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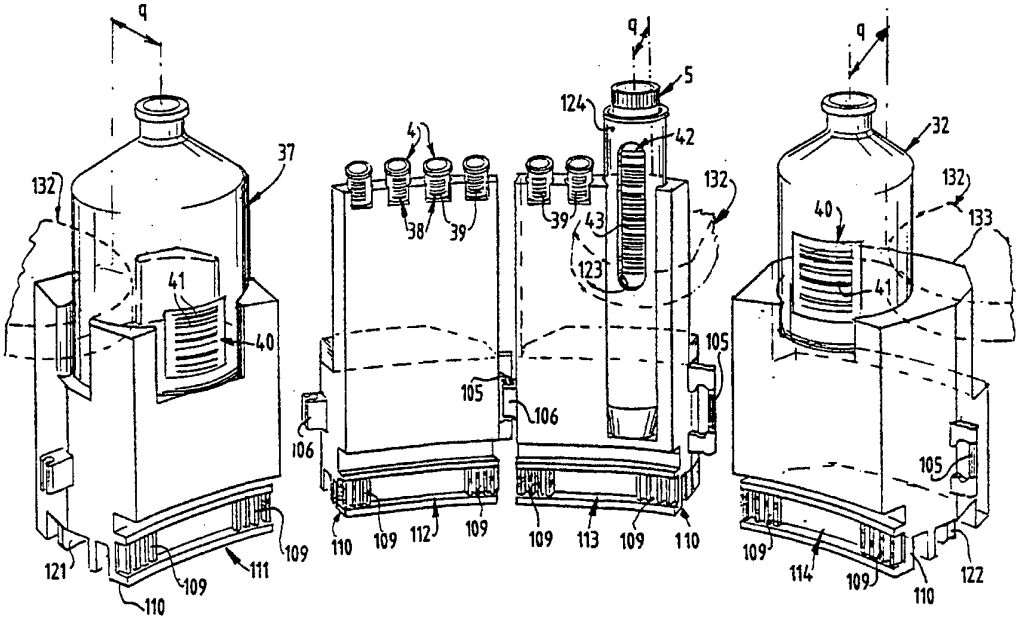

(57) Abstract

The invention relates to a method for performing ELISA tests. Catastrophic errors occur during performing of immunological tests due to incorrect combination of ingredients used. The invention has for its object to avoid such errors. For this purpose the method according to the invention has the feature that the coated cups and the additive containers for the other test ingredients, for which particular calibration values of optical density or fluorescence are determined subject to concentration, each carry a code which designates these coated cups and other test ingredients as forming part of determined lot, and that the computer program is programmed to exclude production of a measurement value of a test with coated cups not forming part of the determined lot and/or other test ingredients not forming part of this lot.

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METHOD AND AUTOMATED DEVICE FOR PERFORMING IMMUNOLOGICAL TESTS AND A LOT OF INGREDIENTS THEREFOR

The invention relates to a method according to the preamble of claim 1.

Catastrophic errors occur during performing of immunological tests due to incorrect combination of ingredients used.

The invention has for its object to avoid such errors. For this purpose is proposed the method of claim 1.

The invention also relates to an automated device as according to claim 6 and a lot of ingredients as according to claim 7.

Mentioned and other features of the invention will be elucidated in the description following hereinbelow and given by way of example.

In the drawings in schematic form:

Fig. 1 and 2 show a perspective view of an automated device according to the invention respectively in closed and opened situation,

Fig. 3 shows on larger scale a section along the line III-III in fig. 1,

Fig. 4 shows on larger scale a perspective view of detail IV in fig. 2,

Fig. 5A, 5B and 5C each show on a larger scale a perspective view of detail V in fig. 2 in different positions,

Fig. 6, 8 and 9 show on a larger scale a perspective view respectively of details VI, VIII and IX in fig. 3,

Fig. 7 shows on larger scale a perspective view of detail VII of fig. 3 in another formation,

Fig. 10 shows a fluid circuit diagram for the automated device of fig. 1, and

Fig. 11 is a broken away perspective view of detail XI in fig. 5B.

The automated device 1 according to the drawing comprises a manipulation cabinet 2, a storage compartment

23 for containers 202, 205 and 206 of diverse liquids required in ELISA tests and a vacuum vessel 209, a feed platform 24, platforms 25 for carrying a computer 6 with monitor controlling the automated device, keyboard 26 and recorder 27. The cabinet doors 29 can only be opened by operating an electric switch 30 after a relevant key has been entered as password in computer 6 by an authorized person. Errors due to interference in the inside of the automated device 1 by unauthorized persons is hereby avoided.

The manipulation cabinet 2 contains inter alia (see fig. 3):

a storage compartment 13 for holders 3 which are each adapted for receiving, in this embodiment, four microtitre cups 4;

a storage compartment 15 for receiving primary tubes 5 which contain serums for testing, for instance blood serums of patients, respectively standard samples;

storage compartments 16 for receiving diluent tubes 36;

storage compartments 17 with locations 237 for receiving containers 37 for different conjugates, substrates and stop liquids;

incubation areas 18 and 19 which are held at a temperature of 22°C respectively 37°C with a variation of at most 2°C in which holders 3 with cups 4 are kept for a prescribed time in accordance with the type of test;

a pipette storage compartment 20 in which are accommodated three grids filled with unused pipettes 7;

a pipette storage compartment 21 for storing used, still usable pipettes 7;

a checking device 118 for checking whether a pipette is hanging on the pipette arm 10;

a cooling space 22 with locations 232 for receiving conjugate containers 32 which are each intended for a conjugate or other additive (The containers 32 are removed from this cooling space when a test must be taken therewith. For this purpose these containers 32 are then transferred to a storage compartment 17 to be brought to room temperature prior to being used);

a device 33 for feeding and discharging test ingredients and primary tubes 5;

an optical density measuring device 34;

a washing device 35;

a switching device 28;

and a waste disposal device 31.

When a doctor prescribes tests for a patient, an extracted serum is sent in a primary tube 5 together with a form indicating the desired Elisa test or tests to a laboratory which performs such tests by means of the automated device 1. In this laboratory the test assignment is numbered and entered in computer 6 matched with antecedents of the patient with mention of all required Elisa tests. It is conceivable that in a hospital or in a laboratory the test authorization is entered into a central computer coupled to computer 6. At the time of entry into the computer 6 a label 42 with bar code 43 containing the assignment number is printed and adhered to the primary tube 5. It is noted that throughout this text an automatically readable code, for instance bar code or dot code, can be understood instead of bar code.

The computer 6 contains the necessary instruction for all types of Elisa tests with respect to the manner of performing thereof, including the designation of the ingredients to be used. Among these ingredients can be included microtitre cups which are coated inside with antibodies and/or antigens, hereinafter designated as cups 4, and conjugates which are held in conjugate containers 32 which are each provided with a label 40 with bar code 41 which designates the relevant conjugate associated with a lot of testing ingredients of a particular Elisa test.

The cups 4 which together with a determined conjugate or number of conjugates form part of a particular lot also carry this information in their bar code together with the identification of these cups 4.

The code 39 on cups 4 contains for instance six letters X X P W W Y. Herein are intended:

X X for code of test type

P for production serial number

W W for production week
Y for production year
The code 41 on containers 32 and 37 contains for instance ten letters C C X X P W W Y E E. Herein are intended:
C C for code of the type of additive
X X for code of test type
P for production serial number
W W for production week
Y for production year
E E for designating the number of weeks of the time limit on use.
The primary tubes 5 which contain standard samples have for instance a fifteen-letter code
S D X X N N V V V V V V F F F. Herein are intended:
S D for distinguishing these standard tubes 5 relative to primary tubes of patient samples
X X for test type
N N the method of standard test, namely:
concentration calibration;
negative check;
positive check;
or reference check.
V V V V V V designations relating to use in respect of concentration;
F F F for designating use time limits in months and year.

For each lot a testing instruction is entered into the computer 6 in the form of a diskette, which instruction also contains directions for realizing calibration values with limited time periods for the use of these calibration values and therefore directions for recalibration, in addition to directions for refusing the input of ingredients of a determined lot when the reliable lifespan thereof has been exceeded.

The code is arranged on each cup 4 as bar code with a width of 6 mm which is printed with a fine-print printer, for instance a 12-dot printer, on a label of woodfree paper adhered to one side of cup 4. Eight or twelve such thus coded cups 4 open at the top are mutually joined on their upper edge by injection moulding to form a strip. Twelve or eight strips are received into a

packing grid. During use these cups 4 are broken loose of each other.

In the manipulation cabinet 2 the frame 44 of a collective manipulator 8 is driven and guided three-dimensionally as according to fig. 4. Horizontal rails 45, 46 guide a horizontal traverse 47 which is driven by a motor 48, a toothed belt 49, a shaft 50 and two toothed belts 51. A frame 52 is guided relative to traverse 47 in horizontal direction along rails 53 and is driven in horizontal direction by means of a motor 54, toothed belt 55, spline shaft 56 and toothed belt 57. A frame 58 is guided in vertical direction relative to frame 52 by means of its rail 59, wherein the relevant guide rollers 60 are mounted on the same shafts 61 as the guide rollers 62 of the horizontal guiding. Frame 58 is driven in vertical direction by means of a motor 63 via a toothed belt 64, spline shaft 65 and toothed belt 66, which in addition to horizontal parts on the traverse 47 has also guided vertical parts on the frame 58, wherein transition guide rollers 67 are mounted on the frame 52.

All positions in the diverse storage compartments for containers 32, 37, holders 3, cups 4 in holders 3, pipettes 7 as well as all other operational positions of manipulator 8, such as stampers 88, pick-up position 115, fountain 35, optical densimeter 34 and waste disposal device 31 are stored in the computer memory in accordance with a co-ordinate system and the stepping motors 48, 54 and 63 steer the manipulator 8 exactly to the required positions using as starting point some reference reflection means 79 with which a sensor 78 to be described later co-acts in order to correct any eventual small deviation in its position.

The frame 58 bears a gripper 9, a pipette carrier 10 and a washer 12 (fig. 5A). Gripper 9 consists of Neurenberger scissors 14, the gripper arms 68 of which are rotatably mounted on a pivot shaft 69 fixedly attached to frame 58, while the other pivot shaft 70 is moved in vertical direction by means of a stepping motor 71 via a threaded rod 72 with a nut 73 which is displaceable in vertical direction in a bearing block 74 but which is

pulled into the lowest position against a stop 77 by means of pins 75 and draw springs 76 so that, when gripper 9 clamps shut when taking hold of an object, the upper pivot shaft 70 is pulled downward as long as the nut 73 is held in engaged position with the stop 77 of bearing block 74. When an object is clamped sufficiently fixedly in gripper 9 the spring tension of draw springs 76 is overcome and the nut 73 can displace somewhat further.

Built into the gripper 9 is a sensor 78 which protrudes downward when gripper 9 is opened but which is carried upward during closing of the gripper 9 by a pressure spring 80 which pushes against a support 81 which is fixed to the lower pivot shaft 69 and in which the sensor is vertically guided for sliding, while the pressure spring 80 presses against a transverse pin 82 of sensor 78 which is guided in vertical slots 83 of the frame 58. The opened gripper position is detected by a switch 84, whereafter the motor 71 is stopped and computer 6 has the information that sensor 78 is exposed.

The pipette carrier 10 is displaceable between its rest position of fig. 5A and its operative position of fig. 5B in that it is adapted on its top end 85 for snap engagement into a per se known coupling 86, as shown for instance in fig. 11, which is released when the bottom end 87 of the pipette carrier 10 receives an upward impact which is brought about by stamping this bottom end 87 onto a fixed upright stamper 88. When coupling 86 is released the draw springs 89 pull the pipette carrier 10 downward until a support 90 thereof strikes on a guide bearing 91. A switch 191 signals the pulled-up position of pipette carrier 10 to the computer 6. When pipette carrier 10 lifts up a pipette 7 the manipulator 8 shows the picked up pipette 7 to the checking device 118 prior to pipetting. Should the checking device 118 signal the absence of a pipette 7, the computer 6 then gives the alarm and stops the pipetting operations until the error is corrected.

The washer 12 is displaceable between its rest position of fig. 5A and its operational position of fig.

5C in that it is adapted on its top end with a coupling 86 which is released when the washer 12 receives an upward impact by stamping it onto a stamper 88. When this coupling 86 is released a pressure spring 92 presses the washer downward until a stop head 93 of a stop rod 94 strikes against a guide bearing 95. A switch 96 actuated by the stop head 93 signals the rest position of the washer 12 to computer 6.

According to fig. 6 a toothed belt 98 with external toothing is guided along the inside of a curved guide rail 97 by means of guide rollers 99 and guide discs 100 while this toothed belt is driven by means of a stepping motor 101 and tooth wheel 102. Guide rail 97 extends from an inlet 103 to an outlet 104.

Fig. 7 shows four different carriers 111, 112, 113 and 114 which can be mutually coupled by means of a vertical pin 105 and a clamp 106 engaging elastically thereon. A plurality of each type of carrier 111-114 is present. Each carrier 111-114 has a curved foot 110 which during transport in manipulation cabinet 2 is displaced between the rail 97 and the toothed belt 98 which then engages in external teeth 109 of these carriers. Carriers 111-114 have on their underside a characteristic difference, which can be detected by means of two switches 108 and 107; carriers 111 and 113 have a rear switch member 121 which co-acts with switch 107; carriers 113 and 114 have a front switch member 122 which co-acts with switch 108 and carrier 112 has no switch member 121, 122. The carriers 111-114 are recognized by the combination of signals from switches 107, 108. Carrier 111 is adapted for a substrate container 237 or a large conjugate container 37; carrier 112 for four cups 4; carrier 113 for two cups 4 and a primary tube 5 which is held in a sleeve 124 provided with a slot 123; and carrier 114 for a small conjugate container 32. When a train of carriers 111-114 is fed manually according to arrow 125, a switch 126 switching on motor 101 is actuated by incoming carriers. The frame 127 of a level scanner 128 can swivel on a vertical shaft 129 and is pressed by a torsion spring 130 as according to arrow 131 with a stop nose 132 against a

conjugate container 37 of carrier 111 or against a shoulder 133 of carrier 114. In the case carriers 112 and 113 pass through, the frame 127 strikes against a vertical rod 134. These parts are herein dimensioned such that a sensor 135 carried by the frame 127 is situated in each case at distance q from the nose 132 above the centre line of the containers 32, 37 or primary tube 5, so that sensor 135 can scan the liquid level therein. Sensor 135 operates as a per se known light reflector and is carried by a rod 136 which is guided vertically in frame 127 and which is pulled downward through a determined stroke by a magnet 137 and pressed upward by a pressure spring 138. When the liquid level in a container is known and the container with its particular inner diameter is identified, the volume of the container is known.

Each carrier 111-114 subsequently passes a light sensor 139 which responds to the leading edges of the carriers so that the motor 101 moves the relevant carrier further until a code detector 140 has read the bar codes 41, 39, 43. If necessary the motor 101 moves the carriers 111-114 reciprocally. Should for any reason a code not be readable, the computer 6 then controls the automated device 1 such that the relevant containers or cups are not picked up by the gripper 9 but leave the manipulator cabinet 2 by the outlet 104. If the codes have been read and the carriers 111-114 or cups 4 identified, they are then picked up one by one by the gripper 9 from the carriers 111-114 at a determined pick-up location 115 of the conveyor belt and set down in a free place in cabinet 2 adapted for this purpose. Conjugate for a determined type of Elisa test not belonging to the same lot of already introduced cups 4 is refused. Conversely, cups not belonging to the same lot of already introduced conjugate are refused. Likewise refused are ingredients which exceed the 'use by' date. When the duration limit of the calibration values of a lot has been exceeded or a new lot is introduced, the computer requests feed of standard samples, which are then introduced in primary tubes.

Situated in the storage compartment 13 (fig. 3) are

holders 3 which are each adapted to receive four cups 4. Fig. 8 shows such a holder 3 gripped by the gripper 9. Holders 3 with another multiple of four receiving spaces for cups 4 are conceivable. The capacity of the automated device 1 is enlarged in that cups are collected in each case in a holder 3 on which the same type of Elisa test must be performed. The collective manipulator (gripper 9), which must perform many movements, and also other members of automated device 1 are thereby used more effectively. At the beginning of a working day the automated device 1 starts from a starting position in which storage compartment 13 is entirely filled with empty holders 3. Incoming cups 4 which are identified by their bar codes 39 are placed sorted into holders 3 such that only cups 4 are found in the same holder 3 which are identical in respect of the tests to be performed therewith and which are thus only suitable for the same type of Elisa test. The test is only started when a holder 3 is full. In the case of rarely occurring tests the testing with cups 4 is nevertheless still started after a predetermined period, for instance six hours, or still in due time before the end of a working day, also in the case the holder 3 is not full. A test with cups from an incompletely filled holder 3 are moreover started when the ingredients and serum for an urgent assignment which has been entered into the computer 6 are present in cabinet 2.

According to fig. 8 the automated device 1 comprises a waste disposal device 31. By means of the gripper 9 the finished cups 4 are placed with an edge 145 of their holder 3 on a swivel plate 143, and into a recess 144. After removal of gripper 9 the swivel plate 143 is turned over as according to arrow 146 by means of a stepping motor 147, while a fork-like detainer 150 mounted on the swivel shaft 148 and coupled to this swivel shaft via a torsion spring 149 is carried along from a raised rest position to a position above the inlet 152 of a waste container 151. The holder 3 is herein held in place by the detainer 150. In the return stroke of motor 147 the empty holder 3 is set down again and is then picked up by

gripper 9 and placed in storage compartment 13.

Used and no longer usable pipettes 7 are placed by pipette carrier 10 as according to arrows 154 through a large hole 155 in device 31 and stripped off in the slot 156. All the waste falls into a plastic bag 157.

According to fig. 9 the optical densimeter 34 comprises the usual light source 158, light filters 159 and glass fibre cables 160 which cast the light rays 161 through cups 4 and their content onto the light sensors 162. Four sensors 162 herein receive light for measuring of cups 4 while one sensor 163 is intended for a comparative zero object 164. The densimeter 34 comprises a closed box 165 into which a holder 3 with cups 4 is introduced by being placed in a slide 166 by the gripper 9 and the slide 166 then being pushed inside using the pipette carrier 10 which for this purpose performs together with gripper 9 the movement as according to arrows 167, while the pipette carrier 10 engages in a hole 168 of the handle 169.

According to fig. 9 four washing tubes 170 of the washer 12 are washed in a fountain 171, wherein washing liquid is supplied by feed tubes 172 and sprayed on the outside of the washing tubes 170. This washing water is then drained via a drain tube 173 to waste washing liquid containers 205. The washing treatment with the fountain 171 is started by computer 6 only when the washing tubes 170 are situated in fountain 171.

The switching device 28 of fig. 10 comprises a vacuum pump 211 of 0.7 bar which is driven by a motor 210 and which creates a vacuum in a vacuum vessel 209 which is connected to two mutually communicating containers 205 for used liquid which are connected via valves 215 and 216 to the washing tubes 170 of the washer 12 respectively the drain tube 173 of fountain 171. An air pressure pump 219 driven by a motor 218 is connected to a buffer vessel 220, to containers 206 with different diluents and to containers 202 with different washing liquids. These containers 202 are selected by means of valves 21 in the case of a determined washing treatment and then connected via valves 213 onto washing tubes 170. They are herein

all opened simultaneously when four cups 4 are situated in a holder 3 or a relevant smaller number when holders 3 are not completely filled. During washing of the inside of washing tubes 170 in the washing fountain 171 selected washing liquid is supplied via an opened valve 212 and an opened valve 215.

The device 186 for filling diluent tubes 36 with diluent from one of the containers 206 comprises a large cylinder 182 of 500 µl and a small cylinder 183 of 250 µl which are connected according to the diagram of fig. 10 to the containers 206 via rotating valves 181, 188 driven by motors 180, 187 and to the tubular pipette carrier 10. Prior to filling of the diluent tubes the conduit system is flushed with the diluent for use, wherein the pipette carrier 10 is held in the fountain 171 and this flushed diluent passes into the containers 25. A plurality of diluent tubes 36 is now preferably filled one after another with this same diluent using the filled conduit system, this as required by means of one or more complete or partial fillings of cylinders 182 and/or 183 which are driven reciprocally for this purpose by motors 189, 190.

The storage compartments 16 are continually shaken by means of a shaker 230 except during filling with diluent and during pipetting. During pipetting the rotating valve 188 is closed and the cylinder 183 then first presses diluent out of the pipette carrier 10 into the fountain 171 so that an air buffer is situated therein, while the bottom end is washed with water. A pipette 7 is then lifted out of the storage compartment 20 or 21 and a measured quantity of serum is drawn up out of a primary tube 5, wherein the small cylinder 183 makes a measured stroke and this serum is transferred into a cup 4 or a diluent tube 36. These operations can be repeated quickly with the same pipette 7 in the case of one or more filled holders 3 with cups 4 for identical tests. After ending of the filling process of one or more diluent tubes 36 this still usable pipette 7 is stored in the storage compartment 21. The computer 6 records the amounts of used washing agents, diluents, conjugates and serums so that the pipette 7 is immersed each time to the correct

level into the liquid to be drawn up and computer 6 detects, if necessary, a practically empty container 32, 36, 5, 202, 206. The pipettes 7 employed for instance for serum which can no longer be used are removed immediately through the slot 156. Serums are either carried directly from primary tubes 5 into cups 4 and/or carried into the diluent tubes 36, from which they are transferred in diluted state into cups 4 after some shaking of the mixtures using a shaker 230.

At the beginning of a working day a start is made with filled containers 202 and 206, empty containers 205, cleaned conduits, filled pipette storage compartment 20, storage compartments 16 filled with empty diluent tubes 36, holder storage compartment 13 filled with empty holders 3, empty incubation spaces 18, empty pipette storage compartment 21, empty cooling space 22, an empty storage compartment 15 for primary tubes 5, an empty storage compartment 217 for substrate containers 237 and an empty storage compartment 17 for conjugate containers 37.

The automated device 1 checks everything relating hereto in that the manipulator 8 scans all positions. Thereafter the substrate containers, conjugate containers, primary tubes 5 and cups 4 can be introduced, which can take place throughout the day in random sequence as test assignments arrive, wherein the automated device 1 itself collects together the test assignments according to types and, in an efficient manner, performs the same tests simultaneously as far as possible, wherein even tests requiring the same washing agent and/or the same diluent, the same conjugate and/or substrate are preferably performed successively. The test results are linked by the computer 6 to the relevant assignments and thereby to the correct patient due to the coupling of the tests and test results to the assignment number read from the primary tube 5.

The automated device 1 not only operates efficiently because similar tests are collected and performed simultaneously and/or immediately after one another and because operations for tests with use of the same washing

agents and/or diluents are performed immediately one after another, but also operates reliably in the sense that directions for incubation times and any required short intervals between successive operations are respected, in any case within the tolerance time limits. To this end the automated device 1 operates according to a manipulator agenda in which the utilization periods of the manipulator 8 for all operations of initiated test assignments are reserved. An incubation will for instance never be initiated if the manipulator 8 would not be available to perform the operations required at the end of the incubation.

When an urgent assignment arrives it is treated with priority. The computer 6 is preferably adapted to search for free periods in the manipulator agenda and preferably even such that periods already reserved for other non-urgent tests are deferred, while respecting the required directions relating to already initiated tests.

When the cabinet doors 29 are opened the storage compartments are removable and thus easy to clean thoroughly and to autoclave.

The computer 6 detects any disturbance and any obstacle which prevents performing of the test in accordance with the assignment, for instance the absence of a required cup 4 and other ingredients. It is conceivable that instead of only one manipulator 8 the automated device 1 has a number of mutually adjacent manipulators 8, in which case the computer 6 controls the operations for performing and these manipulators 8 such that they do not conflict with each other. The gripper 9, the washing device 12 and the pipette carrier 10 could be carried by different manipulators.

The carriers 111-114 may as alternative carry an identification code which is read by the code detector 140.

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CLAIMS

1. Method for performing immunological tests of the ELISA test type, comprising the following steps:

a serum for testing and thereafter a conjugate is added in each case to a cup (4) which is coated with antibodies and/or antigens;

after an incubation period the cup (4) is washed with a washing liquid;

a substrate for the purpose of bringing about a colour reaction is added and thereafter optionally a stop liquid, for instance sulphuric acid;

whereafter the concentration of the substance for measuring possibly present in the serum is determined by comparing the optical density or fluorescence measured on the relevant cup to calibration values of optical density respectively fluorescence determined on standard samples while making use of the same test ingredients, namely cups with identical coating, identical conjugate and optionally identical substrate,

wherein a plurality of tests is performed automatically in an automated device (1), into which are introduced cups (4), serum containers (5) with the serums for testing and additive containers (37) with additives;

and wherein the cups (4) and the serum containers (5) are provided with an automatically readable code, for example a bar code,

characterized in that the coated cups (4) and the additive containers (37) for the other test ingredients, for which particular calibration values of optical density or fluorescence are determined subject to concentration, each carry a code (39, 41) which designate these coated cups (4) and other test ingredients as forming part of a determined lot,

and that the computer program is programmed to exclude production of a measurement value of a test with coated cups (4) not forming part of the determined lot and/or other test ingredients not forming part of this lot.

2. Method as claimed in claim 1, **characterized in that** the computer program is programmed to exclude production of a measurement value of a test with test ingredients, the time limit of use of which, applying the determined calibration values, has been exceeded.

3. Method as claimed in claim 1 or 2, **characterized in that** the instruction for performing a determined type of ELISA test with a combination of mutually associated coated cups (4) and other test ingredients is entered into a computer (6) which controls the automated device (1), preferably by means of a diskette.

4. Method as claimed in claim 3, **characterized in that** the instruction comprises calibration directions for the determined type of ELISA test relating to calibration tests with standard samples of different concentrations of substance for measuring in order to produce calibration values of optical density or fluorescence applying to the combination of coated cups (4) and other test ingredients associated therewith for a particular lot, which calibration values are stored in the computer program related to a code corresponding with the codes carried by the coated cups (4) and the containers (37) of the associated other test ingredients of this lot.

5. Method as claimed in claim 4, **characterized in that** after lapse of a determined time limit of use of the calibration values the calibration tests are repeated and that after performing of the repeated tests a new time limit of use for the relevant lot is entered into the computer program.

6. Automated device (1) for performing the method as claimed in any of the foregoing claims comprising a computer (6); means for adding to a coated cup a serum for testing, a conjugate, washing liquid, a substrate and optionally a stop liquid, in addition to measuring means for measuring optical density or fluorescence and for generating a measurement value of optical density to the computer (6) which is adapted to compare the measured optical density or fluorescence with relevant calibration values, **characterized in that** the automated device (1) is adapted to identify codes (39, 41) carried by coated cups

(4) and containers (37) of other ingredients for a determined ELISA test, and that the computer program of the computer (6) is programmed to exclude from production a measurement value of a test with coated cups 4 not forming part of a particular lot and/or other test ingredients not forming part of this lot, for which lot valid calibration values are recorded in the computer program.

7. Lot of ingredients for a determined ELISA test comprising coated cups (4) and conjugate, **characterized in that** the coated cups (4) and each container (37) of another ingredient for a particular ELISA test each carry a code (39, 41) which identifies them as belonging to this lot of ingredients.

8. Lot of ingredients as claimed in claim 7, **characterized in that** it is provided with an instruction, preferably in the form of a diskette, for performing the determined ELISA test, comprising directions for performing and/or repeating standard tests for determining calibration values.

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AMENDED CLAIMS

[received by the International Bureau on 16 May 1994 (16.05.94); original claims 1 and 7 amended; other claims unchanged (3 pages)]

1. Method for performing immunological tests of the ELISA test type, comprising the following steps:

a serum for testing and thereafter a conjugate is added in each case to a cup (4) which is coated with antibodies and/or antigens;

after an incubation period the cup (4) is washed with a washing liquid;

a substrate for the purpose of bringing about a colour reaction is added and thereafter optionally a stop liquid, for instance sulphuric acid;

whereafter the concentration of the substance for measuring possibly present in the serum is determined by comparing the optical density of fluorescence measured on the relevant cup to calibration values of optical density respectively fluorescence determined on standard samples while making use of the same test ingredients, namely cups with identical coating, identical conjugate and optionally identical substrate,

wherein a plurality of tests is performed automatically in an automated device (1), into which are introduced cups (4), serum containers (5) with the serums for testing and additive containers (37) with additives;

and wherein the cups (4) and the serum containers (5) are provided with an automatically readable code, for example a bar code,

characterized in that the coated cups (4) and the additive containers (37) for the other test ingredients, for which particular calibration values of optical density or fluorescence are determined subject to concentration, each carry a code (39, 41) which designate these coated cups (4) and other tests ingredients as forming part of a determined lot,

that the computer program is programmed to exclu-

de production of a measurement value of a test with coated cups (4) not forming part of the determined lot and/or test ingredients not forming part of this lot.

and that said automatically readable codes of cups (4) and said additive containers (37) for said other ingredients are automatically read after introduction of said cups (4) and said containers (37) into said automated device (1) which during operation is kept in closed condition.

2. Method as claimed in claim 1, **characterized in that** the computer program is programmed to exclude production of a measurement value of a test with test ingredients, the time limit of use of which, applying the determined calibration values, has been exceeded.

3. Method as claimed in claim 1 or 2, **characterized in that** the instruction for performing a determined type of ELISA test with a combination of mutually associated coated cups (4) and other test ingredients is entered into a computer (6) which controls the automated device (1), preferably by means of a diskette.

4. Method as claimed in claim 3, **characterized in that** the instruction comprises calibration directions for the determined type of ELISA test relating to calibration tests with standard samples of different concentrations of substance for measuring in order to produce calibration values of optical density or fluorescence applying to the combination of coated cups (4) and other test ingredients associated therewith for a particular lot, which calibration values are stored in the computer program related to a code corresponding with the codes carried by the coated cups (4) and the containers (37) of the associated other test ingredients of this lot.

5. Method as claimed in claim 4, **characterized in that** after lapse of a determined time limit of use of the calibration values the calibration tests are repeated and that after performing of the repeated tests a new time limit of use for the relevant lot is entered into the

computer program.

6. Automated device (1) for performing the method as claimed in any of the foregoing claims comprising a computer (6); means for adding to a coated cup a serum for testing, a conjugate, washing liquid, a substrate and optionally a stop liquid, in addition to measuring means for measuring optical density or fluorescence and for generating a measurement value of optical density to the computer (6) which is adapted to compare the measured optical density or fluorescence with relevant calibration values, **characterized in that** the automated device (1) is adapted to identify codes (39, 41) carried by coated cups (4) and containers (37) of other ingredients for a determined ELISA test, and that the computer program of the computer (6) is programmed to exclude from production a measurement value of a test with coated cups (4) not forming part of a particular lot and/or other test ingredients not forming part of this lot, for which lot valid calibration values are recorded in the computer program.

7. Lot of ingredients for a determined ELISA test comprising coated cups (4) and conjugate, **characterized in that** the coated cups (4) and each container (37) of another ingredient for a particular ELISA test each carry a code (39, 41) which identifies them as belonging to this lot of ingredients, said cups having small dimensions viz a height of about 13 mm and a diameter of about 8 mm.

8. Lot of ingredients as claimed in claim 7, **characterized in that** it is provided with an instruction, preferably in the form of a diskette, for performing the determined ELISA test, comprising directions for performing and/or repeating standard tests for determining calibration values.

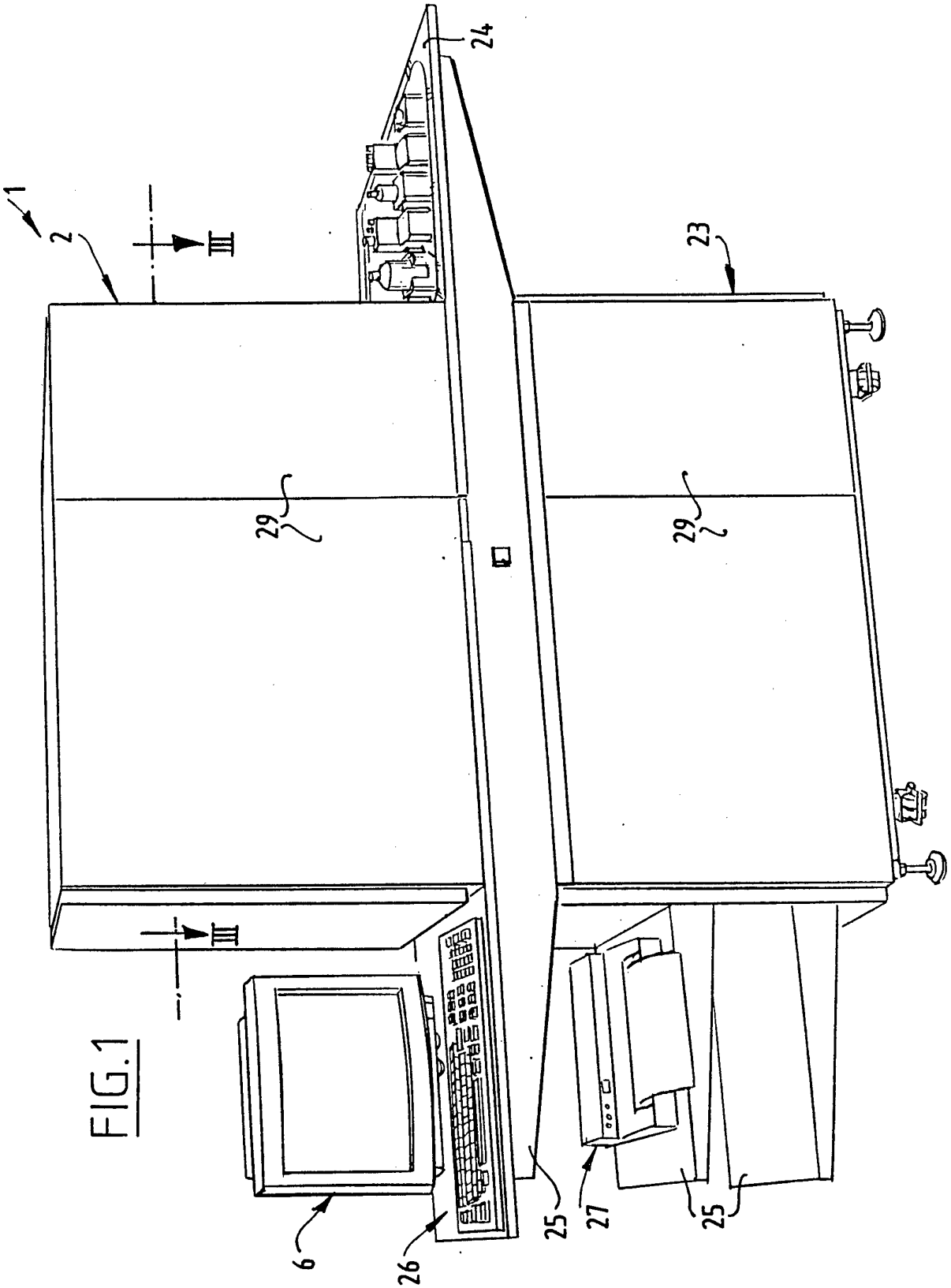


FIG.1

FIG.2

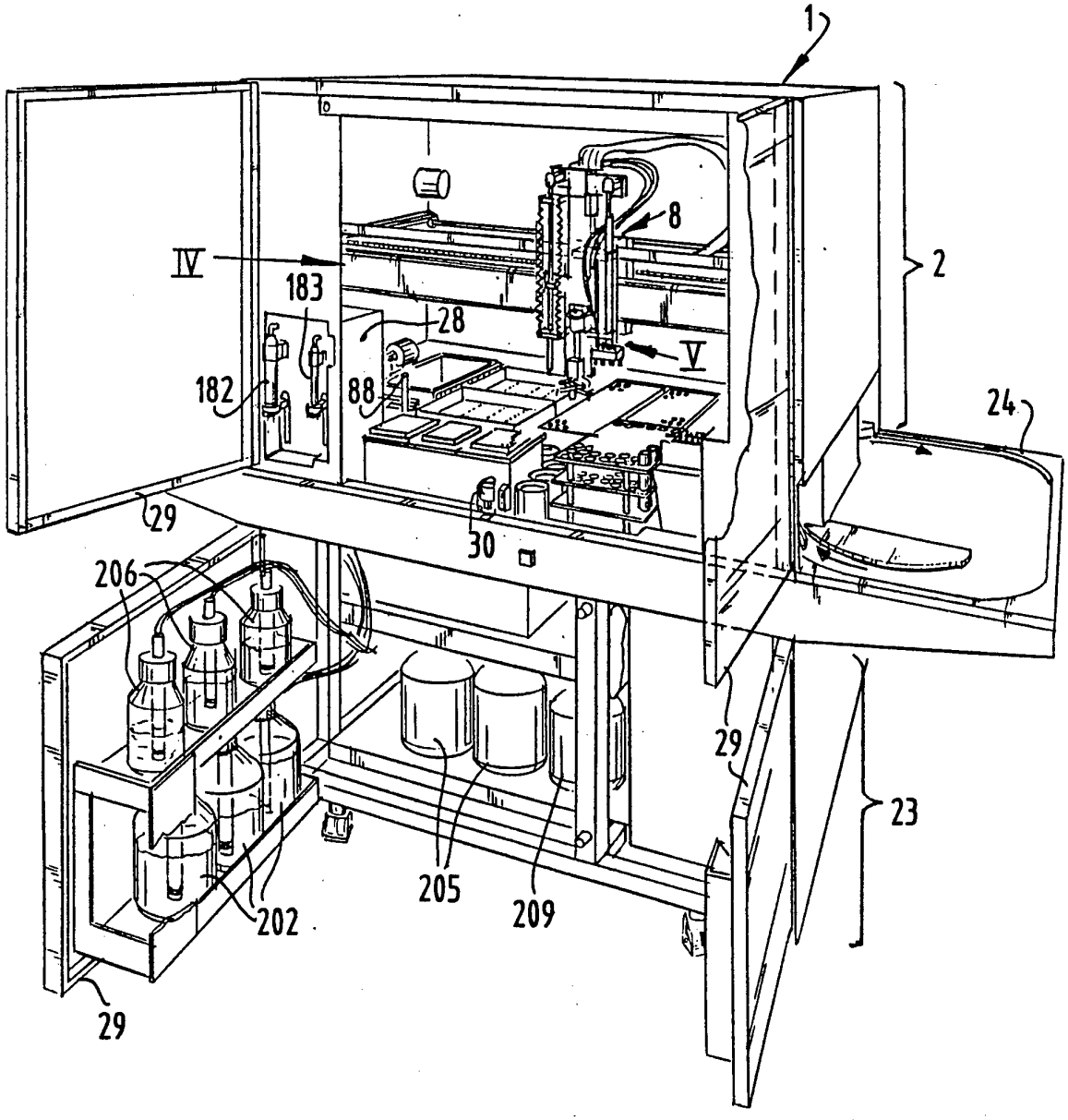
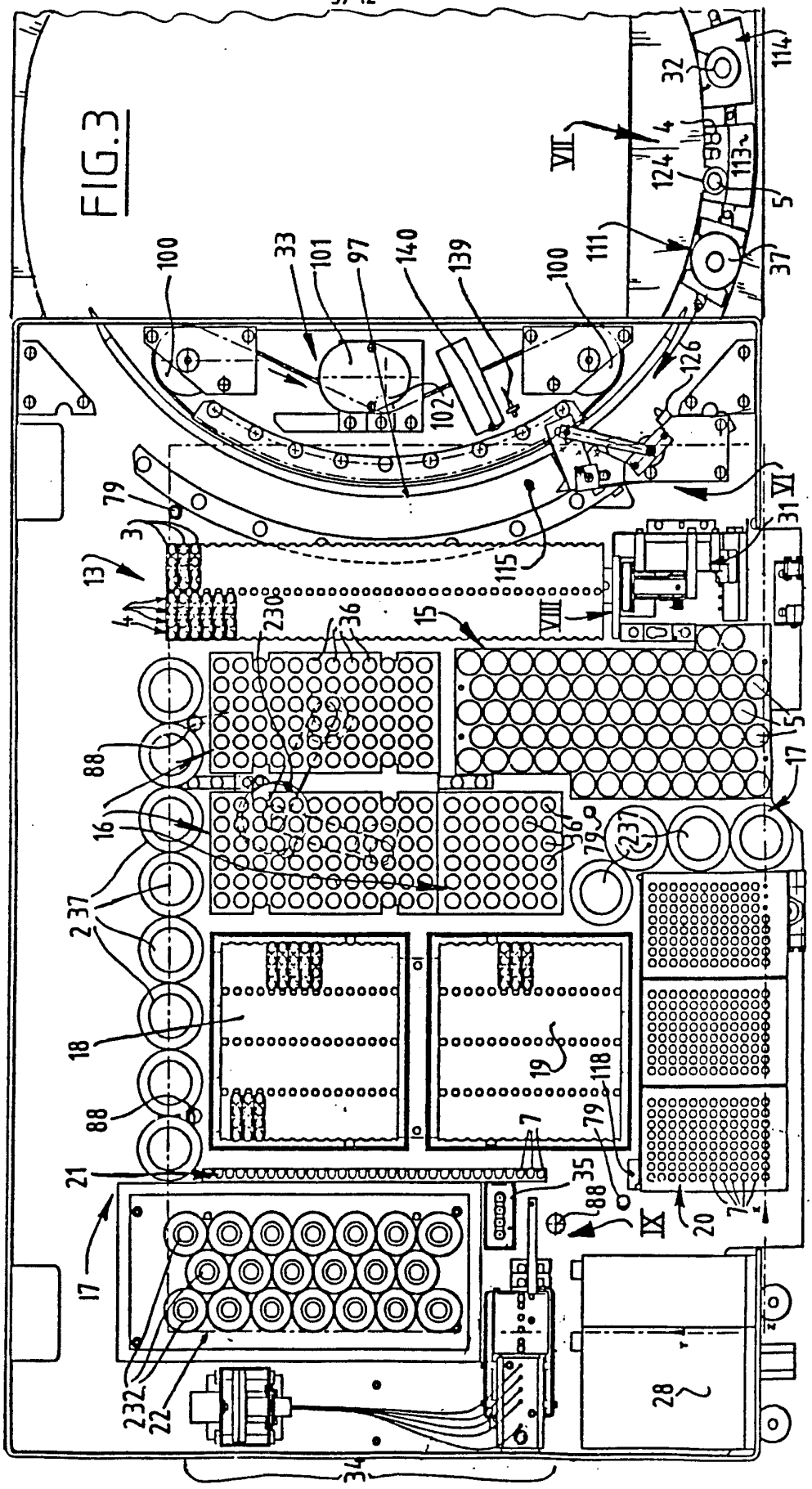


FIG.3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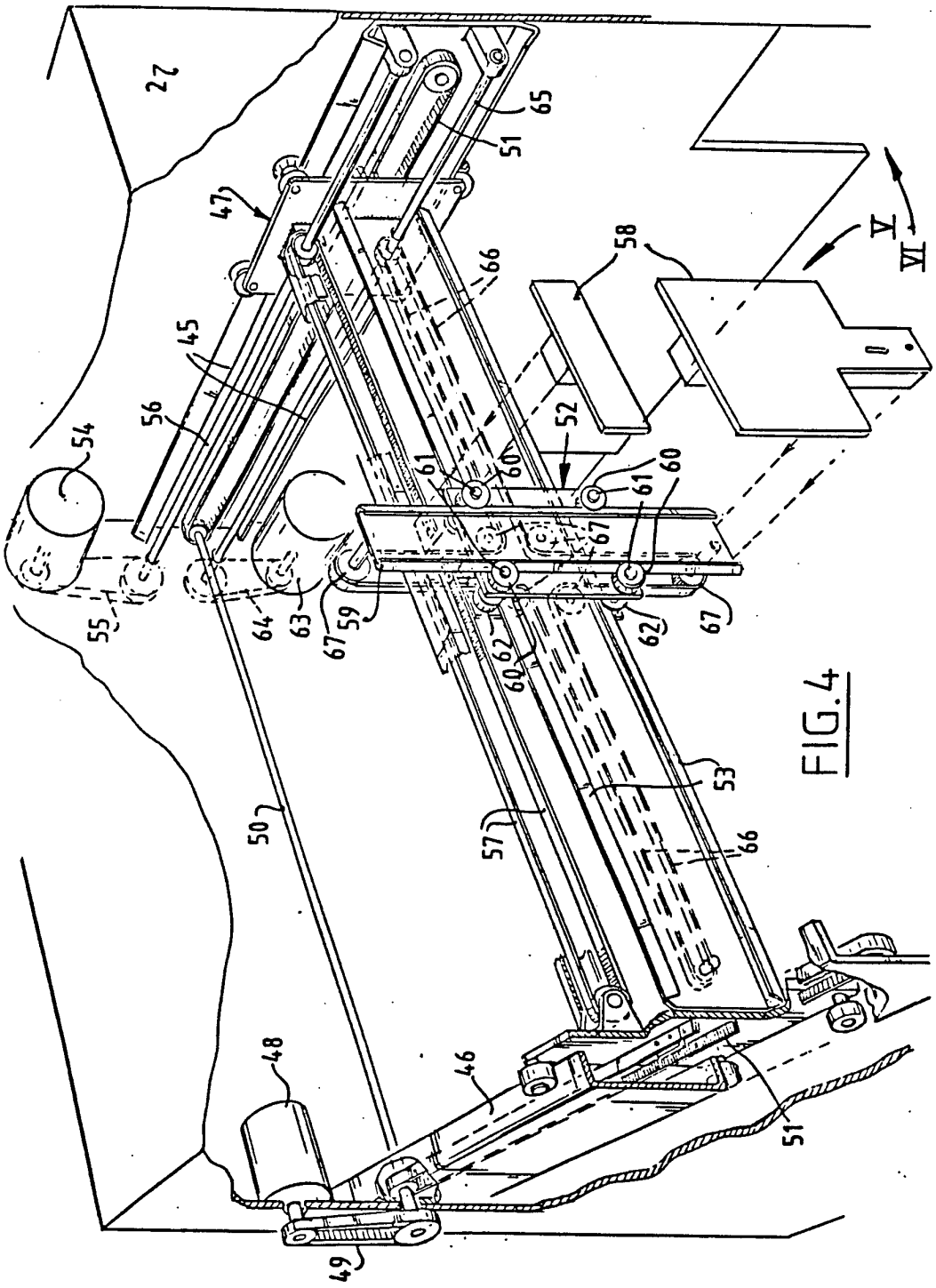
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FIG.4

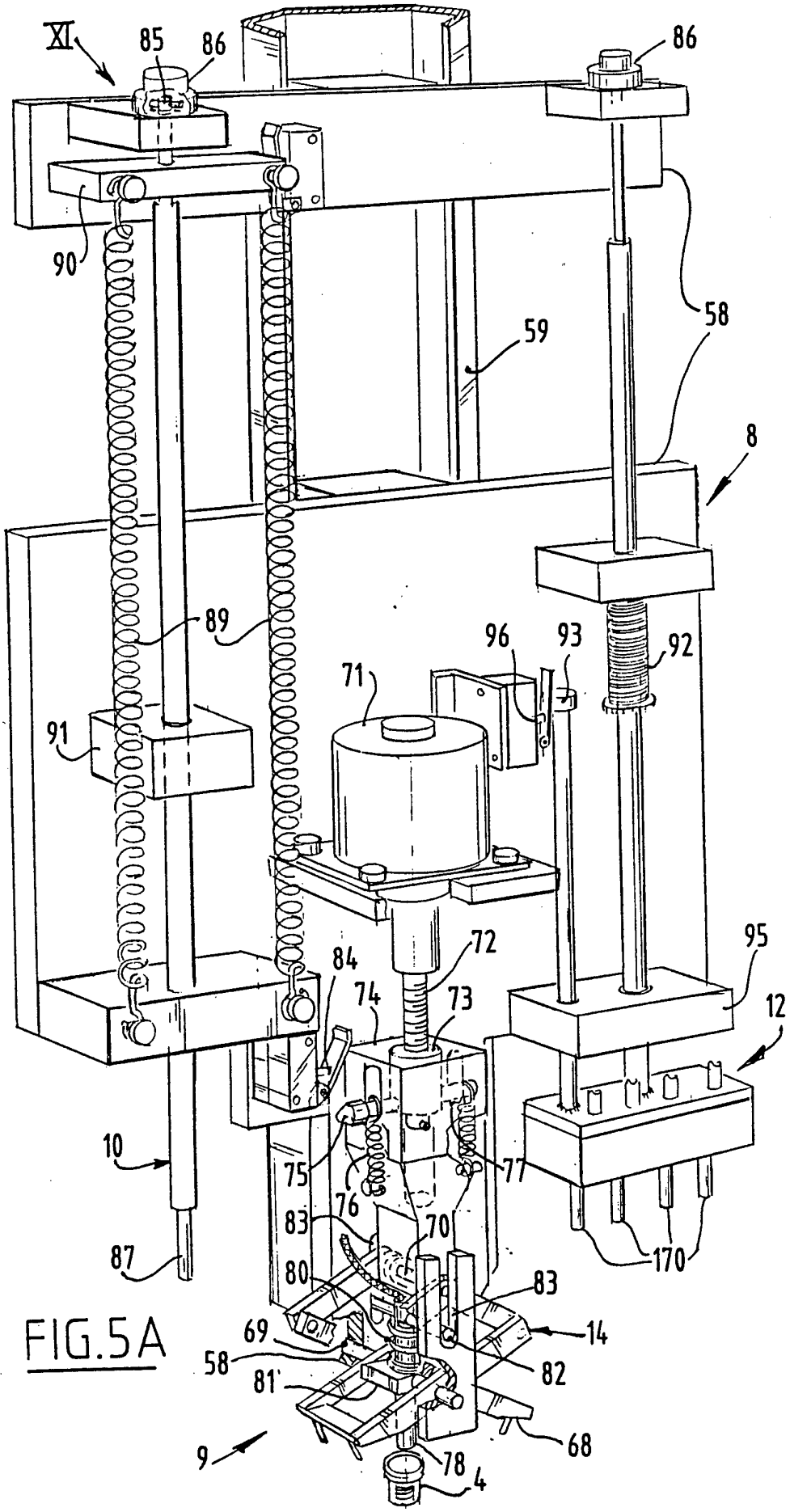
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FIG.5A

FIG.5B

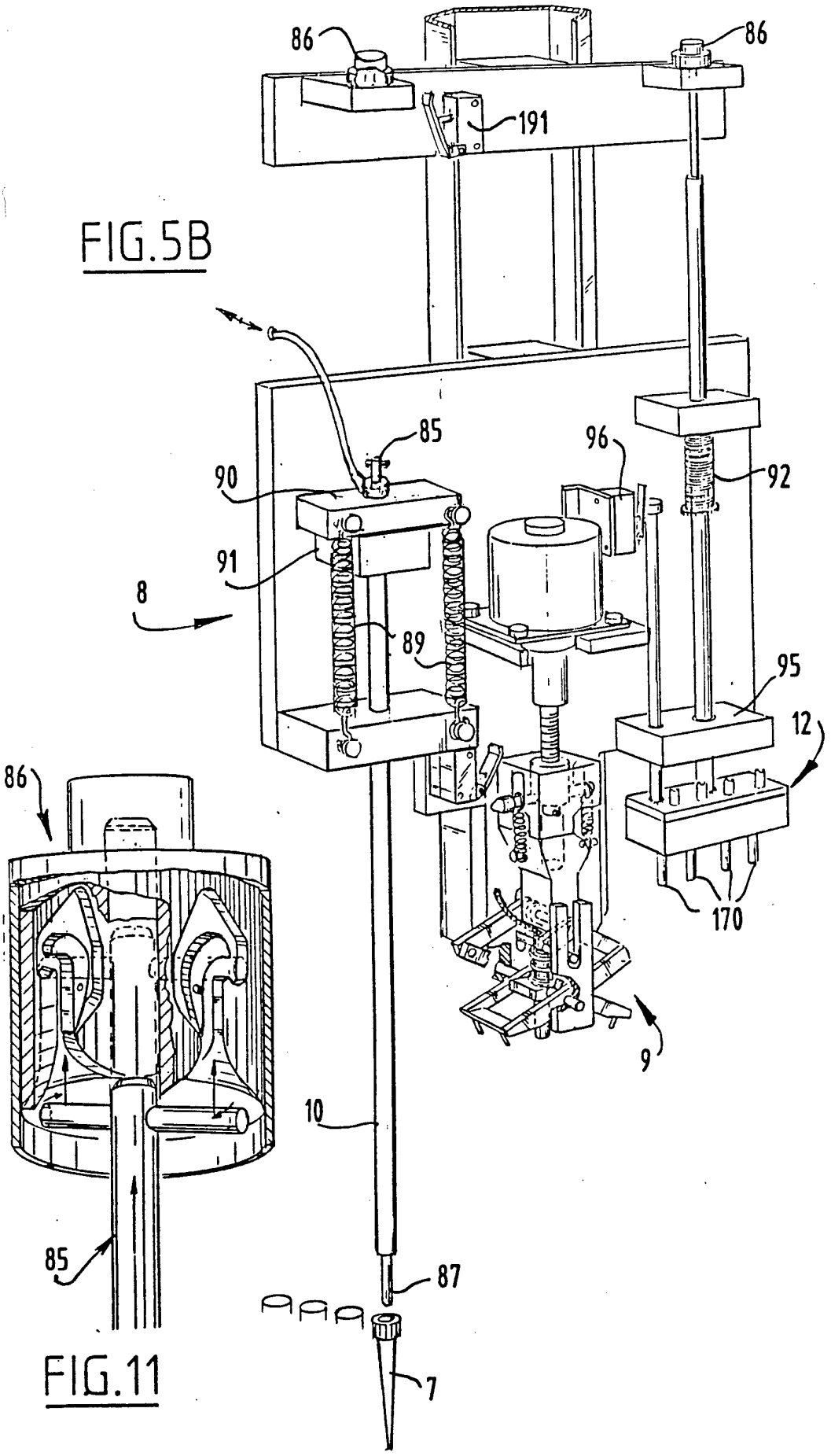


FIG.11

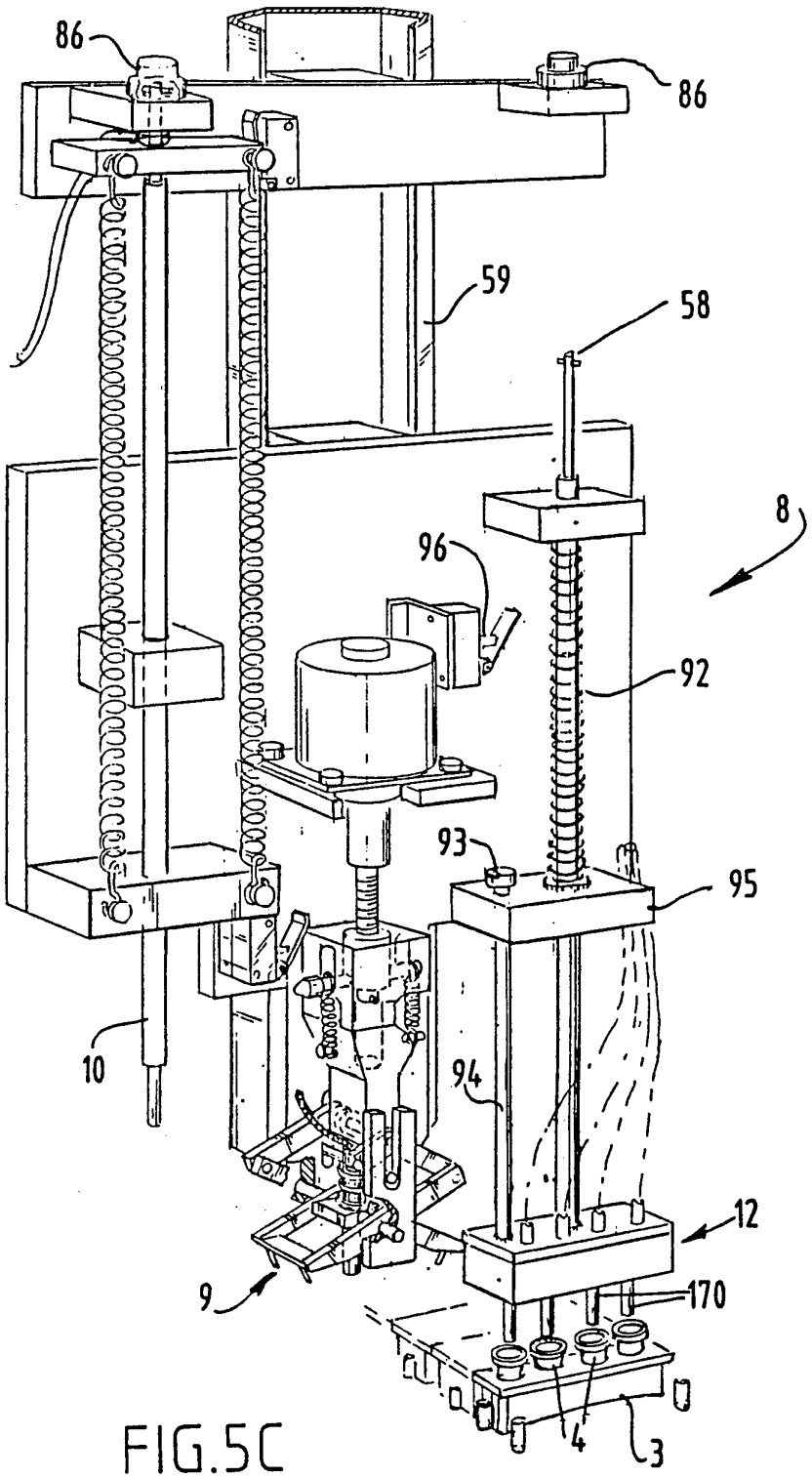
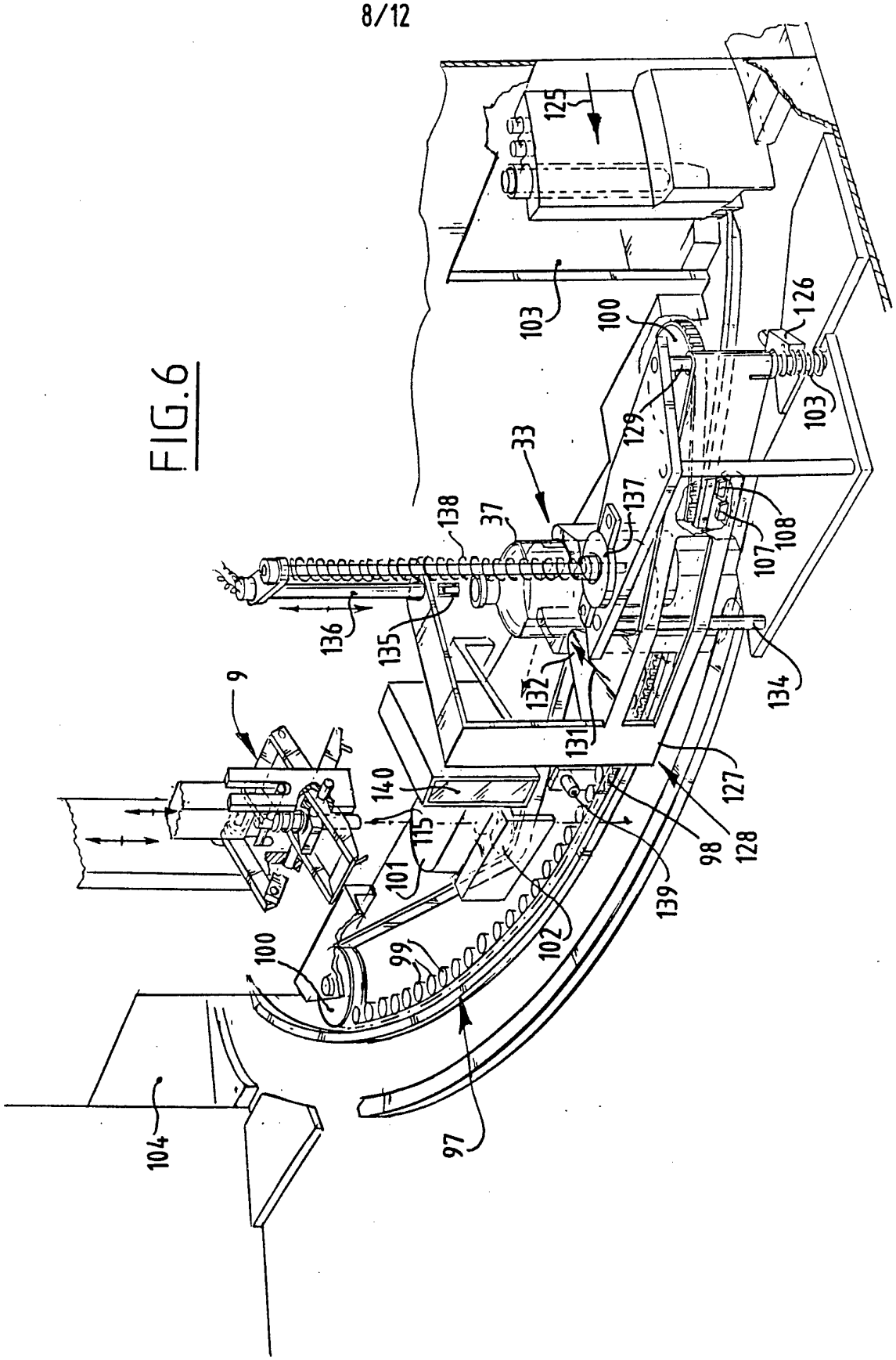


FIG.5C

FIG.6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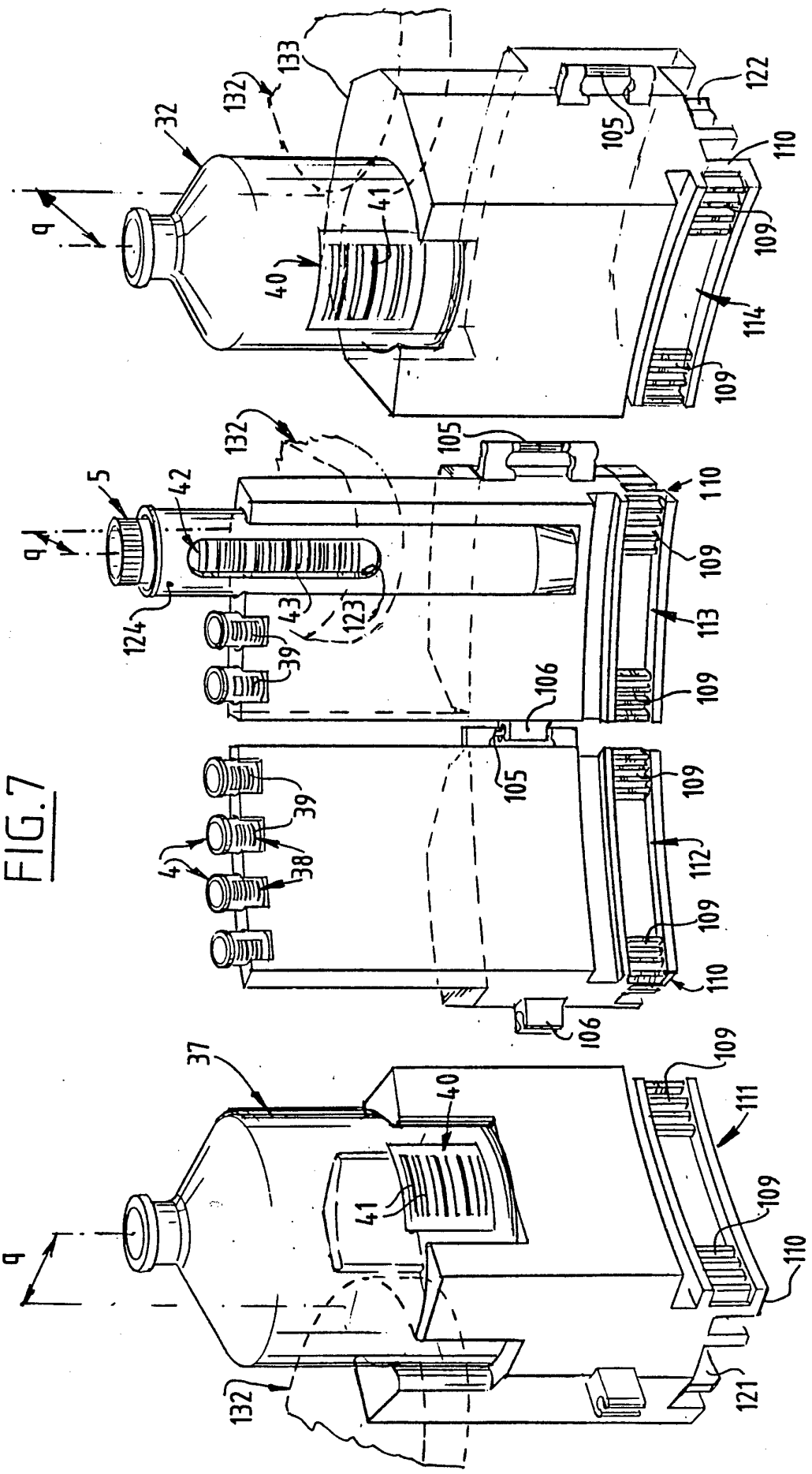
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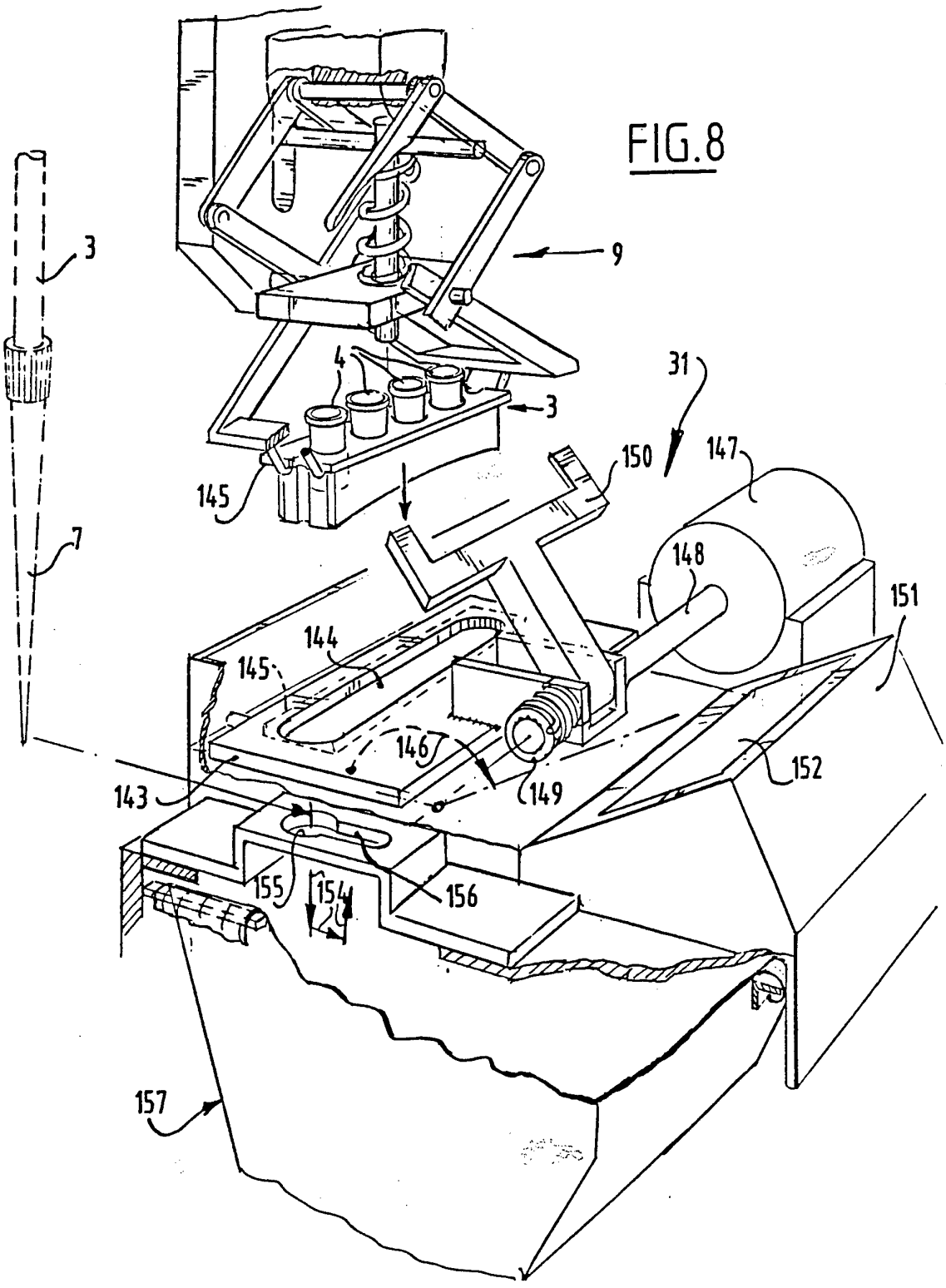
FIG.7

FIG.8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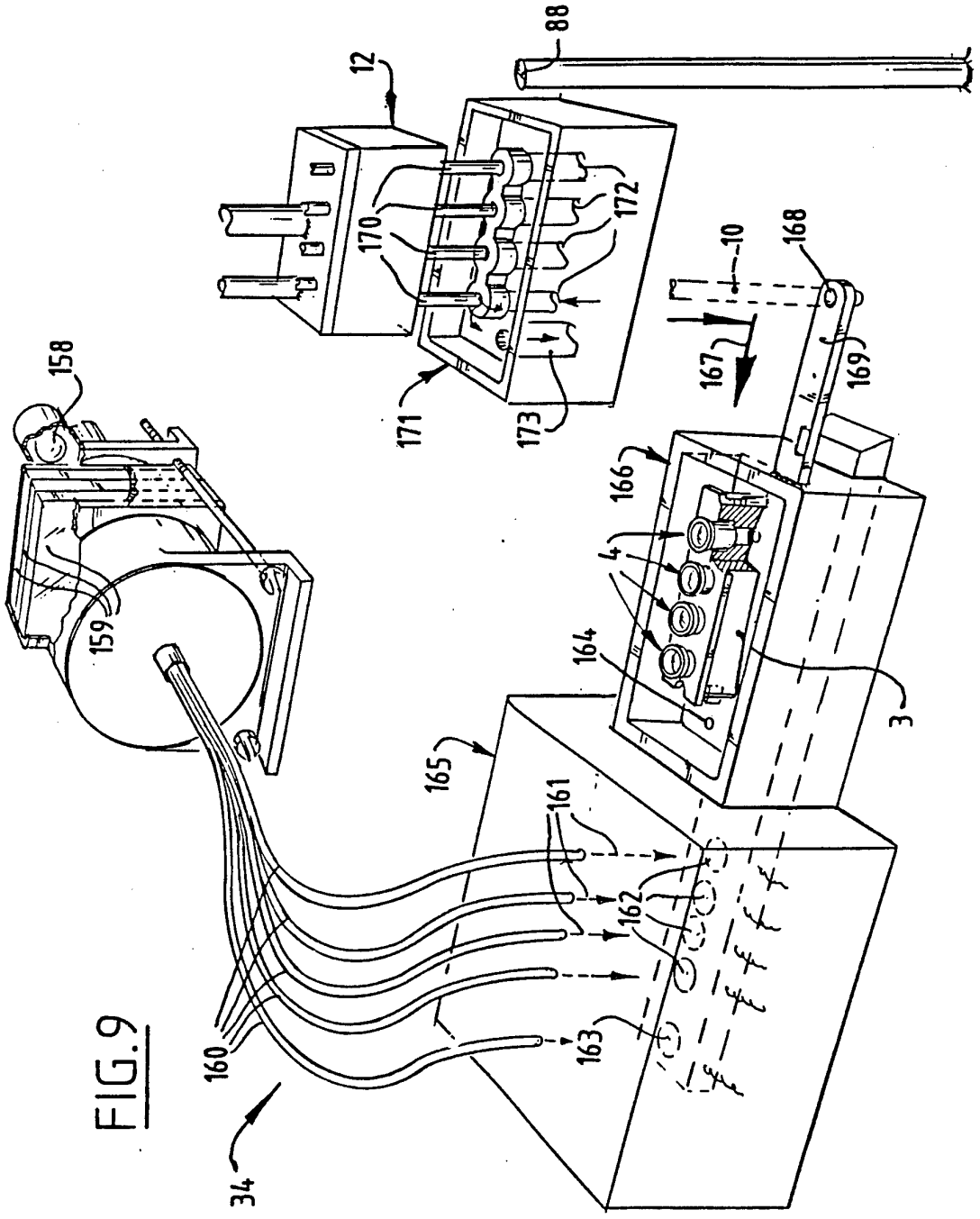
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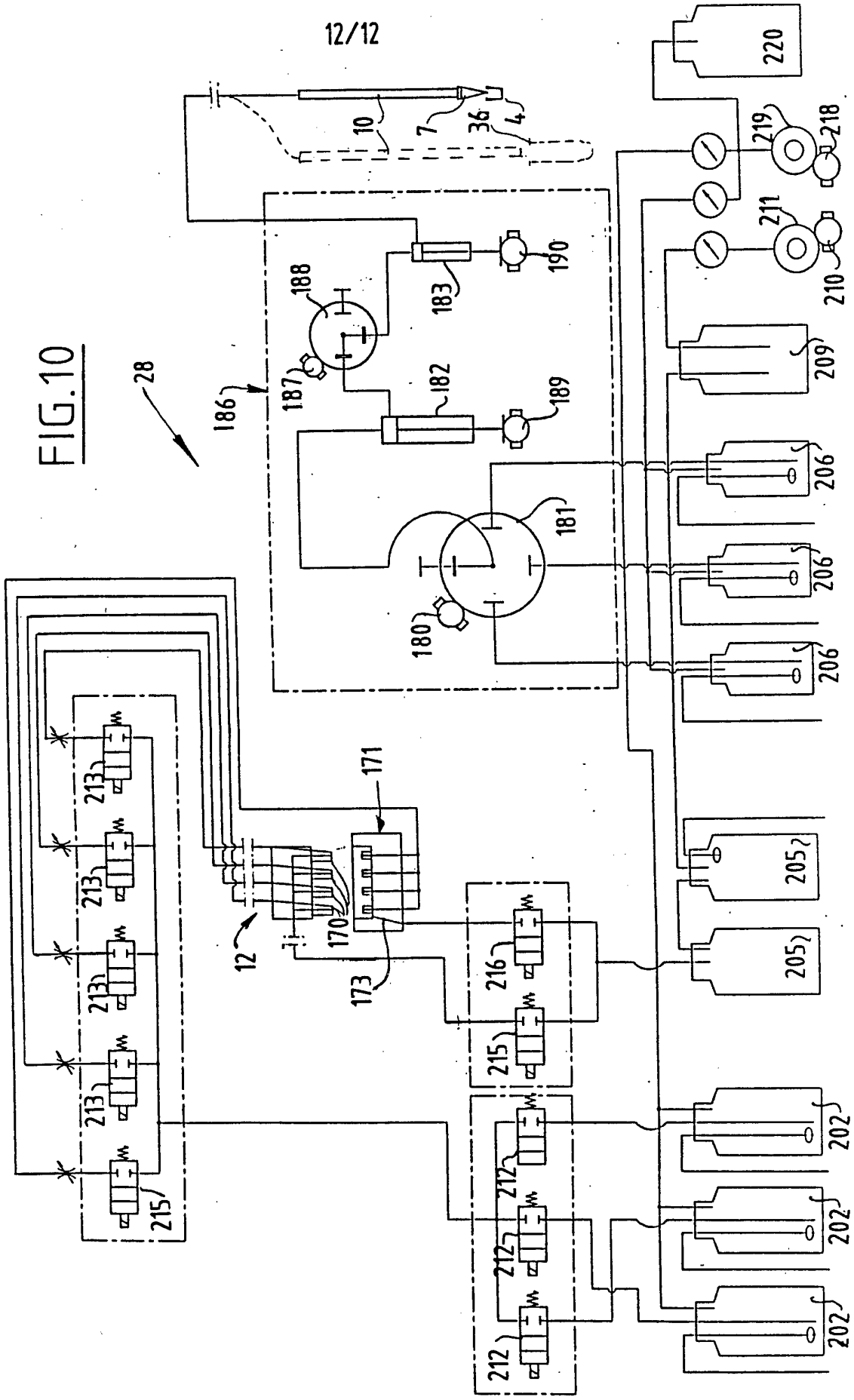
FIG.9

FIG.10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INTERNATIONAL SEARCH REPORT

Inter ıal Application No
PCT/BE 93/00070

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 G01N35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 G01N B01L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP,A,0 410 688 (TOSOH CORPORATION) 30 January 1991 see column 1, line 29 - line 53 see column 3, line 56 - column 4, line 53 see column 8, line 40 - column 11, line 20	1-8
A	US,A,4 678 755 (SHINOHARA ET AL.) 7 July 1987 see abstract	1,2,5,6
A	WO,A,92 05448 (ANAGEN LTD) 2 April 1992 see page 12, line 8 - page 22, line 16 see page 37, line 16 - page 39, line 5	1,6
A	WO,A,88 02866 (SERONO DIAGNOSTICS PARTNERS) 21 April 1988 see page 12, line 5 - line 19	1,6

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
8 March 1994	16. 03. 94

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl, Fax (+ 31-70) 340-3016	Bindon, C

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INTERNATIONAL SEARCH REPORT

...information on patent family members

Inter nal Application No
PCT/BE 93/00070

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