June 27, 1967 P. J. L. SEQUEIRA 3,327,535

MULTIPLE PIPETTING APPARATUS

Filed Aug. 24, 1964 11 Sheets-Sheet 1

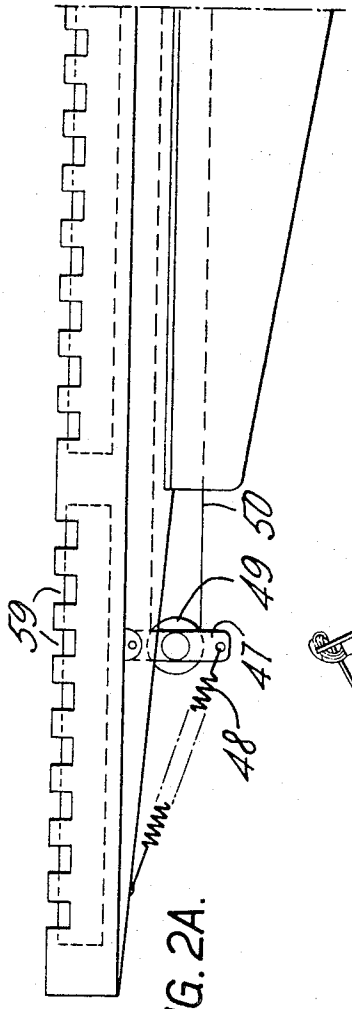


FIG. 2A.

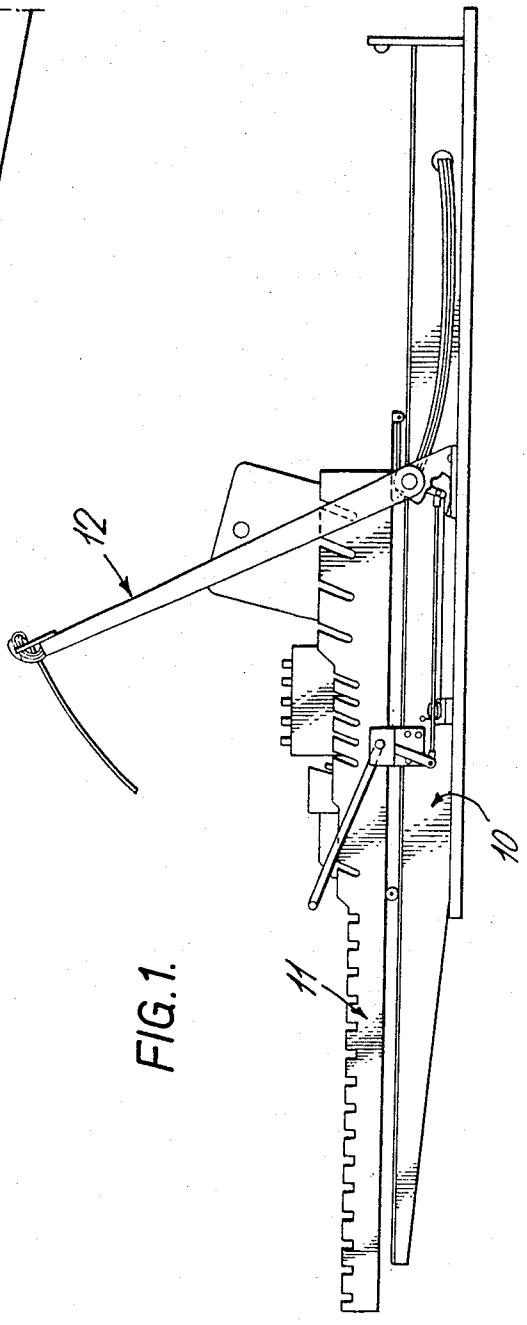


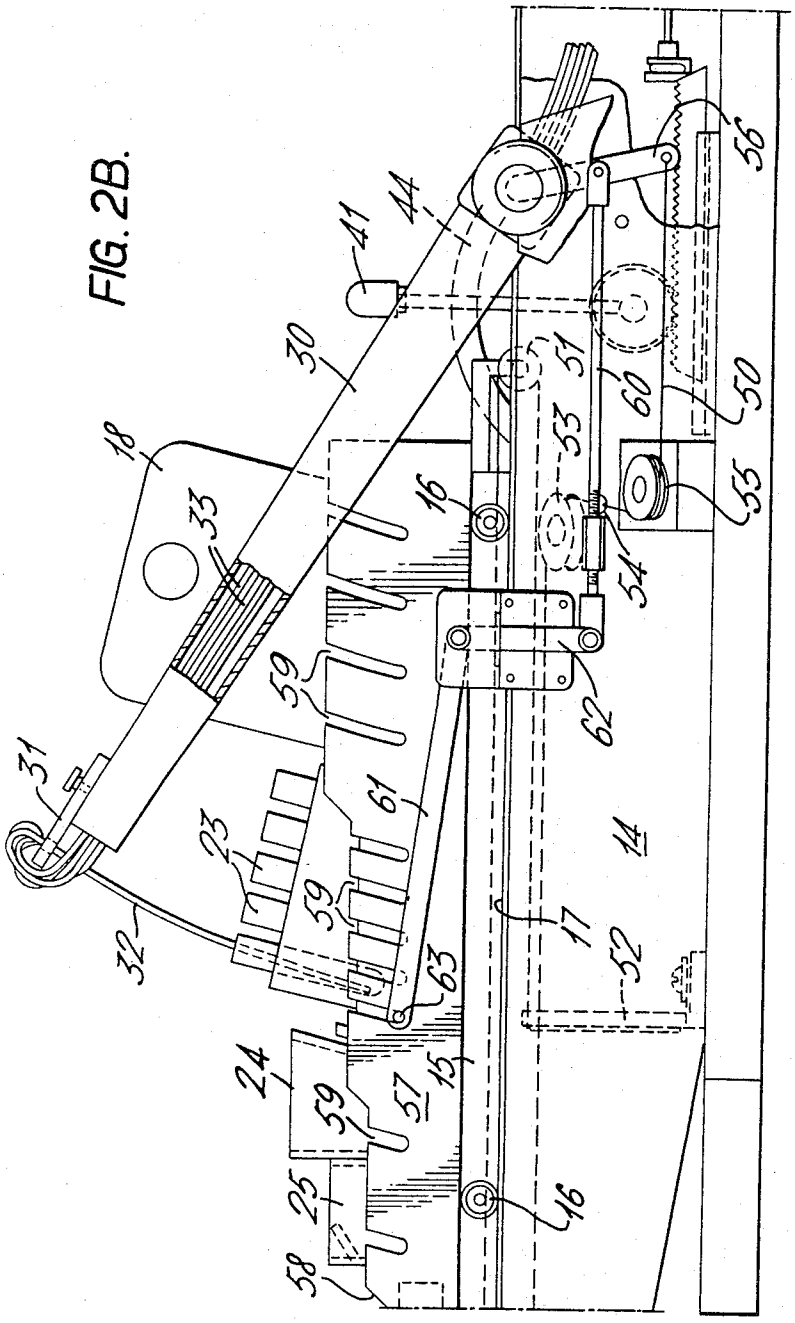
FIG. 1.

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FIG. 2B.



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FIG. 2C.

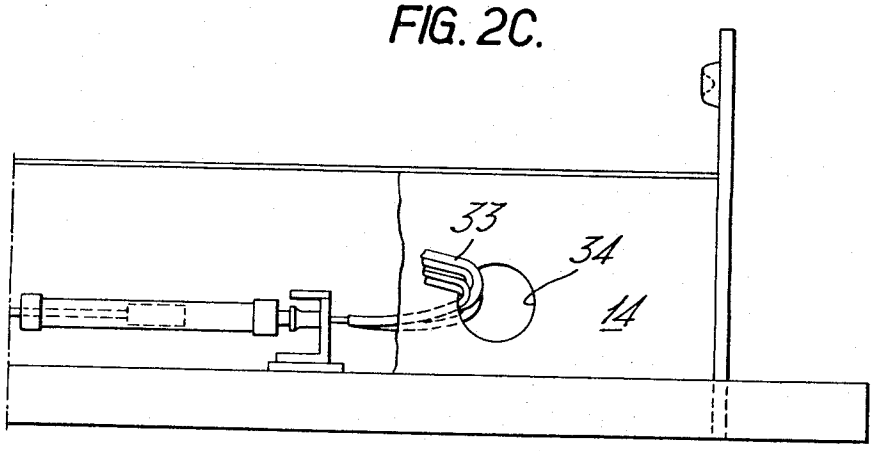
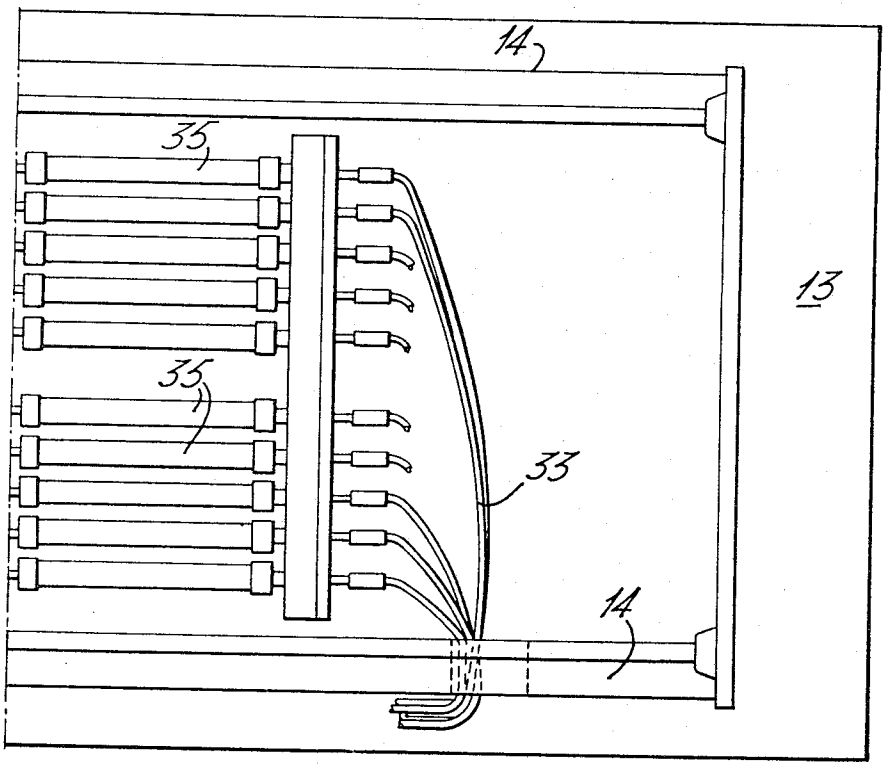


FIG. 3C.

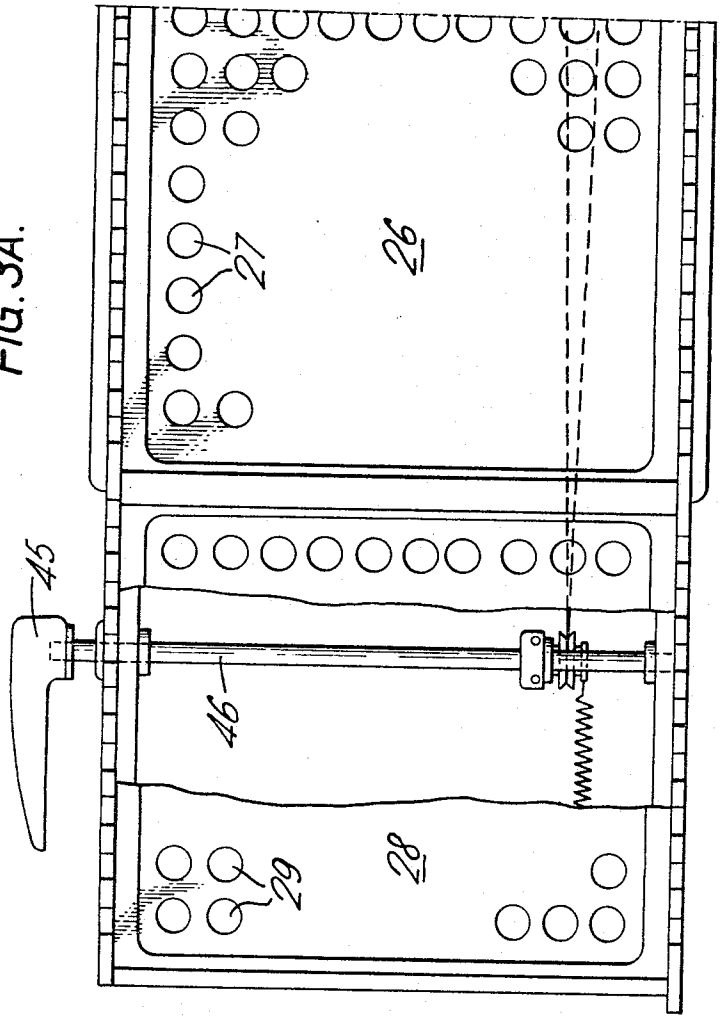


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FIG. 3A.



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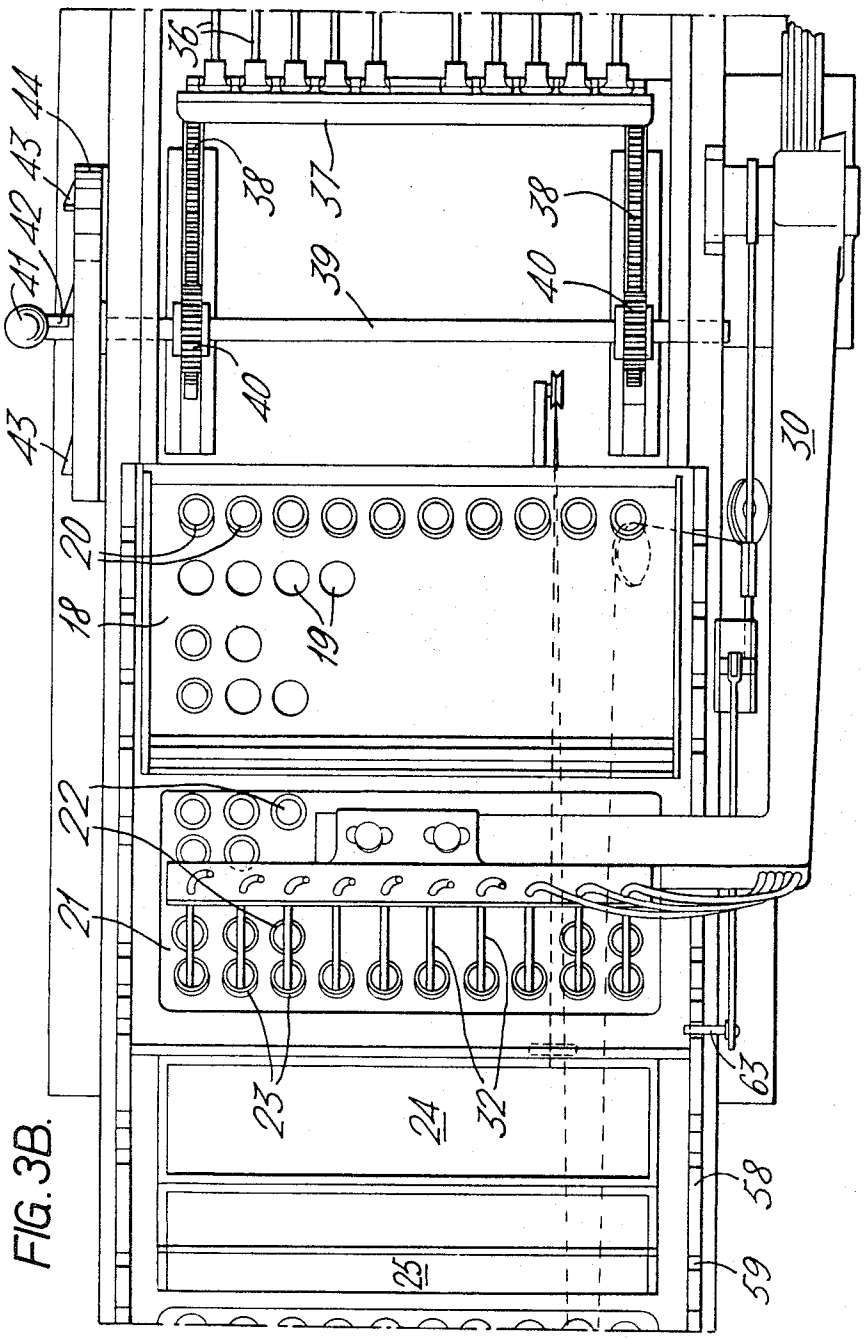


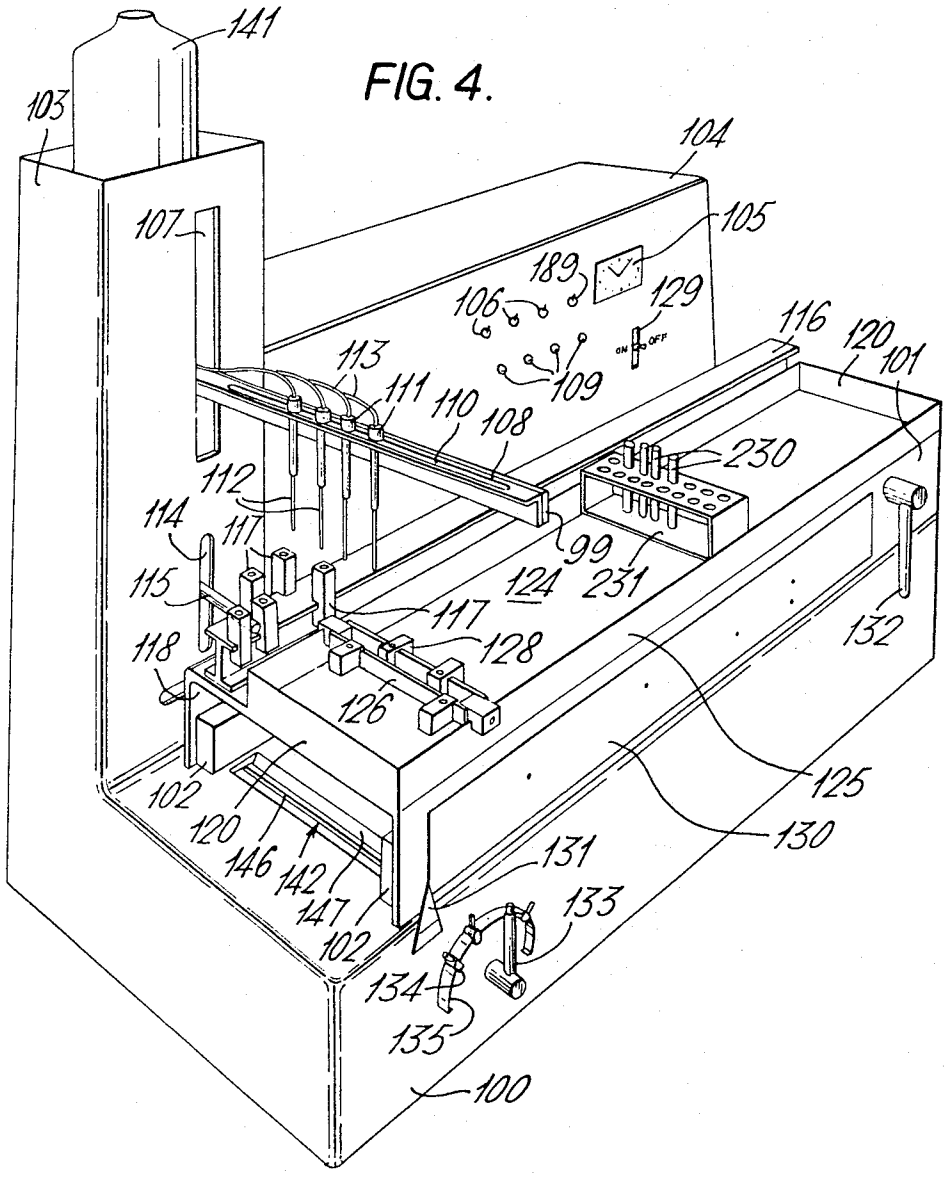
FIG. 3B.

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FIG. 4.

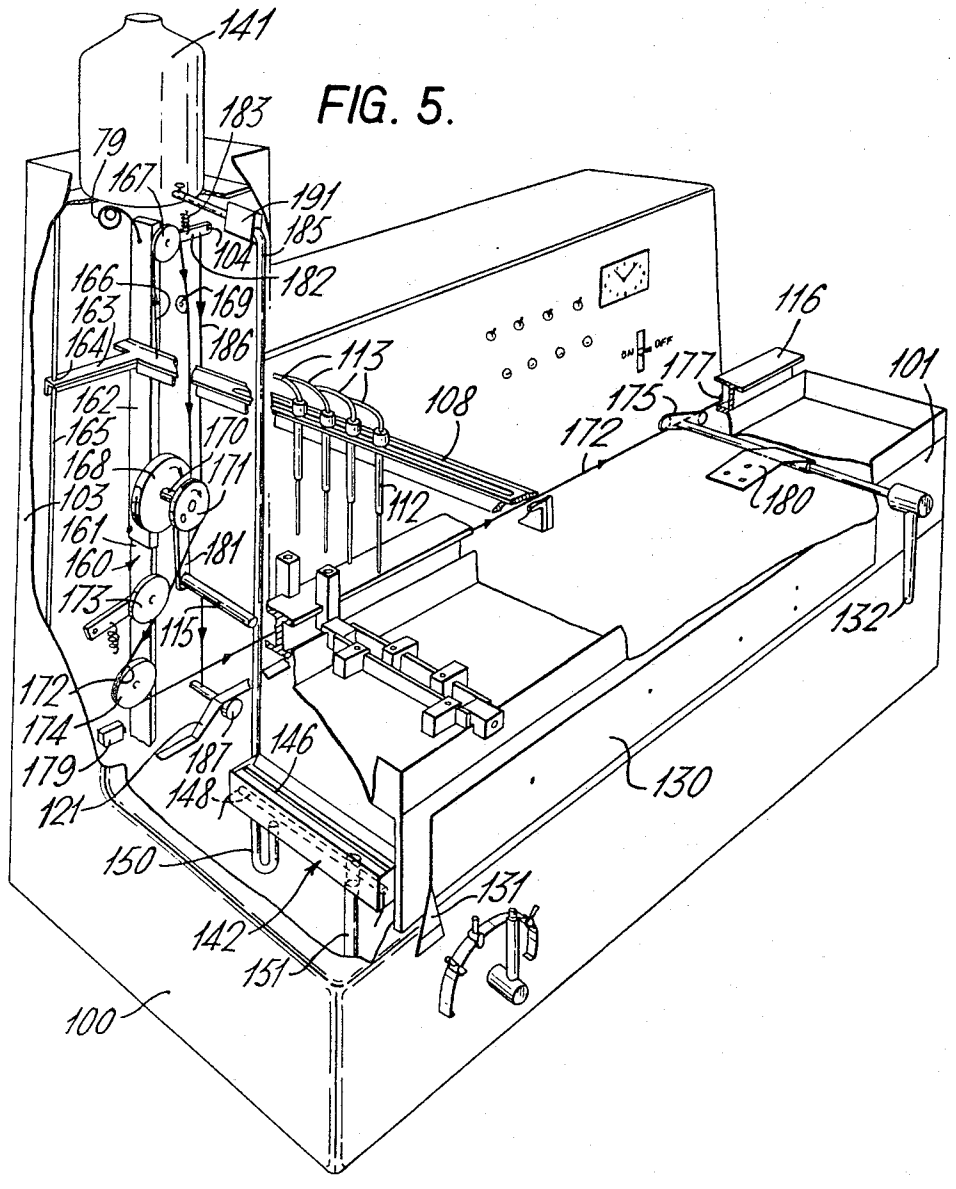


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FIG. 5.



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FIG. 6A.

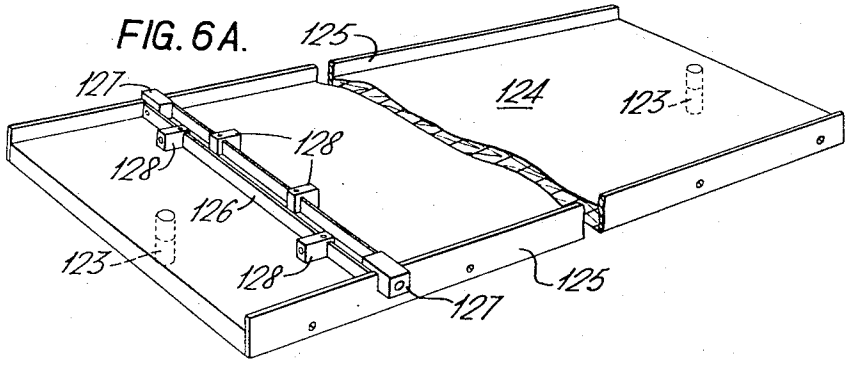


FIG. 6B.

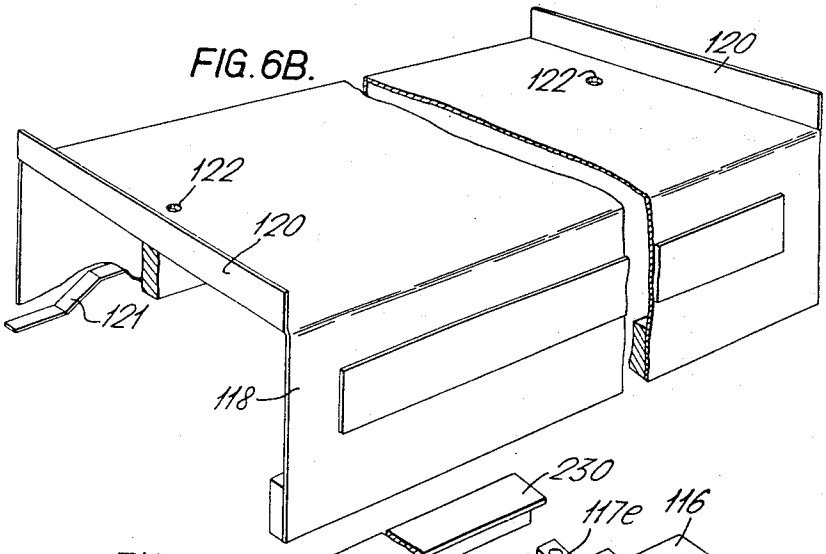
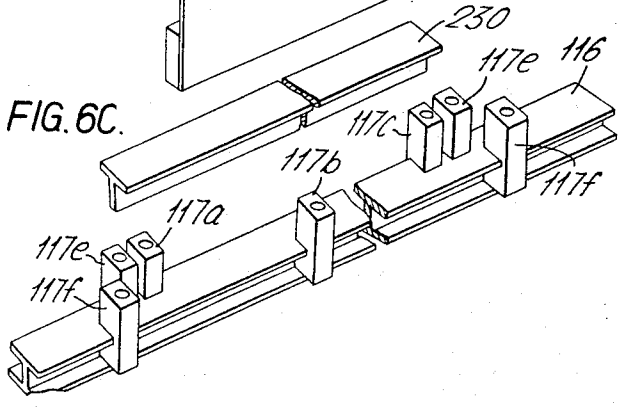


FIG. 6C.



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FIG. 7.

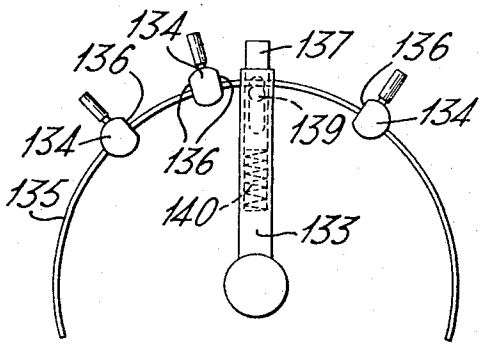


FIG. 9.

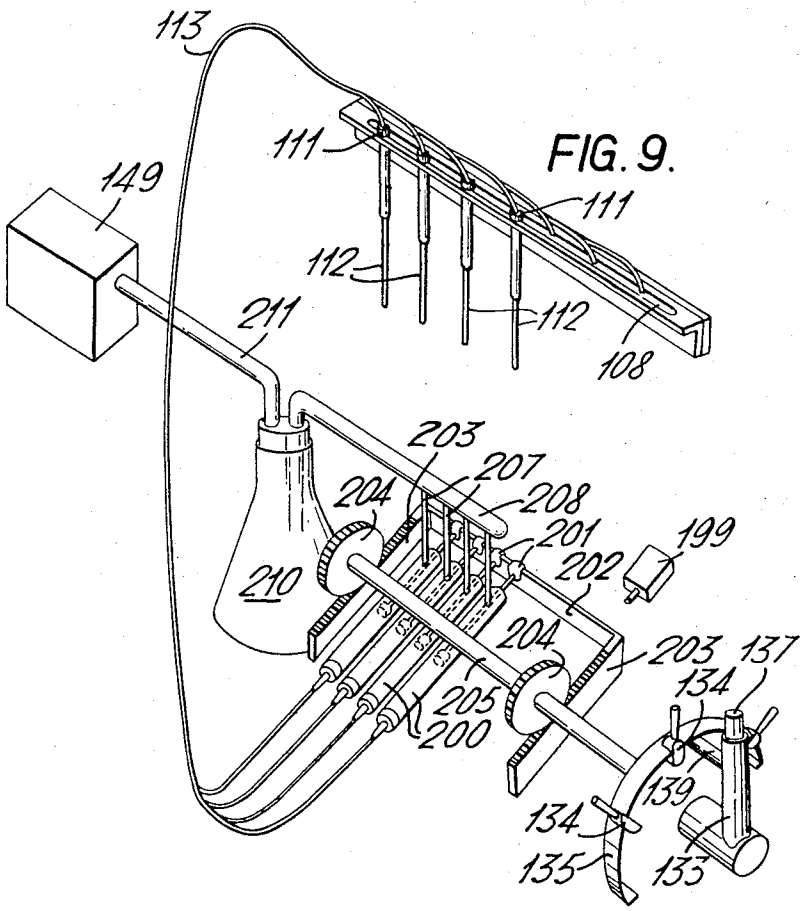


FIG. 8.

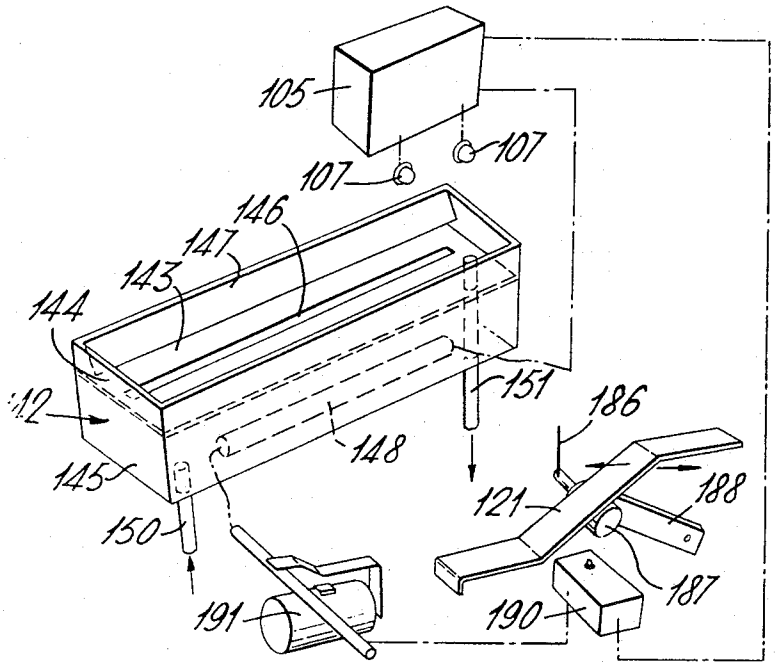
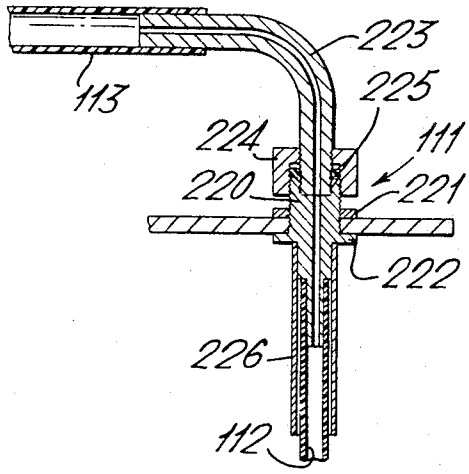

105
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FIG. 10.

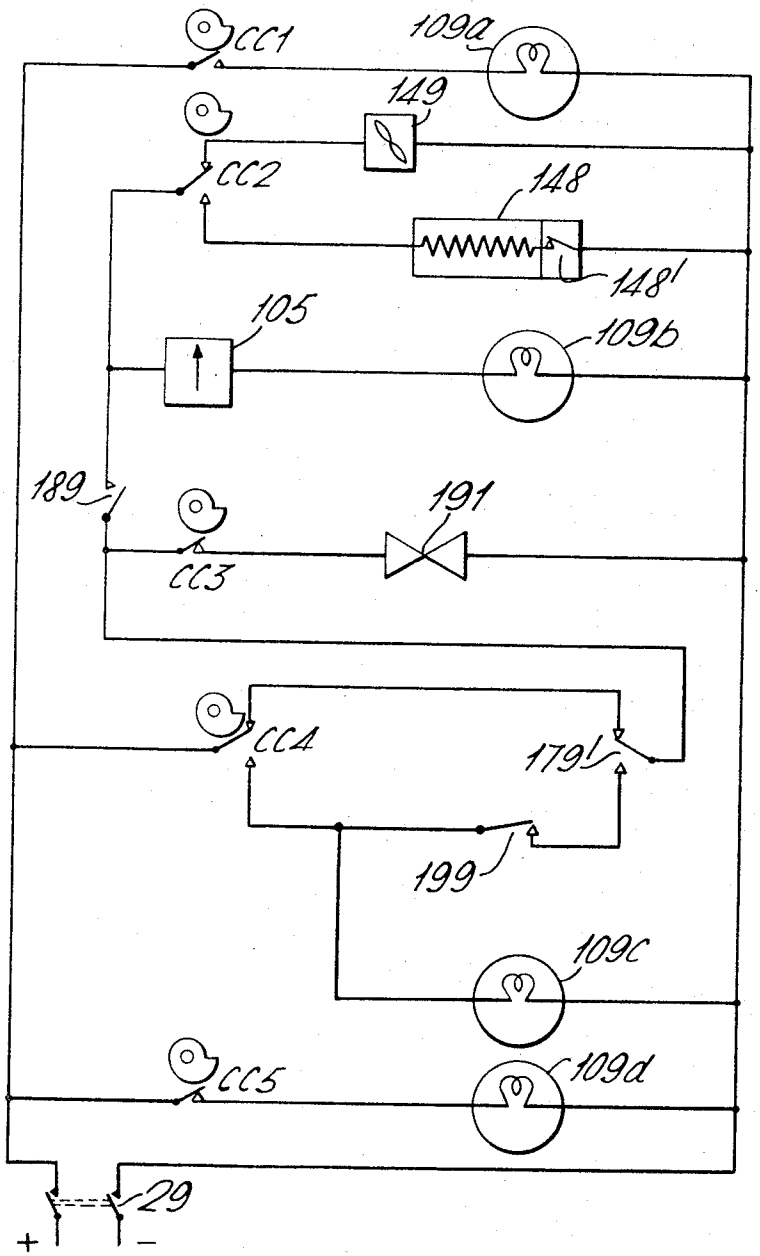

223
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226
112

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FIG. 11.



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Patented June 27, 1967

3,327,535

MULTIPLE PIPETTING APPARATUS

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Filed Aug. 24, 1964, Ser. No. 391,436
Claims priority, application Great Britain, Aug. 24,1963, 33,611/63
14 Claims. (Cl. 73—423)

This invention concerns a multiple pipetting apparatus adapted to dispense known proportions from each of a plurality of liquid samples into a plurality of receptacles.

According to the present invention a multiple pipetting apparatus comprises a base having a support for carrying receptacles arranged in rows extending along the support and in columns extending across the support, a member extending across the support and spaced above it, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted on the member and individually communicating through pipes with respective piston-and-cylinder units operated in synchronism to draw liquid simultaneously into the pipetting tubes or expel liquid simultaneously from the pipetting tubes, and a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles. Preferably the units comprise syringes.

Pipetting apparatus in accordance with the invention has the advantage that it enables routine pipetting such as is necessary for serological and biochemical work to be carried out more rapidly than is possible when done manually and with greater average accuracy.

Preferably the support is movable with respect to the base although it is not outside of the scope of the invention to have the support fixed to the base and the pipetting tubes movable lengthwise of the base.

Preferably the pipetting tubes are made of polytetrafluoroethylene as this substance is hydrophobic and there is little tendency for aqueous liquids to be retained on its surfaces and be carried from one receptacle to another during use and thus spoil the accuracy of the apparatus.

The invention will now be described in more detail, by way of examples, with reference to the accompanying drawings, in which:

FIGURE 1 shows, in side elevation, one form of apparatus;

FIGURES 2A, 2B and 2C are side elevations respectively of the front portion, intermediate portion, and rear portion of the apparatus of FIGURE 1 on an enlarged scale;

FIGURES 3A, 3B and 3C are respectively plan views of the three portions of the apparatus shown in FIGURES 2A, 2B and 2C;

FIGURE 4 is a greatly simplified perspective view of an alternative form of multiple pipetting apparatus;

FIGURE 5 is a view corresponding to FIGURE 4 but with sections broken away to expose the interior of the apparatus and in particular a pulley system used to raise and lower a line of pipetting tubes;

FIGURE 6A is a perspective view, with parts broken away of a tray forming part of a support used in the apparatus of FIGURE 4;

FIGURE 6B is a perspective view with parts broken away of a carriage also forming part of the support;

FIGURE 6C is a perspective view with parts broken away of a rail, clamping pieces and T-piece, which may be used on the rail which forms part of the support;

FIGURE 7 is a scrap view of the apparatus of FIGURE 4 and shows a handle and associated stops for limiting its movement;

FIGURE 8 shows schematically parts of the apparatus of FIGURE 4 and their interconnections;

FIGURE 9 illustrates a mechanism for drawing liquid into and expelling liquid from the pipetting tubes of FIGURE 4; and

FIGURE 10 is a sectional view of a mount used for supporting a pipetting tube in FIGURE 4; and

FIGURE 11 is an electrical circuit diagram.

The apparatus shown in FIGURES 1 to 3 is very suitable for serological work and is capable of being loaded with samples of serum, each of which is to be dispensed into a number of receptables in various predetermined proportions of dilution as will be explained hereafter. Whilst the apparatus may be loaded with many samples, it can dispense 10 of them simultaneously and in 4 complete cycles of operation can dispense all the samples with which the apparatus is loaded.

Referring now to FIGURE 1 it will be seen that the apparatus essentially comprises a base, generally indicated by the reference numeral **10**, a carriage, generally indicated by the reference numeral **11**, and a pipetting assembly, generally indicated by the reference numeral **12**.

The base **10** is generally of channel cross-section, comprising a bottom member **13**, and side walls **14**, which extend beyond the bottom member **13** at the front end of the apparatus. The carriage **11** essentially comprises a rectilinear platform **15** which carries a number of rollers **16** on each of its longitudinally extending sides. The rollers **16** engage rails **17** provided on the upper edge of each of the side walls **14** of the base portion **10**, in such a manner that the carriage **11** may be freely moved longitudinally over the base portion **10**.

The carriage **11** provides a support for a multiplicity of removable receptacles for liquid, which will now be described. An aluminum frame **18** extends transversely over the rear end of the carriage **11**, and is provided with forty holes **19**, each of which is adapted to locate a test tube **20** for a sample of liquid which is to be dispensed by the apparatus. The forty holes **19** are arranged in four columns of 10, each of which extends transversely across the carriage **11**. The frame **18** is followed by a frame **21**, which is provided with forty holes **22** each of which is adapted to locate a test tube **23**. The holes **22** in the frame **21** are arranged in a like manner to the holes **19** in the frame **18**. The frame **21** is followed by a rectangular bath **24** which extends transversely over the entire width of the carriage. The bath **24** is intended to receive waste material as will be explained in greater detail hereinafter. The bath **24** is followed by a further bath **25** which likewise extends transversely over the entire width of the carriage. The bath **25** is adapted to hold a diluent for the samples which are to be dispensed by the apparatus. The bath **25** is followed by a plate **26**, which is provided with eighty blind holes **27**, each of which forms a receptacle for liquid. The eighty holes **27** are arranged in eight colums of ten, each of which extends transversely over the width of the carriage. The plate **26** is followed by a plate **28** which is provided with eighty blind holes **29** arranged in a like manner to the holes **27** in the plate **26**.

The pipetting assembly **12** essentially comprises an L-shaped member having one limb formed by a tubular arm **30** pivotally mounted at its lower end to one of the side walls **14** of the base portion **10**. The arm **30** carries at its upper end a bar **31** forming the other limb of the L and extends transversely over the upper face of the carriage **11**. The bar **31** supports ten pipetting tubes **32** which extend therefrom in spaced parallel relationship downwardly towards the upperface of the carriage **11**. The tubes **32** are formed from a polytetrafluoroethylene material. Each pipetting tube **32** is connected to a pipe or tube **33** which extends from its upper end through the arm **30** and an aperture **34** in one of the side walls **14** of the base **10** to the interior of the channel-section of

the base. Each tube 33 is connected to one of a set of syringes 35 disposed between the side walls 14 of the base. The ten syringes 35 extend longitudinally of the apparatus and are arranged in parallel spaced relationship in a line which extends transversely across the apparatus. The plungers 36 of the syringes 35 are all connected rigidly to a bar element 37 which is in turn connected to a toothed rack 38 at each of its ends. An axle 39 extends transversely of the apparatus and is carried in bearings mounted in each of the side walls 14. The axle 39 carries pinions 40 which are in engagement with the racks 38. One end of the axle 39 carries a radially directed handle 41 which is provided with releasable locking means 42 adapted to co-operate with a plurality of stops 43 mounted on an arcuate guide frame 44. Rotation of the handle 41 causes actuation of the plungers of the syringes 35 by means of the pinions 40, racks 38 and bar 37.

A device in the form of a handle 45 is provided for controlling the raising and lowering of the pipetting tubes 32 and also the longitudinal position of the carriage 11 on the base 10, in a manner which will now be described.

The handle 45 is rigidly secured to one end of an axle 46 which extends transversely of the carriage at a position adjacent the front end thereof. A short arm 47 is firmly secured to the axle 46 and projects downwardly therefrom, its lower end being connected with the underside of the carriage 11 by a tension spring 48. The arm 47 carries a freely rotatable pulley 49 around which passes a wire or cord 50. One side of the cord 50 extends backwardly from the pulley 49 to a further pulley 51 freely and rotatably mounted at the rear end of the carriage 11. The cord passes round the pulley 51 and forwardly to a position beneath the pipetting tubes 32 where it is firmly secured to a bracket 52. The other side of the cord 50 extends rearwardly from the pulley 49 to a pulley 53 mounted on one of the side walls 14. The cord 50 passes round the pulley 53 and through a small aperture 54 in the side wall and round a further pulley 55 freely mounted on the outside of the side wall 14, whence it extends to the end of a lever 56 connected with the arm 30 at the position where the latter is pivoted to the wall 14.

The side of the platform 15 constituting the carriage 11 adjacent the arm 30 is provided with a side wall 57, whose upper edge defines a cam surface 58 provided with a slot or notch 59 transversely opposite each transversely extending row of receptacles 20, 23, 24, 25, 27 or 28. A rod 60 is pivotally connected to the lever 56 by its rear end, and is pivotally connected to a bell crank lever consisting of arms 61 and 62 at its front end. The upper end of the arm 61 carries an interlock pin or peg 63 which is adapted to rest either on the cam surface 58 provided by the wall 57 or in one of the slots or notches 59.

When the handle 45 is rotated, the cord 50 moves in such a manner as to operate on the lever 56 as to pull same forwardly and cause the arms 30 and 61 to rise, whereby the lower ends of the pipetting tubes 32 are removed to a position wherein they are spaced from the receptacles supported by the carriage 11, and whereby the pin 63 is moved to a position wherein it disengages with the notches 59 and the cam surface 58. When the arms 30 and 61 are in their raised position, the handle 45 may be used to pull the carriage forwardly or to push same rearwardly. The carriage may be halted in any desired position and the handle 45 released so as to allow the arms 30 and 61 to fall. It will be appreciated that the arm 30 can only assume its lowermost position when the peg 63 can engage one of the notches 59, and the latter are arranged so that the arm 30 can only be lowered completely when the carriage is in such a position that the pipetting tubes 32 will engage one transversely extending column of the receptacles carried by the carriage 11. The cam surface 58 and pin 63 provide interlocking means designed to ensure that the carriage cannot be moved along until such time as the pipetting tubes 32 are in a sufficiently raised position to ensure the free passage of the receptacles beneath the lower end of same.

The apparatus may be used in a variety of different ways, but one particular way will now be described. Initially, the forty tubes 20 are filled with forty different samples of serum which it is desired to dispense, the receptacles 23, 24, 27 and 29 being empty, and the receptacle 25 being filled with a diluent. The handle 41 is operated to ensure that the plungers 36 are fully depressed into the syringes 35, and the carriage 11 is aligned so that the rearmost column of the tubes 20 is aligned beneath the pipetting tubes 32, which are then lowered so that they penetrate the samples of serum contained in these tubes. The handle 41 is operated to draw off a known volume of serum from each of the ten tubes 20 in the rearmost column thereof into the ten pipetting tubes 32. The carriage 11 is then moved backwardly until the rearmost column of the tubes 23 are aligned beneath the pipetting tubes 32 which are then lowered so as to penetrate same. The handle 41 is then operated to discharge a known volume of the serum from each of the pipetting tubes 32 into their respective tubes 23. The carriage is again moved backwards, and the pipetting tubes lowered into the receptacle 25 when the handle 41 is operated to draw off a known volume of the diluent into each pipetting tube 32. The carriage is again moved backwardly until the pipetting tubes are aligned with the rearmost column of holes 27 when the tubes 32 are again lowered to engage such holes. The handle 41 is operated to discharge all the fluid from the pipetting tubes 32 into the holes 27 to ensure mixing of the serum with the diluent. The handle 41 is then operated to draw off a known volume of the serum from each of the holes 27 into the tubes 32 leaving a predetermined volume therein. The carriage is again moved backward until the tubes 32 are aligned over the next column of holes 27, whereupon the tubes 32 are lowered, and the handle 41 operated to discharge a known volume of the serum into each of the holes 27. This last operation is repeated twice in the two following columns of holes 27, whereupon the carriage is moved forwardly to bring the receptacle 24 for waste beneath the pipetting tubes 32, which are lowered thereinto and the handle 41 operated to discharge any remaining serum and diluent from the pipetting tubes 32 into the receptacle 24. The entire cycle of operations thus far described is then repeated for each of the three remaining columns of tubes 20 containing samples of serum, in each case, the carriage being moved to align the tubes 32 with the desired receptacles at each stage of the cycle.

The stops 43 on the guide 44 for the handle 41 may be arranged at predetermined positions to facilitate the operation of the handle 41 to draw up and discharge the desired and predetermined volumes of fluid at each stage of the operation cycle.

It will be appreciated that the apparatus can be used to dispense forty samples of serum each into a plurality of receptacles at known volumes and known dilutions in a very short time, both on account of the fact that ten samples may be dispensed simultaneously and also on account of the simple operations required to effect the dispensing.

A second example of multiple pipetting apparatus in accordance with the invention is shown in FIGURE 4. The apparatus comprises a base 100 on which a support 101 is slidably mounted by means of runners 102 fixed to the base. A tower 103 extends upwards behind the support 101 alongside a casing 104 containing electrical control apparatus to be described later. The front of the casing 104 is fitted with a timer 105 and various control knobs 106 and indicating lights 109.

The tower is provided with an upper rectangular slot 107 through which extends an angle member 108 detachably mounted on a bracket 99. The horizontal web of

the angle member is formed with a slot **110** extending above the support **101** and in which are slidable mounts **111** each supporting a pipetting tube **112**. Although only four pipetting tubes are shown more may be mounted in the slot **110** as required. Pipes **113** pass from the tops of the mounts **111** along the member **108** and through the slot **107** into the tower **103**. A second slot **114** is spaced directly beneath the slot **107** and a vertically movable interlocking pin **115** serving for indexing the support **101** projects through the slot **114** so that its end overlies the top surface of a rail **116** fixed to the support and extending in the direction of its movement. Locating pieces **117** of which only five are shown, are movable to different positions along the top flanges of the rail **116**. When the pin **115** is in the top of the slot **114** the locating pieces pass beneath the pin when the support **101** is moved along the base **100**. When the pin **115** is in the lower position shown, it is spaced close to the top surface of the rail **116**. Whether or not the pin **115** is allowed to assume the position shown, depends on the positions of the pieces **117**. If the pieces **117** on the side nearest the pin are closely spaced so as to provide a continuous top surface the pin **115** will be prevented from assuming its lower position. However, if the pieces **117** are spaced sufficiently to provide a slot between them into which the pin **115** can fit then it will enter the slot and will assume the position shown. The length of the pin **115** is such that it can be stopped from entering a slot by the pieces on both sides of the rail **116**. Thus the clamping pieces **117** on one side of the rail can be used to form one side of each of a series of transverse slots and the precise positions of the other sides of the slots formed from further locating pieces mounted on the other side of the rail and overlapping those on the first side where a fraction of a width of a locating piece is required.

The support **101** comprises a carriage **118** of inverted channel shape with the runners **102** being fitted to the inside faces of the downturned flanges of the carriage. FIGURE 6B shows the carriage in more detail from which it will be seen to have a pair of end flanges **120** and a camming surface **121** formed on the outside of one downturned flange. In its top surface the carriage is provided with two locating holes **122** for accommodating studs **123** projecting downwards from the underside of a tray **124** shown in more detail in FIGURE 6A which rests on the top surface of the carriage **118** as shown in FIGURE 4. The tray **124** is provided with parallel upstanding side flanges **125** each of which serves as a guideway for opposite ends of a U-channel partition **126** which is movable to different positions along the tray **124**. At its ends each of the partitions **126** is provided with a clamp **127** which may be tightened to lock the partition in a desired position. The partition is of channel shape and clamp blocks **128** are slidable to different positions along opposite sides of the channel. There is sufficient spacing between the clamp blocks on opposite sides of the partition to enable them to be slid past one another without obstruction.

Referring again to FIGURE 4 the support **101** is provided with fixtures into which a programme card **130** can be fitted in order to suit a particular sequence of operation to be carried out. A pointer **131** on the base indicates the particular point in the programme at any instant and a hand lever **132** close to one end of the support **101** enables the support to be moved along the base **100** to different positions in accordance with the programme **130**. The handle **132** is also rotatable to raise and lower the pipetting tubes **112** as will be described later.

The base **100** is provided with a handle **133** shown in more detail in FIGURES 7 and 9. The handle is movable to different angular positions determined by adjustable stops **134** set to positions corresponding to volumes of liquids to be drawn into or expelled from the pipetting tubes **112**. Each of the stops **134** is mounted on an arcuate frame **135** concentric with the axis of the handle **133**, and one or both sides **136** of each stop **134** is planar to provide an abutment for the handle **133**. An override button **137** is fixed in the top of the handle and is fixed to a peg **139** which cooperates with the abutment surfaces **136** when the button is not pressed. Where no planar abutment surface **136** is permitted the peg **139** is able to ride over the curved undersurface of the stop **134**. However if the button **137** is pressed the peg **138** is also able to move past the abutment surfaces **136** so that the handle **133** is able to be moved to different positions past the stop. The button **137** acts against a spring **140** mounted inside the handle **133**.

Turning to FIGURE 5, the top of the tower **103** provides a stand on which a reservoir bottle **141** may be placed. Piping **185** extends from the bottle through the tower to a wash trough **142** mounted in the base **100** directly beneath the number **108**. When the wash trough is not in use the support **101** is able to pass freely over it.

The length of the wash trough is the same as the length of the slot **110** in the member **108** and is shown in more detail in FIGURE 8. It comprises a rectangular trough divided by a horizontal plate **143** into an upper compartment **144** and a lower compartment **145**. A slot **146** slightly wider than the cross-sections of the lower end-portions of the pipetting tubes **112**, is formed in the plate **143** directly beneath the pipetting tubes and a removable sloping glass plate **147** slopes into the upper compartment **144** and terminates above the slot **146**. An electrically operated immersion heater **148** provided with a thermal cut-out is mounted in lower compartment **145** and a liquid inlet pipe **150** opens through the bottom of the compartment **145**. A liquid outlet pipe **151** opens into the top compartment **144** through the plate **143** and extends downwards through the floor of the bottom compartment **145**.

FIGURE 5 shows the method of raising and lowering the member **108** on which the pipetting tubes **112** are mounted. The bracket **99** supporting the member **108** is mounted inside the tower **103** on a telescopic guideway **160** having a lower part **161** which is fixed inside the tower and an upper part **162** which is vertically slidable along the lower part. The bracket **99** is fixed to the upper part **162** and a cross brace **163** extends horizontally away from the member **108** and is provided at its end-portion with a hole **164** which is a sliding fit along a slide rod **165** fixed at its upper and lower ends inside the tower. The cross brace **163** prevents undesirable horizontal movement of the member **108** about the guideway **160**.

The weight of the member **168** is carried by a wire **166** which extends around a first pulley **167** in the upper end portion of the tower and around a deflector pulley **169** which is movable horizontally to vary the effective length of the wire **166**. A tensator spring **79** in the top of the tower and attached to the sliding part **162** counter-balances much of the weight of the pipetting tubes. The other end of the wire **166** is fixed to the periphery of a second pulley **168** mounted on a shaft **170** journalled into the tower between the slots **107** and **114**. A third pulley **171** is also fixed to the shaft **170** and a second wire **172** is fixed to the periphery of the third pulley **171**. The second wire **172** extends around an idler pulley **173** which maintains it in tension and around a stationary mounted pulley **174** fixed in the base **100** at one end. The other end portion of the wire **172** extends through a tensioner **175**, which is rotated by the hand lever **132** fixed to the carriage **118**, to an anchorage **177** at the other end of the base **100**. A helical spring **180** ensures the engagement of the tensioner **175** with the wire **172**.

A hanging link **181** is pivoted at its upper end to the third pulley **171** eccentrically with respect to its axis and carries the interlocking pin **115** at its lower end.

The first pulley **167** is fixed to one end of a lever **182** which is biased upwardly by a coil spring **183** against an adjustable stop. The lever is pivoted at **104** and is positionally controlled by a wire **186** which extends downwards through the tower **103** and is anchored at its lower end to a cam rider **187** mounted at the free end of a spring loaded lever **188** as shown in FIGURE 8. The cam rider **187** is positioned in the path of movement of the cam surface **121** provided on the side of the carriage **113** as shown in FIGURE 6B. The camming surface **121** is so positioned that it engages the cam rider **187** to press it downwards when the support **101** is so far to the right of FIGURE 4 that is is not interposed between the pipetting tubes **112** and the wash trough **142**.

The supply of liquid to the wash trough **142** is controlled by a solenoid operated valve **191** mounted in the top of the tower **103** beneath the reservoir bottle **141**. Operation of the valve **191** is controlled by an electrical circuit shown in FIGURE 11 and described in detail later. The electrical circuit also controls operation of the immersion heater **148** in the wash trough **142**, the indicating lamps **107** in the casing and an air pump **149**.

The pipes **113** from the mounts **111** extend through the slots **107** in the tower **103** and downwardly to a set of syringes **200** mounted in a line across the base **100** and shown in FIGURE 9. There is one syringe **200** provided for each of the pipetting tubes **112** and their plungers are held by fixtures **201** to a cross element **202** which is fixed at its ends to a pair of racks **203**. The racks are engaged by pinions **204** fixed to an axle **205** extending through the side of the base and on which the handle **133**, is mounted. The cylinders of the syringes **200** are provided close to their rear ends with branch pipes **207** opening into a manifold **208** which extends into a flask **210** containing a drying agent, such as silica gel, and a bacteriological filter. The flask **210** is mounted in the foot of the tower **103** and is accessible through a door (not shown) at the back of the tower. A pipe **211** extends through the back of the tower to the air pump **149** (see FIGURE 11) for driving air into the drying flask **210**. The branch pipes **207** open into the cylinders of the syringes at positions which enable them to discharge dried air through the syringes **200** and the pipes **113** when the plungers are in their rearmost positions with respect to the syringes **200**. At this position, which is indicated by one of the stops **134** associated with the handle **133**, a microswitch **199** is operated.

FIGURE 10 shows one of the mounts **111**. This comprises a bush **220** flanged at **222** and having its upper portion threaded and passing through the slot **110** where it is clamped into position by a lock nut **221** which clamps the member **108** to the flange **222**. An elbow tube **223** is held in a socket at the upper end of the sleeve **220** by a cap nut **224** and a packing ring **225**. The other end of the elbow passes into the end of the pipe **113** which is conveniently made of polyethene tubing. The pipetting tube **112** is made of polytetrafluoroethylene and its upper end is a force fit on a spigot formed in the underside of the mount **111**. A stainless steel sleeve **226** closely surrounds the junction of the pipetting tube **112** with the mount **111** and prevents undue flexing of the pipetting tube at this point and assists their alignment.

FIGURE 6C shows the rail **116** in more detail and also illustrates the use of a T-piece **230** to bridge between locating pieces **117** when a slot is not to be formed between the clamping pieces over a relatively large distance.

The T-piece **230** is gripped between the locating pieces **117***a*, **117***b* and **117***c*, to prevent lowering the pin **115**, and slots for reception of the pin are formed between the pairs of clamping pieces **117***e*, **117***f* at each end of the T-piece. The locating pieces **117** are provided in different sizes to suit different lengths of receptacles **230** into which pipetting is to be carried out.

Referring again to FIGURE 4 the receptacles **230** into which liquid is to be pipetted are mounted in a test tube rack **231** of standard size. Although only one such rack is shown in FIGURE 4 it is to be understood that several such racks, arranged side by side, would normally be used and they are standard items of laboratory equipment. The racks **231** may come in several different sizes according to the purpose for which they are intended and the number of receptacles which are to be carried. For clarity a rack having two columns of eight openings and containing four test tubes **230** has been shown, the rack extending entirely across the width of the tray **124**. However different sizes of rack may be of different lengths but can nevertheless be firmly clamped in position on the tray by the partitions **126** as is described below.

FIGURE 11 shows the electrical wash control circuit for the apparatus. It comprises a main ON/OFF switch **29** which closes to complete electrical circuits to a number of cam operated contacts CC1, CC2, CC3, CC4 and CC5. The cams controlling the contacts are driven in unison by the timer **105** and are so arranged that the washing sequence is completed in one complete revolution of the timer **105**. During one complete revolution of 360° the contacts CC1 and CC2 are closed between 1° and 201°; the contact CC3 is closed between 340° and 20°; the contact CC4 is closed between 0° and 200°; and, the contact CC5 is closed at 360°.

The contact CC2 is a change-over contact and selectively controls operation of the pump **149** and the heater **148**. During the arc 1°–201° the heater **148** is energised and during the arc 201°–1° the pump **149** is energised. The electrical supply to the timer **105** and the contact CC2 is controlled by a manually operable switch **189** which, when opened, allows the pipetting tubes to be washed out with cold water, but which is closed if the washing sequence employing the timer **105** is to be used. Various lamps **109***a–d* are used to signify different stages in the washing sequence. The contact CC4 is also a change-over contact and is in the position shown during the 0°–200°.

A change-over contact **179′** controls the supply to the manual switch **189**, the contact **179′** being operated by a microswitch **179** in the tower **103** as shown in FIGURE 5. The microswitch **179** is so arranged that the contact **179′** is in the position shown in FIGURE 11 if the pipetting tubes **112** are lowered sufficiently for their tips to reach the surface of the liquid in the wash trough **142**. If the pipetting tubes are above this point the contact **179′** assumes its lower position. Operation of the microswitch **179** is carried out by its engagement with the movable part **162** of the slideway **160** during lowering of the pipetting tubes **112**.

To prepare the apparatus for use the operator places the test tube racks **231** which are required onto the tray **124**.

Each of the test tube racks is held in place by two partitions **126** which are moved against opposite sides of the rack. The partitions **126** are only able to move parallel to themselves so that they ensure, by engaging the sides of the racks **231**, that the columns of receptacles **230** extend parallel to the line of pipetting tubes **112**. The spacing between the pipetting tubes **112** is arranged to be the same as that between the receptacles of each column and the test tube racks **231** are clamped in the position at which the pipetting tubes engage with the receptacles, by adjustment of the clamping blocks **128**, which are then tightened. The locating pieces **117** are then positioned to ensure that the interlocking pin **115** can pass between two adjacent pieces **117** when the pipetting tubes **112** rest centrally in each row of receptacles. The columns of receptacles are next brought into exact agreement with the programme card **130** and to do this the pipetting tubes **112** are raised and each column is brought beneath the row of pipetting tubes **112** which are then lowered by means of the hand-lever **132** into respective receptacles **230** of a column. The programme card **130** is then marked

at the point indicated by the pointer **131**. When this has been done two of the locating pieces **117** on opposite sides of the rail **116** are then locked in position.

When all of the test tube racks or similar such devices which may be used for different forms of receptacles are clamped into their correct positions and the programme card **130** completed the bottle **141** is placed on top of the tower **103** and connected to the piping **185** extending to the wash trough **142**. Also, the stops **134** are placed at different positions along the path of movement of the handle **133** according to volumes of liquids it is required to draw into and expel from the pipetting tubes **112**. The positions of the stops **134** are signified by a calibrated scale (not shown) extending around the path of movement of the handle **133**. The apparatus is now ready for use.

To use the apparatus the hand lever **132** is rotated counter-clockwise to raise the line of pipetting tubes so that their lower ends are lifted clear of the tops of the receptacles **230**. The action of rotating the hand lever **132** tensions the wire **172** and causes the pulley **171** to rotate in a clockwise direction as will be clear from FIGURE 5. This rotation is transmitted through the shaft **170** to the second pulley **168** so that the wire **166** is drawn around the top pulley **167** and pulls the member **108** upwards. This upward movement is permitted by the telescopic guideway **160** and any tendency for the line of pipetting tubes to twist is resisted by the engagement of the cross-brace **163** with the slide rod **165**. During rotation of the said pulley **171** the hanging link **181** is also drawn upwardly so that the interlocking pin **115** is lifted clear of the clamping pieces **117** or T-pieces arranged along the rail **116**. The height of the locating pieces **117** selected is such that the interlocking pin **115** does not clear the slot formed between them until the lower ends of the pipetting tubes **112** are clear of the tops of the receptacles **230**.

The support **101** is now displaced by the hand lever **132** along the base **100** to the first position indicated by the pointer **131** on the programme card **130**. At this position the handle **132** is allowed to rotate in a clockwise direction. If the pipetting tubes **112** are not correctly aligned with a column of receptacles the interlocking pin **115** will not enter the corresponding slot formed between the clamping pieces **117** but will engage the top surface of one or either of the clamping pieces. This prevents further rotation of the third pulley **171** so that further lowering of the member **108** is prevented before the pipetting tubes **112** reach the level of the tops of the receptacles **230**.

Assuming the apparatus has been set up correctly the interlocking pin **115** passes between the clamping pieces **117** defining the slot associated with the first position and allows the lower ends of the pipetting tubes to be lowered into the column of receptacles. When the pipetting tubes are in their lower positions their weight is carried by the wires **166** and **172** and the interlock pin **115** is just clear of the top surface of the rail **116**.

The operator draws the desired volumes of liquids into the pipetting tubes **112** by rotation of the syringe-operating handle **133** up to a stop **134** as shown in FIGURE 9. The hand lever **132** is then rotated in the reverse direction to raise the pipetting tubes and after they are lifted clear of the receptacles **230** the interlocking pin **115** allows the support to be moved to the next position indicated by the programme card **130**. It will be appreciated that the engagement of the interlocking pin **115** in the slot formed between the clamping pieces **117** ensures that the support **101** cannot be moved as long as the pipetting tubes are engaged in the receptacles **230**.

At the next position the procedure is repeated and perhaps a second liquid is drawn into the pipetting tubes.

At a third position denoted by the programme card it may be required to mix the two liquids contained in the

pipetting tubes, in a column of receptacles. To accomplish this the pipetting tubes **112** are lowered into respective recepetacles **230** of the column, as described above, and the handle **133** is moved in the reverse direction. This expels the liquid from the pipetting tube into the column of receptacles. To mix the liquid in the receptacles thoroughly the handle **133** may be worked backwards and forwards a few times. Samples of the mixed liquid may then be transferred by the pipetting tubes **112** to other columns of receptacles as required.

Between different programmes, or at periods during a single programme it may be required to clean the pipetting tubes thoroughly. This may be carried out either by a cold wash, in which case the manual switch **189** is opened, or by a hot wash, in which case the manual switch **189** is closed.

The procedure for cold washing will first be described. The manual switch **189** is opened and the support **101** is moved as far as the right of FIGURE 4 as possible so that the camming surface **121** of FIGURE 5 forces the cam rider **187** downwards. This draws wire **186** downwards also so that the pulley **167** in the top of the tower **103** is pulled downwards against the spring **183**. This lowers the line of pipetting tubes **112** from their upper positions by twice the downward movement of the pulley **167**.

The hand lever **132** is then rotated to lower the line of pipetting tubes **112** and, as a result of the upper pulley **167** being lowered, the lower ends of the pipetting tubes are able to descend below the level of the support **101** and into the slot **146** of the wash trough **142**.

When the tips of the pipetting tubes reach the top of the wash trough **142** the descending upper part **162** of the slideway **160** operates the microswitch **179** so that its changeover contact **179'** moves to the position shown in FIGURE 11. At this time the contact CC4 is in the position shown so that the solenoid-operated valve **191** is energised by way of the closed contact CC3 and opens to allow wash liquid to flow from the reservoir **141** into the bottom compartment **145** of the wash trough **142**. The liquid from the lower compartment **145** flows upwards past the lower end portions of the pipetting tubes **112** with a millrace effect so that the end portions are thoroughly cleaned by the continuously flowing hot liquid. At the end of the washing time the operator turns the hand lever **132** to lift the pipetting tubes **112** a small amount so that their tips are drawn out of the slot **146** and rest against the top surface of the sloping glass plate **147**. Glass is hydrophilic whereas the polytetrafluoroethylene of the pipetting tubes is hydrophobic so that any drops of water on the tips of the pipetting tubes are transferred to the glass plate **147**. This reduces the risk of dilution of the next liquid into which the pipetting tubes are dipped by water adhering to the outside of the pipetting tubes from the wash trough **142**.

The hand lever **132** is fully rotated counter-clockwise to raise the pipetting tubes **112** to their original positions.

As a result the microswitch **179** returns to its original state and its contact **179'** breaks the electrical circuit to the valve **191**. Valve **191** is de-energised and closes to stop the flow of wash liquid into the wash trough **142**. Throughout the washing the timer **105** remains unenergised and the contact CC5 is closed to light the lamp **109***d*.

In certain circumstances it is necessary to thoroughly clean and dry the end-portions of the pipetting tubes **112** and for this purpose the hot wash, which is time sequenced by the timer **105**, is necessary.

To use the hot wash the switch **189** is closed and the lower end-portions of the pipetting tubes **112** are lowered into the wash trough **142** in exactly the same way as described above. However in this case operation of the microswitch **179** energises the timer **105** as well as the

solenoid. The cams driven by the timer **105** are rotated and almost immediately the contacts CC1, CC2, and CC5 are operated as they all respond to 1° of rotation. The contact CC2 changes over to energise the immersion heater **148** and the contact CC1 lights the lamps **109***a* to signify operation of the heater. Should the reservoir bottle **141** inadvertently be empty, over-heating of the immersion heater is prevented by a thermal cut-out **148** so that excessive heating of the lower end-portions of the pipetting tubes is prevented.

The contact CC3 remains closed until the cams have rotated through 20° during which time the end-portions of the pipetting tubes are washed in cold water. After 20° of cam rotation contact CC3 de-energises the valve **191** which interrupts the supply of wash liquid from the bottle **141**. As a result the liquid in the trough **142** is raised to its boiling temperature. The wattage of the immersion heater **148** and time taken for the cams to rotate through 180° are so selected that the wash liquid, which may be water, is just brought to its boiling point and held there while the pipetting tubes may be worked up and down by the handle **132** to rinse thoroughly. The temperature of the wash liquid is sufficiently high to kill vegetative micro-organisms which might be present and the time taken for the cams to rotate to 200° is sufficient for this purpose.

At 200° the contact CC4 changes over to break the electrical supply to the timer **105** and energises a lamp **109***c*. This indicates that the rinsing sequence is completed.

When the operator observes light **109***c* he lifts the pipetting tubes by the hand-lever **132** to their upper position after allowing their tips to rest momentarily on the glass plate **147**, and this causes microswitch **179** to operate and contact **179'** to change-over.

If at this stage the plungers of the syringes **200** are not wound back to their furthest extents the microswitch **199** will not be operated and the electrical circuit to the timer **105** will be broken. To complete this circuit the operator winds back the plungers until he reaches a stop **134**. He will then see the lamp **109***b* light to indicate that the timer is again operating and therefore the microswitch **199** has been closed. Simultaneously with the timer **105** operating the valve **191** is opened to allow cold water from the bottle **141** to flush out the hot rinse liquid from the trough **142**.

A second or so later after operation of the timer the cams are rotated to 201° and the contacts CC2 and CC1 operate to transfer the electrical supply from the immersion heater to the pump **149** and to signify that this has taken place.

The pump **149** drives dry air from the flask **210** through the syringes **200**, this being permitted by the withdrawn plungers, and through the piping **113** to the pipetting tubes **112**. The dry air absorbs any moisture remaining inside the tubes **112** and this is facilitated by the tubes **112** still being warm from the previous rinsing operation. The pump continues to run until the cams have rotated through the remainder of the 360° when cam contact CC4 again changes over to break the electrical circuit to the timer **105**. At 360° cam CC5 also closes to indicate the cams have completed the entire sequence and the circuit is ready to start a fresh sequence when desired.

During operation of the pump **149** the cam pass the 340° position at which the contact CC3 is once again closed to open the valve **191** and allow cold liquid from the bottle **141** to flush the hot contaminated rinse liquid from the trough **142**. At the end of the washing and drying sequence the support **101** is returned to its original position shown in FIGURE 4 so that the cam surface **121** no longer bears against the cam rider **187**. The spring **183** returns the pulley **167** to its topmost position to lift the pipetting tubes **112** to their upper positions in readiness for the next sampling operation.

Although the operation of the immersion heater **148**, pump **149**, and timer **105** has been described in a sequence controlled circuit it will be understood that each may be provided with its own over-riding switch to enable it to be switched on and off independently if desired.

It will be appreciated that it is not intended to limit the scope of the invention to the above examples only, many variations, such as might readily occur to one skilled in the art, being possible, without departing from the principles of the invention.

Thus, for example, the mechanical construction of the apparatus may be varied in any number of ways without departing from the principles of operation. For example, in place of the solenoid valve shown in FIGURE 8 the control of wash liquid from the flask **141** may be carried out by mechanically pinching the piping **185** extending from the flask **141** to the wash trough. Such pinching may be carried out by sandwiching the piping between a portion of the lever **182** so that the pinch is relieved when the pulley **167** is drawn downwardly by the wire **186**.

The pipetting arrangements may be different and the pipetting tubes need not be formed from polytetrafluoroethylene though this material is preferred, since as there is no tendency for liquids to wet the surfaces of such tubes very accurate quantities of fluid can be dispensed.

The apparatus may be used in any desired manner to effect any known method of dispensing serological or other fluid samples for analysis. Thus the carriage may support receptacles for reagents of various kinds for mixing with the samples under test, or receptacles for rinsing media for the pipetting tubes between any desired stages or cycles of operation.

The apparatus of the invention is able to dispense liquids with accuracy and at great speed.

As an example of the speed of use of the first apparatus described above, it was used by a skilled operator to prepare serial dilutions of 1 in 8, 1 in 16, 1 in 32 etc. The sequences necessary took approximately 2½ minutes, 1¼ minutes and 1¼ minutes respectively whereas to do the job manually a skilled operator took 20 minutes, 10 minutes and 10 minutes respectively. The accuracy of measurement was superior to that attainable by manual methods and in general, in serological work, the speed of use is between 5 and 10 times faster than with conventional methods. In another example using routine procedures which required eight measurements for each specimen, a single technician has, by using the apparatus of FIGURES 1 to 3, been able without difficulty or fatigue to dispense 500 specimens in an hour. Were conventional manual methods to be used it would require two technicians each working three hours to dispense 500 specimens.

I claim:

1. Multiple pipetting apparatus comprising a base, a support on the base for holding receptacles disposed in rows and columns extending along and across the support respectively, a member extending across the support above the level of the receptacles, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, an element for operating the syringes in synchronism, a device for simultaneously raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, said support including a rectangular tray having slidable partitions movable parallel to one pair of sides of the tray and carrying adjustable clamping blocks movable parallel to the other pair of sides of the tray.

2. Apparatus as claimed in claim **1**, in which the support is movable with respect to the base.

3. Multiple pipetting apparatus comprising a base, a support mounted on said base for holding receptacles disposed in rows and columns extending along and across the support respectively, a tower extending upwards from the base at one side of the support, an upright telescopic guide mounted inside the tower, a member extending horizontally away from the guide to an opening in the tower and extending across the support above the level of the receptacles, a mechanism for moving the support along the base, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, an element for operating the syringes in synchronism, a device for simultaneously raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, and interlock means for preventing operation of the device until alignment of said lower ends.

4. Apparatus as claimed in claim 3, including inside the tower a slide rod extending parallel to the base, and a brace extending transversely in a horizontal direction away from the member and slidable along the slide rod at its free end.

5. Multiple pipetting apparatus comprising a base, a support on said base for holding receptacles disposed in rows and columns extending along and across the support respectively, a member extending across the support above the level of the receptacles, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted in the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, an element for operating the syringes in synchronism, a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, means defining slots spaced along the support, an interlock pin vertically movable between two positions at one of which it engages in a selected slot to prevent relative movement between the support and the pipetting tubes and at the other of which it is spaced from the slot to allow such relative movement, and a linkage operatively connected between the pin and the member so that they are moved in synchronism.

6. Apparatus as claimed in claim 5, in which the linkage includes a bell crank lever.

7. Apparatus as claimed in claim 5, including a pulley in said linkage and rotated by said device, and a swinging link depending from said pulley and having the interlock pin projecting from its lower end through a vertical slot confining movement of the pin to a vertical direction.

8. Apparatus as claimed in claim 5, in which said means defining slots comprise adjustable clamp blocks slidable to different positions along a track extending along one side of the support.

9. Multiple pipetting apparatus comprising a base, a support on said base for holding receptacles disposed in rows and columns extending along and across the support respectively, a member extending across the support above the level of the receptacles, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, a rack and pinion unit, a handle for rotating the pinion, an element movable with the rack towards and away from the syringes, fixtures connecting the plungers of the syringes to the element for operating the syringes in synchronism, a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, adjustable stops for co-operating with the handle to limit its movement, and an over-rider button on the handle for permitting it to ride over the stops when desired.

10. Multiple pipetting apparatus comprising a base, a support on the base for holding receptacles disposed in rows and columns extending along and across the support respectively, the member extending across the support above the level of the receptacles, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, branch pipes extending from the rear end portions of respective syringes to a common pipe connection for supplying dried air severally to the syringes so that the dried air passes through the pipes and the pipetting tubes, an element for operating the syringes in synchronism, and a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles.

11. Apparatus as claimed in claim 10, further comprising a handle common to said mechanism and to said device, said handle being movably mounted on said support and operable for producing said relative longitudinal movement and for raising and lowering said pipetting tubes.

12. Multiple pipetting apparatus comprising a base, a support on the base for holding receptacles disposed in rows and columns extending along and across the support respectively, a member extending across the support above the level of the receptacles, a mechanism for producing relative longitudinal movement between the support and the member, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, an element for operating the syringes in synchronism, a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, a wash chamber extending parallel to the columns, means for lowering the lower end portions of the pipetting tubes into the wash chamber to clean them, means for circulating wash fluid past the end portions of the pipetting tubes when dipping into the wash chamber, means in said wash chamber defining upper and lower compartments and an elongated opening extending between said compartments and through which said end portions of the pipetting tubes extend, an inlet for wash liquid in said lower compartment, an outlet for wash liquid in said upper compartment, an immersion heater in said lower compartment and terminating above one edge of said elongated opening.

13. Apparatus as claimed in claim 12, said wash liquid circulating means including a reservoir mounted above the pipetting tubes, a pipe connecting the reservoir to the liquid inlet of the lower compartment, a valve disposed in said pipe for controlling flow of wash liquid therethrough, and means for operating said valve in unison with lowering movement of the end portions of the pipetting tubes into the wash chamber.

14. Multiple pipetting apparatus comprising a base, a support movable on said base and for holding receptacles disposed in rows and columns extending along and across the support respectively, a member extending across the support above the level of the receptacles, a mechanism for producing movement of the support along the base, a line of pipetting tubes mounted on the member above the level of respective rows of receptacles, a set of syringes, pipes individually connecting the syringes to the pipetting tubes, an element for operating the syringes in synchronism, a device for raising and lowering the pipetting tubes when their lower ends are aligned with a column of receptacles, interlock means for preventing operation of the device until alignment of said lower ends, a wash chamber mounted on the base be-

neath the level of the support and extending parallel to the columns, means for lowering the lower end portions of the pipetting tubes into the wash chamber, means for circulating wash fluid past the end portions of the pipetting tubes when in the wash chamber, cam means operated by said support when not interposed between the wash chamber and the pipetting tubes, and a safety element connecting the cam means to the member and preventing said lowering means becoming operative until operation of the cam means.

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