June 3, 1941. J. A. REYNIERS 2,244,082

APPARATUS FOR AND METHOD OF MAINTAINING AND WORKING WITH BIOLOGICAL SPECIMENS IN A GERMFREE CONTROLLED ENVIRONMENT

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FIG. 1.

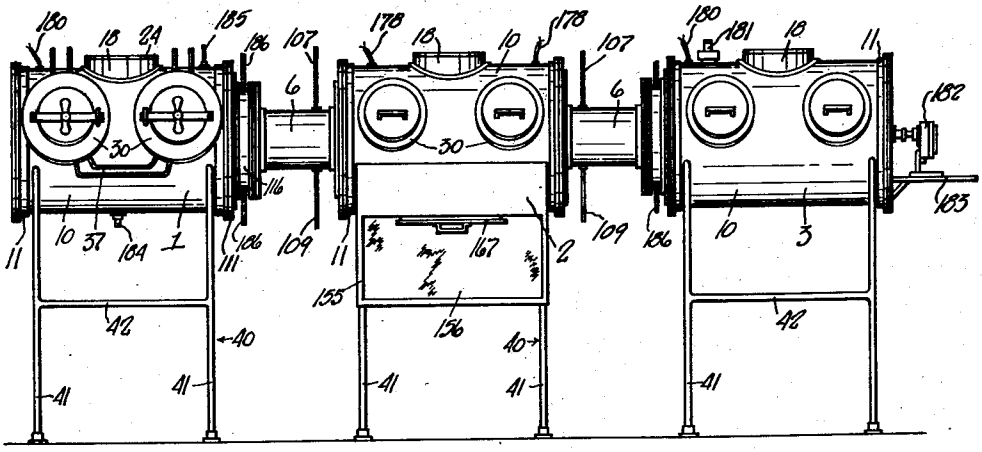


FIG. 2.

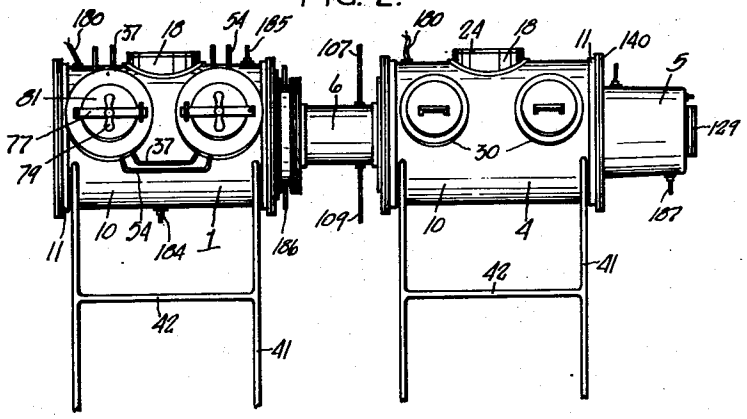


FIG. 3.

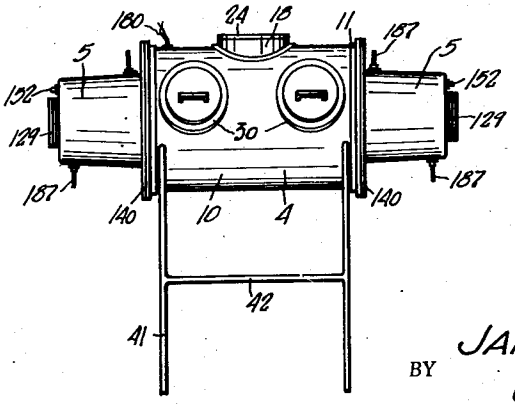
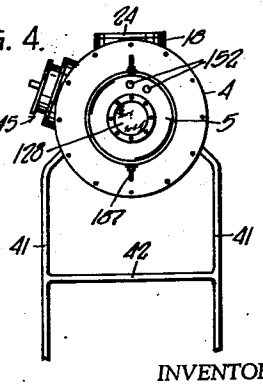


FIG. 4.



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FIG. 5.

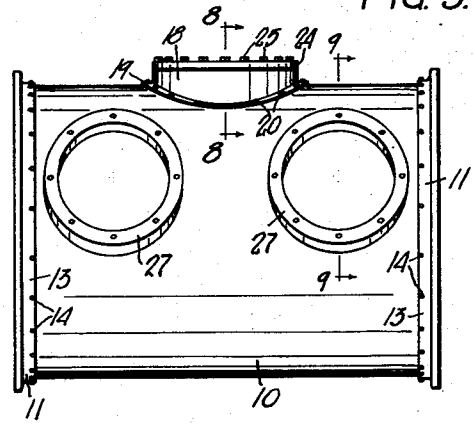


FIG. 6.

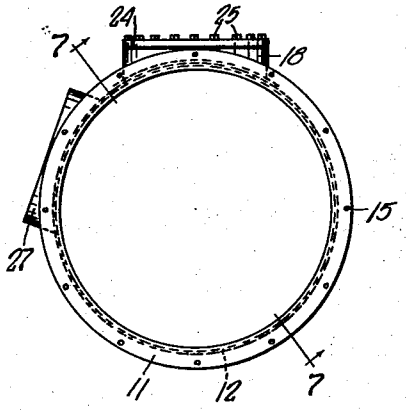


FIG. 7.

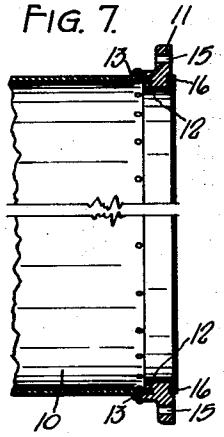


FIG. 8.

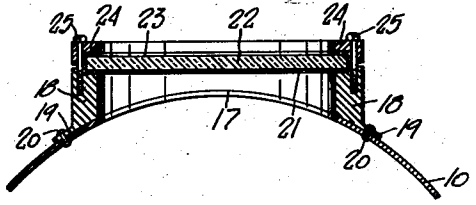


FIG. 9.

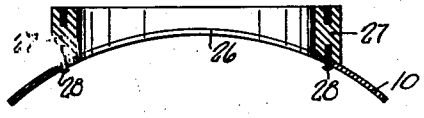
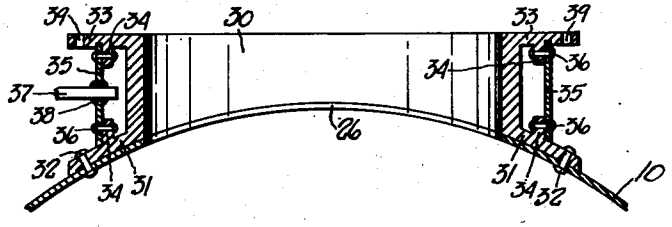


FIG. 10.



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FIG. 11.

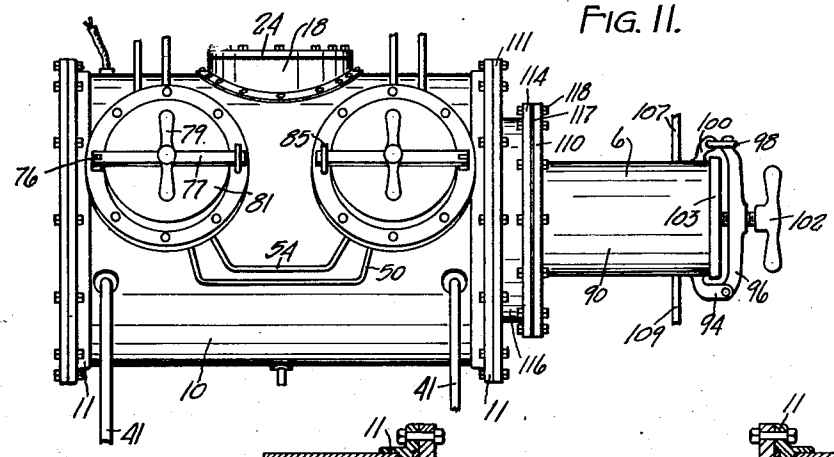


FIG. 12.

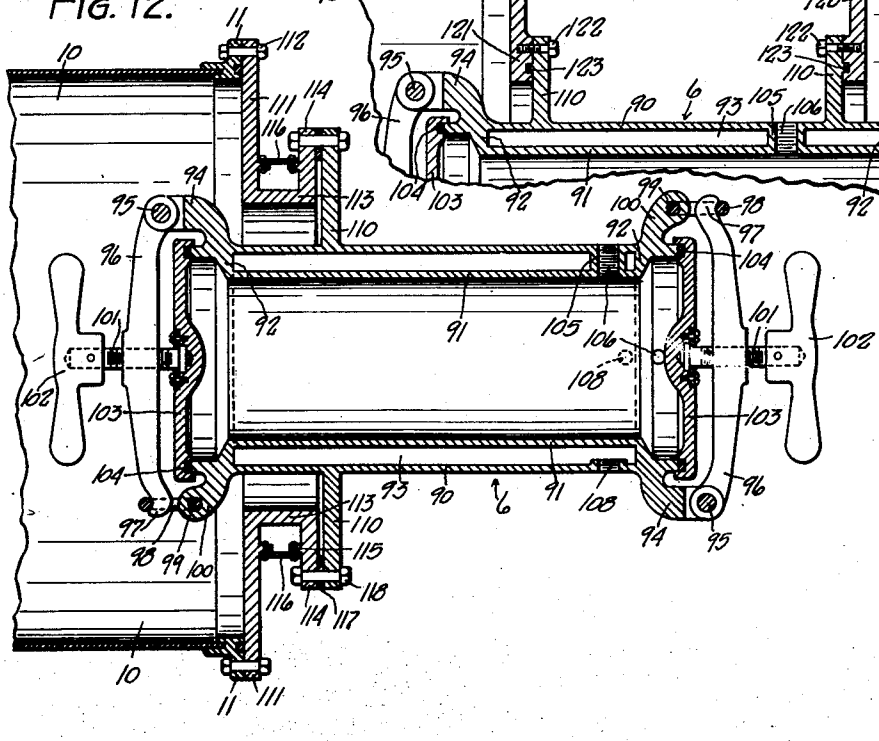


FIG. 13.

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FIG. 14.

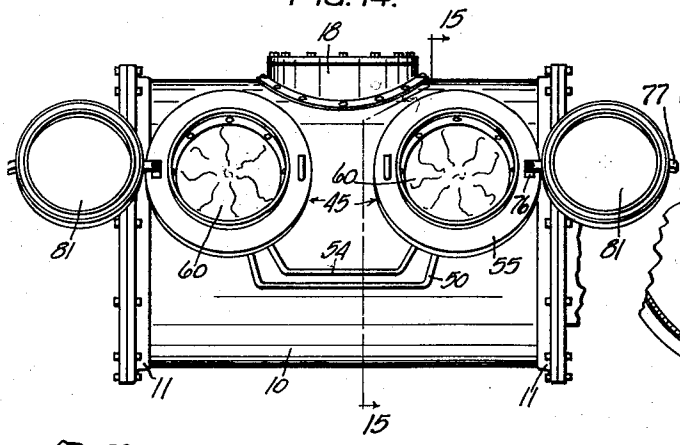


FIG. 15.

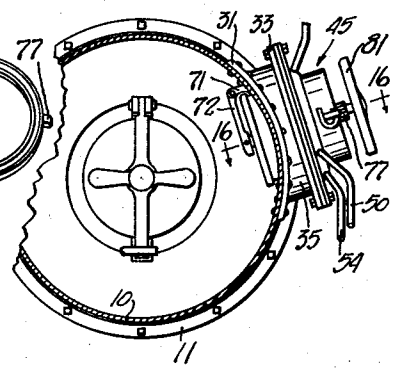


FIG. 16.

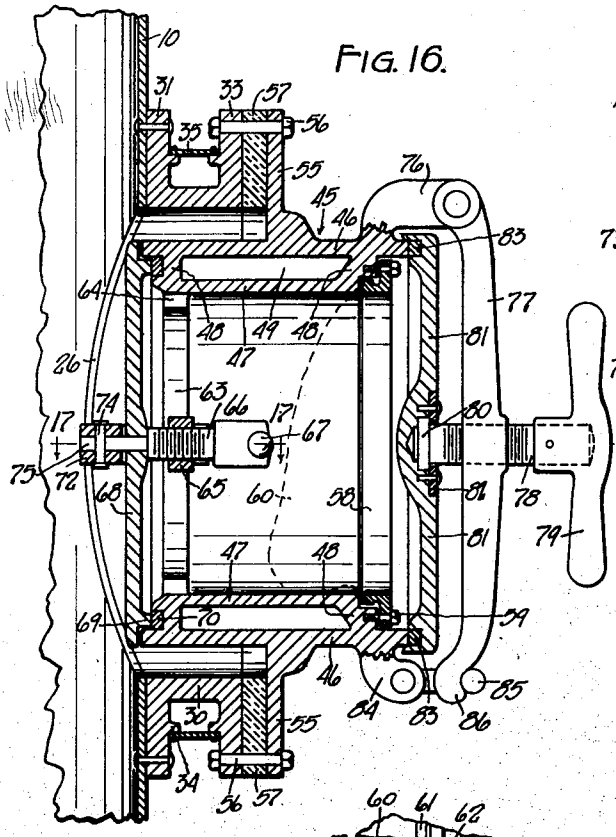


FIG. 17.

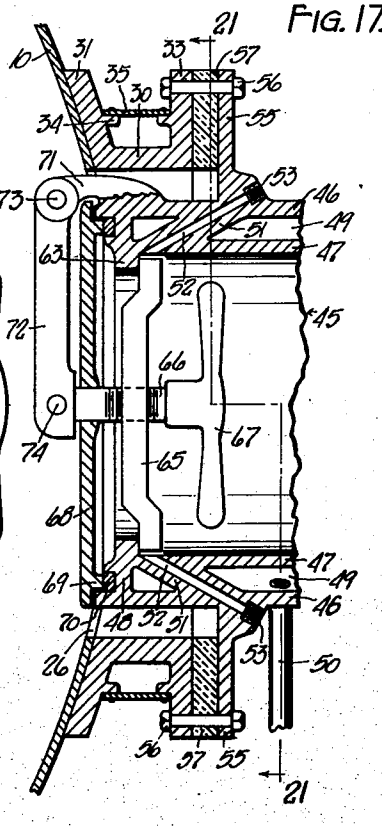
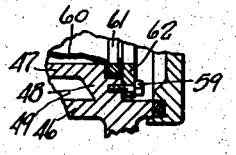


FIG. 18.



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APPARATUS FOR AND METHOD OF MAINTAINING AND WORKING WITH BIOLOGICAL SPECIMENS IN A GERMFREE CONTROLLED ENVIRONMENT

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FIG. 19.

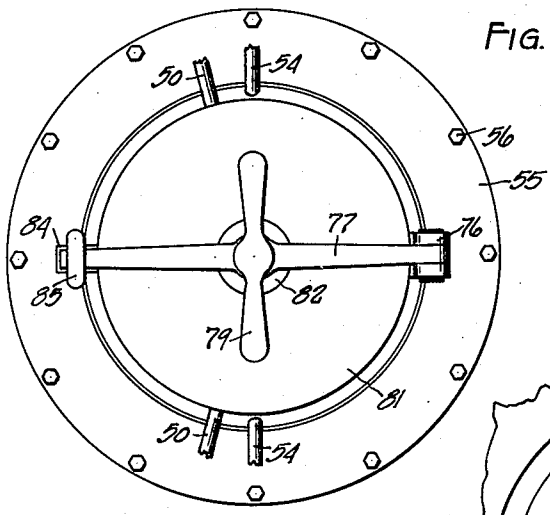


FIG. 20.

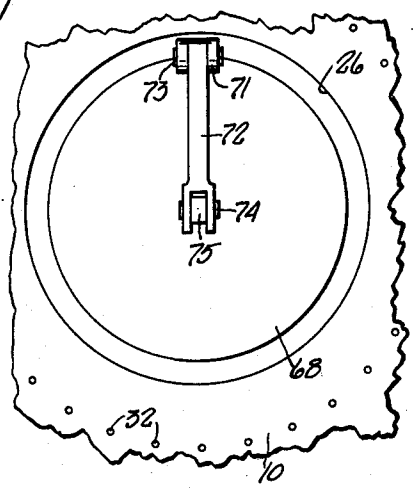
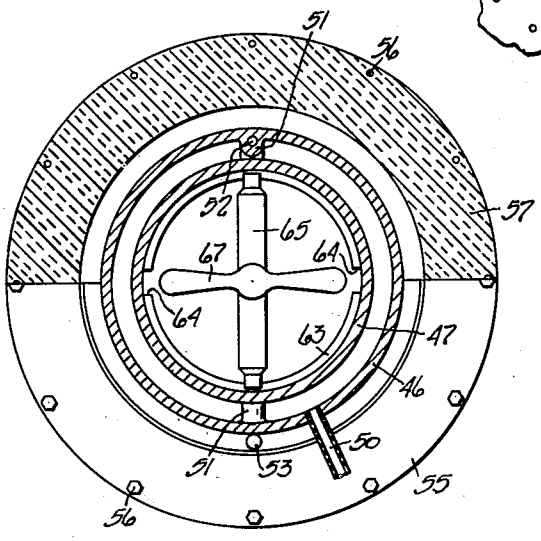


FIG. 21.



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APPARATUS FOR AND METHOD OF MAINTAINING AND WORKING WITH BIOLOGICAL SPECIMENS IN A GERMFREE CONTROLLED ENVIRONMENT

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FIG. 22.

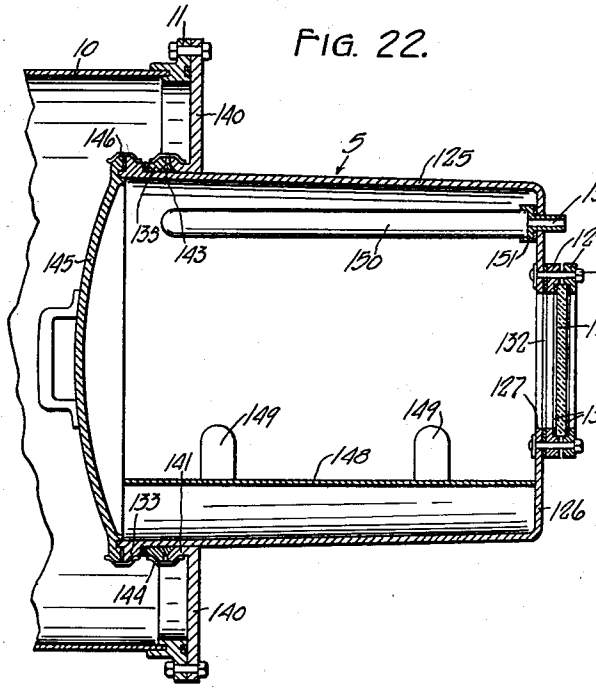


FIG. 25.

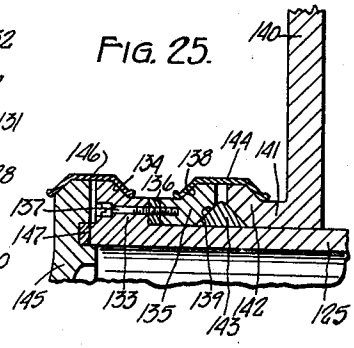


FIG. 23.

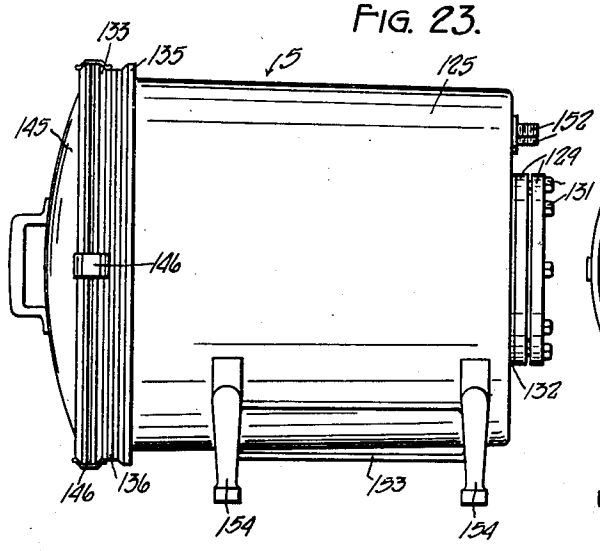
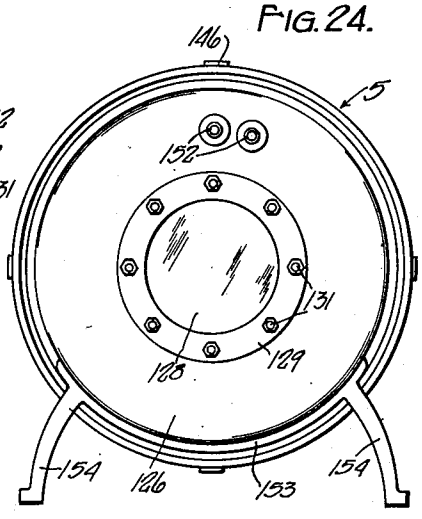


FIG. 24.



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APPARATUS FOR AND METHOD OF MAINTAINING AND WORKING WITH BIOLOGICAL SPECIMENS IN A GERMFREE CONTROLLED ENVIRONMENT

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FIG. 26.

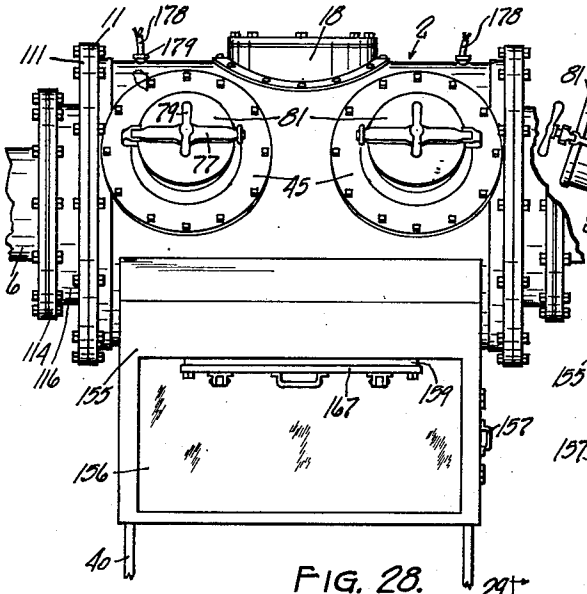


FIG. 27.

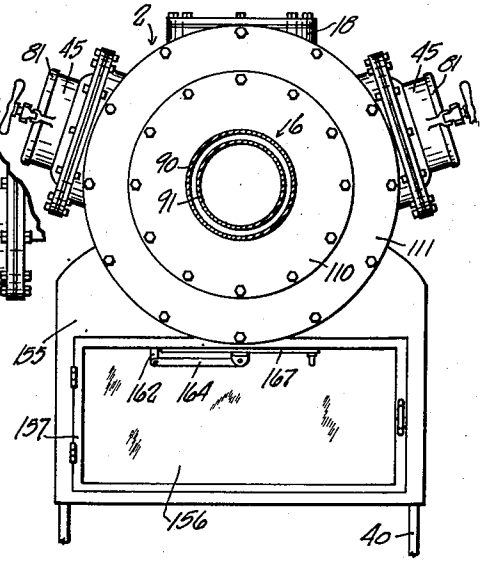


FIG. 28.

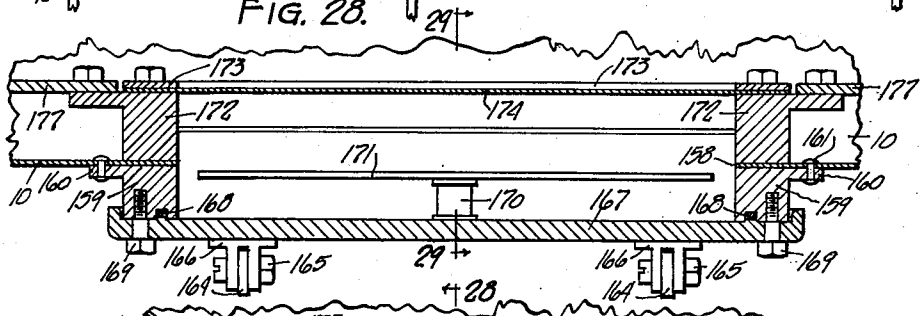


FIG. 29.

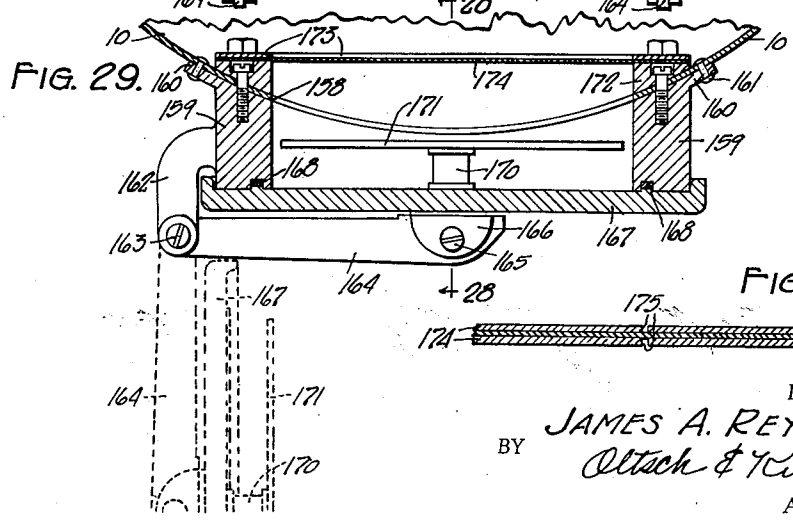


FIG. 30.

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Patented June 3, 1941

2,244,082

UNITED STATES PATENT OFFICE

2,244,082

APPARATUS FOR AND METHOD OF MAINTAINING AND WORKING WITH BIOLOGICAL SPECIMENS IN A GERMFREE CONTROLLED ENVIRONMENT

James A. Reyniers, South Bend, Ind.

Application June 14, 1937, Serial No. 148,102

20 Claims. (Cl. 128—1)

This invention relates to apparatus for, and method of maintaining and working with, biological specimens in a germ-free, controlled environment. More particularly, this invention relates to method and means for operating, examining, raising, maintaining, storing, handling, and breeding animals or plants in a germ-free and controlled environment without risk of contamination.

Various methods and means have heretofore been developed and attempted for the purpose of obtaining, maintaining and working with biological specimens in a germ-free condition and controlled environment for biological and medical research and experimentation; but such have universally been found to be inadequate in various essential respects. The greatest difficulty which has been heretofore experienced with methods and means for this purpose has been the inability to maintain the specimens under the required germ-free and controlled conditions for a length of time adequate to conduct the desired research or experiments; or to permit the preparation, reproduction and growth of the specimen as is necessary for long range tests. Thus, such prior methods and means have failed to provide means for introducing fresh sterilized food and water to the specimens, and to accommodate transfer of the specimens from one container to another while maintaining the required germ-free controlled environment at all times preparatory to, during, and after the transfer. Where the specimens are animals, the need from transfer from time to time to permit cleaning of the cage or other container is obvious, as is also the need for replenishing the food and water supplies and for changing the character of the food as the animal passes through the various phases of a life cycle.

It is, therefore, the primary object of this invention to provide a method and means for maintaining biological specimens in a sterile or germ-free condition and controlled environment for any desired period of time, and to maintain successive generations of animals in such condition and environment.

A further object of this invention is to provide a method and means for working with biological specimens while in a germ-free controlled environment without risk of contamination of the specimens.

A further object is to provide a method and means for transferring biological specimens from one container to another while maintaining its germ-free, non-contaminated condition and the desired controlled environment or atmospheric condition.

A further object is to provide a method and means by which food, water and supplies may be introduced into the apparatus and supplied to the specimen whenever desired or necessary without exposing the specimen to contamination or altering the environment or atmospheric condition in which the specimen is maintained.

A further object is to provide a plurality of containers constructed to accommodate particular phases of the treatment or examination of a specimen and which are readily connectible in hermetically sealed relation, with means for sterilizing a selected container and means for selectively sealing connected containers from each other, said last named means being controllable without danger of contaminating the sterilized containers.

A further object is to provide an apparatus of this character comprising a hermetically sealed, sterilized container, with means for affording access to the interior thereof for manipulation thereof and of the specimens contained therein without contaminating the same.

A further object is to provide an apparatus of this character which may be sterilized while a specimen is contained therein without injuring the specimen.

A further object is to provide a device of this character with novel means for sterilizing the same while desired matter, such as micro-organisms, are contained therein.

A further object is to provide a steam-sterilized apparatus of this character with means for insulating selected connected portions containing specimens against the heat of the steam.

A further object is to provide a sterilized or germ-free apparatus of this character with means for maintaining selected temperature and humidity conditions therein without contamination.

A further object is to provide apparatus of this character by which bacterial and chemical tests, or tests to determine immunology, may be conducted under germ-free conditions.

A further object is to provide apparatus of this character into which material may be inserted, or from which material may be removed, without exposing the specimen contained in the apparatus to contamination.

Other objects will be apparent from the description and the appended claims.

In the drawings:

Fig. 1 is a side view illustrating one arrangement or assembly of the apparatus, and including a raising, an operating and an examining unit interconnected for conjoint use in manipulating and treating the specimen.

Fig. 2 is a side view illustrating another arrangement or assembly of the apparatus, including a raising, a storage and a transfer unit interconnected for conjoint use.

Fig. 3 is a side view illustrating another arrangement embodying two storage units and an interposed transfer unit.

Fig. 4 is an end view of the arrangement illustrated in Fig. 3.

Fig. 5 is a side view of the structure of one of the units.

Fig. 6 is an end view of the structure shown in Fig. 5.

Fig. 7 is a fragmentary longitudinal sectional view taken on line 7—7 of Fig. 6.

Fig. 8 is a fragmentary transverse sectional view taken on line 8—8 of Fig. 5 and illustrating a window construction.

Fig. 9 is a fragmentary transverse sectional view taken on line 9—9 of Fig. 5.

Fig. 10 is a fragmentary transverse sectional view similar to Fig. 9 and illustrating a modified construction provided with a water jacket.

Fig. 11 is a side view illustrating a unit having an access or connecting member in operative relation thereto.

Fig. 12 is a fragmentary vertical longitudinal sectional view of the arrangement illustrated in Fig. 11.

Fig. 13 is a fragmentary longitudinal sectional view illustrating the construction and arrangement of a connector between two units of the device.

Fig. 14 is a side view of one of the units with the outer doors of the glove clave in open position.

Fig. 15 is a transverse sectional view of a unit taken on line 15—15 of Fig. 14.

Fig. 16 is a fragmentary enlarged longitudinal sectional view taken on line 16—16 of Fig. 15 and illustrating the glove clave construction.

Fig. 17 is a fragmentary transverse sectional view taken on line 17—17 of Fig. 16 and illustrating a portion of the glove clave.

Fig. 18 is a fragmentary sectional view of the glove clave illustrating a modified construction of the glove mounting.

Fig. 19 is an end view of the glove clave in closed position.

Fig. 20 is an interior end view of the glove clave.

Fig. 21 is a transverse sectional view of the glove clave taken on line 21—21 of Fig. 17.

Fig. 22 is a fragmentary longitudinal sectional view illustrating a storage unit connected with another unit of the apparatus.

Fig. 23 is a side view of a storage unit mounted on a support and independent of the remainder of the apparatus.

Fig. 24 is an end view of the storage unit and its support.

Fig. 25 is a fragmentary enlarged longitudinal sectional view illustrating the means for interconnecting the storage unit with another unit of the apparatus.

Fig. 26 is a fragmentary front elevation of an operating unit.

Fig. 27 is a fragmentary end view of an operating unit.

Fig. 28 is a fragmentary longitudinal vertical sectional view taken on line 28—28 of Fig. 29.

Fig. 29 is a fragmentary vertical transverse sectional view taken on line 29—29 of Fig. 28.

Fig. 30 is an enlarged fragmentary longitudinal sectional view of the lap cloth of the operating unit.

Referring to the drawings, which illustrate the preferred embodiment of the invention, and particularly to Figs. 1 to 4, the numeral 1 designates a raising unit, 2 an operating unit, 3 an examining unit, 4 a transfer unit, 5 a storage unit, and 6 a connecting or access unit. Each of these units will be more particularly described hereinafter, as will the particular means for interconnecting and manipulating the same for conjoint use as required.

Each of the following: raising unit 1, operating unit 2, examining unit 3, and transfer unit 4, are essentially of the same basic construction, and are all desirably of the same size and especially of the same diameter. The construction of these units is best illustrated in Figs. 5 to 10. Essentially each of these units comprises a sheet metal cylinder 10 whose longitudinal seam (not shown) is suitably sealed, as by welding. To each end of cylinder 10 is secured an end ring 11 (Fig. 7) of generally angle section. Adjacent to the inner portion of the ring 11 in the cylindrical flange thereof is formed an annular groove 12 in which the end of cylinder 10 snugly fits, the outer portion 13 of said grooved flange extending beyond the inner portion thereof, whereby the same may be secured together by rivets 14. The joint between the portion 13 and the cylinder wall may be continuously welded or otherwise treated to form a seal. The radially outwardly projecting flange of the ring is provided with spaced apertures 15. The outer face of ring 11, preferably opposite groove 12, is provided with an annular groove in inwardly spaced relation to apertures 15 to receive an annular gasket 16 of any suitable sealing material, said gasket normally projecting beyond the outer face of ring 11 as illustrated in Fig. 7.

In the center of the cylinder 10 at its uppermost portion is formed an opening 17, preferably substantially circular. A ring 18 whose lower surface conforms to the contour of cylinder 10 at the margin of opening 17, and preferably having an outwardly projecting flange 19 conforming to the cylinder contour, is secured to said cylinder by means of rivets 20 passing through flange 19 and into the cylinder. The joint between ring 18 and cylinder 10 is sealed, as by gaskets or welding. The upper edge of ring 18 is slightly annularly recessed at its inner margin to receive an annular gasket 21. A plurality of spaced longitudinal screw threaded bores are formed in ring 18 at the upper end thereof in outwardly spaced relation to gasket 21. A circular plate 22 of heavy glass which can withstand the application of a high degree of heat and steam such as "Pyrex," is supported at its margin by gasket 21, the diameter of plate 22 being substantially the same as the outer diameter of said gasket. An annular gasket 23 similar to gasket 21 is superimposed on the margin of plate 22. A retaining ring 24 of angle section fits over and around said gasket 23 and plate 22, and is provided with a plurality of apertures registering with the bores in the end of ring 18 to receive bolts 25 which securely fasten ring 24 to ring 18 and compress gaskets 21 and 23 to form a seal. By this construction a posi-

tively sealed sight opening is provided in the cylindrical body of each unit.

One or more pairs of holes 26 are formed in cylinder 10 in complementary relation and adjacent end rings 11. These holes 26 are preferably disposed with their centers approximately 30 degrees above the horizontal center plane of the cylinder, as illustrated in Fig. 6. A ring 27, best illustrated in Fig. 9, having a plane outer edge and an inner edge conforming to the contour of the cylinder is secured to the cylinder at the margin of each hole or opening 26. These rings 27 are preferably provided with spaced longitudinally extending screw threaded bores at their opposite ends. Bolts or screws 28 passing through the cylinder and into the bores at the inner ends of said rings 27 serve to secure the same to the cylinder. Suitable means, such as gasket rings or welded joints, provide the necessary seal between said rings 27 and the cylinder.

In instances where the rings at the openings 26 are to be provided with cooling means, a ring construction as illustrated in Fig. 10 is employed. In this construction a ring 30 of U-section is provided with a lower or inner flange 31 shaped to conform to, and fit in face contact on, cylinder 10. Rivets 32 or other suitable means serve to secure the flange 31 to the cylinder; and suitable means are provided to seal the joint between said flange and cylinder. The upper or outer flange 33 of ring 30 is plane. Annular flanges 34 project from the inner faces of both ring flanges 31 and 33 in opposed relation, and an annular groove is formed in flange 33 with its inner wall forming a continuation of the outer wall of the adjacent flange 34. A strip of sheet metal 35 fits into said groove at its outer or upper edge and engages the outer faces of opposed flanges 34 to which it is secured by rivets 36. The seam of said strip 35 (not shown) is welded or otherwise sealed whereby an annular water chamber is formed at the exterior of ring 30 defined by flanges 31 and 33 and strip 35. One or more holes may be formed in strip 35 to accommodate passage therethrough of the end portions of water tubes 37 which are encircled by suitable gaskets 38 mounted in the openings in strip 35. Suitable spaced apertures 39 are formed in the outer portion of outer flange 33 and radially outwardly spaced from strip 35.

Each cylinder 10 is preferably mounted upon a suitable standard 40 here illustrated as comprising legs 41 secured at their upper ends to the cylinder adjacent the ends and at the under side thereof. These legs are interconnected and reinforced at spaced points by cross bars 42. These standards are of the same height for each of the individual units built upon a cylinder 10.

The openings 26 afford access to the interior of the units whereby the operator of the apparatus may reach into the various units for handling and manipulating the specimen, food, instruments or the like as necessary for the treatment, maintenance, examination or other required technique. For this purpose rubber gloves of a length sufficient to extend from the openings 26 to and preferably beyond the ends of the unit are employed. It is essential that these gloves be so mounted that the surfaces thereof which are exposed to the specimens are absolutely germ-free, and that they are so sealed in their mounting that the use thereof cannot contaminate the apparatus or the specimen. An illustrative form of glove mounting of this character is illustrated in Figs. 14 to 18. In this construction a glove clave 45 is mounted on the water jacketed ring 30, though it will be understood that the same may also be applied to the plain ring 27 illustrated in Fig. 9. The glove clave 45 comprises an outer cylindrical member 46, an inner cylindrical portion 47 spaced from portion 46, and end walls 48 integral with and closing the space between the inner and outer cylindrical portions to provide an annular water jacket 49. The outer end wall 48 is inwardly spaced from the outer end of outer cylindrical portion 46, and is preferably of stepped outer formation best illustrated in Figs. 16 and 18, for purposes to be hereinafter set forth. The ends of suitable water supply and discharge conduits 50 may be threaded in the outer portion 46 to circulate water in water jacket 49. Walls 51 integral with, and spanning the space between, inner and outer portions 46, 47 are provided in the clave and preferably extend diagonally relative to the clave axis. These walls 51 each have a passage 52 extending longitudinally therethrough for communication with the clave interior, and terminate at their outer ends in enlarged threaded portions 53 for connection with steam lines 54. A flange 55 projects radially outwardly from the clave intermediate its ends and is connected by suitable bolts 56 to flange 33 of ring 30, said bolts passing through suitable apertures in flange 55 in registration with apertures 39 in flange 33. An annular gasket 57 is preferably interposed between flanges 33 and 55. The outer diameter of clave 45 is preferably sufficiently less than the inner diameter of ring 30 to facilitate easy assembly of the parts.

The stepped form of the outer end wall 48 accommodates a ring 58 of angle section secured thereto adjacent its outer margin by bolts 59 threaded into suitable tapped bores in said wall 58. The outer end of a glove 60, preferably formed of rubber, fits between said end wall 48 and ring 58 to be locked to place thereby when said ring is tightly applied, said glove at the same time serving to form a seal when tightly pressed between said ring and wall to prevent access of air or dirt into the interior of the clave. In Fig. 18 is illustrated a modified form of glove mounting wherein the outer end of glove 60 is fitted around a ring 61 seated in an annular inner marginal recess in end wall 48 and pressed tightly against said end wall in sealing relation by a flat ring 62 secured by suitable bolts 59 to wall 48 in the manner previously described.

An annular flange 63 projects interiorly from inner clave wall 47 at the inner end of the glove clave, and is provided with a pair of opposed cut-away portions 64. Against this projecting flange 63 the ends of a cross bar 65 are adapted to bear. Bar 65 has a central threaded aperture through which extends a threaded shaft 66 mounting an operating handle 67 at its outer end. Shaft 66 is journaled in the center of an inner closure plate 68 having an annular rib 69 projecting therefrom and adapted to seat against an annular gasket 70 mounted in a suitable groove in the inner end wall 48. An arm 71 is integrally formed with the outer clave wall adjacent its inner end and projects inwardly therefrom. To the end of arm 71 a link 72 is pivoted at 73, the other end of said link being pivoted at 74 to part 75 projecting from plate 68 and accommodating rotation of the shaft 66 with which it is connected. It will be seen that, when the ends of bar 65 bear against flange 63 and handle 67 is rotated to cause shaft 66 to draw closure plate 68 toward said bar, the rib 69 will seat firmly against gasket 70 to seal the interior of cylinder 10 from said clave 45. To open the closure plate, shaft 66 is

rotated to loosen the engagement of bar 65 with flange 63 and permit said bar to be turned on said shaft into registry with cut-outs 64 to thereby release the plate for swinging movement on link 72.

An arm 76 is formed integrally with and projects forwardly beyond the end of outer clave wall 46, and this arm pivotally mounts at its outer end a bar 77 extending diametrically across the outer end of the clave. Bar 77 is provided with a central threaded aperture in which a threaded shaft 78 is mounted. The outer end of shaft 78 carries a handle 79, and a head 80 is formed at its inner end. Head 80 fits in a recess formed centrally in the outer face of a closure plate 81, and a retaining plate 82 secured to plate 81 and encircling shaft 78 serves to connect said shaft and plate. An annular groove is formed in the inner face of plate 81 adjacent its margin, and receives a gasket 83 which is adapted to bear against the outer edge of the outer cylinder 46 of the clave. Opposite arm 76 is provided a projecting lug 84 to which is pivoted a link 85 against which a hook portion 86 on the end of bar 77 is adapted to bear. It will be seen that when hook 86 engages link 85 and shaft 78 is rotated to urge bar 77 outwardly, the closure plate is inwardly urged to tightly seal the outer end of the clave 45, and a reverse rotation of said shaft will permit disengagement of hook 86 from link 85 to permit pivoting of said closure plate 81 to open position.

In the manipulation, treatment and maintenance of the specimen it is necessary that means be provided for the purpose of transferring the specimen from one chamber or unit to another while maintaining the specimen in a germ-free controlled environment at all times. The construction by which this purpose is achieved is best illustrated in Figs. 11 to 13, and involves the use of the connecting or access member 6. As here shown, member 6 is provided with an outer cylindrical wall 90, an inwardly spaced concentric cylindrical wall 91, and integral annular end walls 92 interconnecting said cylindrical walls and providing a closed annular water chamber 93 between the cylindrical walls. The outer wall 90 preferably projects beyond the end wall 92 at each end of the device. Arms 94 project from the member 6 at each end thereof, and to the ends of these arms are pivoted at 95 the cross bars 96. The opposed ends of bars 96 are provided with hooked end portions 97 which are adapted to be held by links 98 pivoted at 99 to ears 100 projecting from the member 6 in opposed relation to the complementary arm 94. Each bar 96 is provided with a threaded opening through its center for the reception of a threaded shaft 101 mounting a handle 102 at its outer end and connected to a closure plate 103 at its inner end for rotation relative to said closure plate. The closure plate 103 is provided with an annular recess in its inner face which mounts an annular gasket 104 adapted to be pressed against the edge of the projecting end of outer wall 90. A plurality of plugs 105 are formed integrally with and extend between the inner and outer walls 90 and 91 and have threaded passages 106 therethrough for connection with conduits 107 which form a steam supply system. Threaded apertures 108 are formed in the outer wall 90 for connection with conduits 109 which form a water circulating system.

Each of the connectors 6 is provided with one or two radially outwardly projecting flanges 110 adjacent its ends, for connection with the adjacent unit or units of the apparatus. One form of connection between unit 6 and the adjacent units is shown in Fig. 12 wherein an adapter ring 111 is connected by bolts 112 to end ring 11 of the adjacent unit and projects radially inwardly therefrom. A cylindrical flange portion 113 integral with ring 111 at its inner margin and preferably outwardly spaced from outer wall 90 of the connector, carries a radially outwardly projecting flange 114 spaced from and parallel to ring 111. The adapter is thus of channel section, and is provided with opposed annular flanges 115 on the adjacent faces of portions 111 and 114. A strip of sheet metal 116 is tightly secured at its margins to said flanges 115 to form an annular water jacket. An annular gasket 117 is interposed between adapter flange 114 and connector flange 110, and securing members 118 connect said flanges. In practice, the adapter rings 111, 114 are connected in operative relation to the connector unit 6 before the same is secured to the adjacent unit and its end ring 11, for convenience in handling and assembly.

A modified construction for mounting unit 6 is illustrated in Fig. 13, wherein a plane adapter ring 120 is connected to end ring 11 of the adjacent unit to which unit 6 is to be connected. In this form, the inner marginal portion 121 of the adapter is preferably of greater thickness to permit the formation therein of tapped bores which extend only partially therethrough, and which receive the inner ends of bolts 122 passing through flange 110 of the connector 6 to secure the adapter to the connector unit. In radially inwardly spaced relation to said bolt holes the adapter ring 120 is provided with an annular groove in its outer face to receive an annular gasket 123 against which flange 110 seats to form a positive seal between rings 110 and 120.

It will be seen from the above that the units are so arranged that specimens may be readily passed from one to another thereof, the whole apparatus being positively and hermetically sealed to maintain the desired germ-free or controlled environment therein during the transfer. Likewise, when necessary or desirable, each of the connected units may be positively sealed from the remaining units of the assembled apparatus, as when a specimen is contained in one unit and food, equipment or other material is to be introduced into the apparatus and then steam sterilized before exposure of the specimen thereto. It will, of course, be understood that the provision of the sealed glove claves in the various units, as heretofore described, is incorporated in the various large interconnected units to permit opening and closing of the various closures between the units and to permit transfer of the specimens, food, etc. from one to another of the connected units.

The storage units 5 afford means by which one or more specimens may be maintained in the desired controlled environment while the remainder of the apparatus is being independently used for the treatment, maintenance, etc. of other specimens. In other words, the storage units 5 may be employed to store individual or groups of specimens while the remainder of the apparatus is used for treating and manipulating the specimens. An illustrative construction of the storage chamber is best illustrated in Figs. 22 to 25 wherein chamber 5 comprises a slightly tapered circular wall 125 and an integral annular end wall portion 126 providing a central circular open-

ing 127 at the small end of the chamber. Opening 127 is provided with a sealed window construction wherein a plate 128 of heat resisting transparent material is held between opposed complementary rings 129 of angle section which mount gasket rings 130 to effect a seal between the same and plate 123. Rings 129 are drawn tightly together and connected to the wall 126 by securing members 131 radially outwardly spaced from transparent plate 128, a gasket ring 132 being interposed between the inner ring 129 and said wall, with said securing members preferably passing therethrough.

At the opposite or large end of the unit, the wall 125 is provided with an integral outwardly projecting circumferential flange 133 preferably spaced slightly from the edge of said wall. The outer periphery of said flange preferably includes a tapered portion 134 best illustrated in Fig. 25. A ring 135 fits closely around wall 125 adjacent flange 133, a gasket ring 136 being interposed between said ring and flange, and a plurality of longitudinally extending securing bolts 137 connecting said ring and flange and drawing ring 135 tight against said gasket. Ring 135 is provided with a tapered portion 138 in its outer periphery in opposed relation to portion 134 of flange 133, and is also provided with a portion of its inner periphery tapered at 139 in complementary or parallel relation to outer tapered portion 138.

For the purpose of connecting the storage unit 5 to one of the other units of the apparatus, an adapter ring 140 is secured to the end ring 11 of said unit. Ring 140 is provided with a substantially cylindrical inner marginal flange 141 adapted to fit closely on wall 125, and said flange terminates in an outwardly tapering flange portion 142. A gasket ring 143 is interposed between flange 142 and ring 135 to be pressed against the wall 125 by the inner face of flange 142 and the tapered inner face 139 of said ring and thereby effect a seal between unit 5 and adapter ring 140. Suitable securing means, such as clips 144 bearing upon the opposed tapered outer faces of flange 142 and ring 135 serve to hold said parts together and tight against jacket 143 to effect the necessary seal.

The unit 5 is provided with a closure plate 145 at its open enlarged end, the periphery of said plate including a portion tapered in opposed relation to face 134 of flange 133 whereby a plurality of securing members 146 similar to members 144 may be applied thereto to hold said closure plate in sealed relation on said unit. A seal is effected between wall 125 and plate 145 by providing an annular groove in the inner face of said plate, which groove mounts a gasket 147 if desired and into which the free forward edge of wall 125 closely fits.

Unit 5 is provided with a suitable flat supporting plate 148 at its lower side to support the specimen, and brackets 149 are associated therewith to mount suitable receptacles (not shown) for holding food and water for the specimen. Adjacent the upper end of the unit is provided an air filter 150 mounted on a suitable holder 151 having nipples 152 for connection with conduits (not shown) for controlling the circulation of air, thus affording means for controlling the temperature and humidity of the air supplied to the unit. It will be seen that, after a specimen has been transferred into unit 5, a supply of food and water provided therein, and the closure plate 145 applied in sealed relation thereto, the storage unit 5 may be removed from the apparatus. To achieve this purpose the adapter 140 is removed from the adjacent unit to disconnect the units, and securing members 144 are then released to permit separation of the adapter from the storage unit. A suitable support may be provided to hold the storage unit independently of the remainder of the apparatus, said support comprising a frame 153 including arcuate cross pieces, and legs 154 mounting said frame. The air filter 150 permits disconnection of the storage chamber from a controlled air supplied source during the time the unit 5 is being manipulated and transferred to and from the apparatus and a storage place having a separate air connection, if such is desired.

Where the specimens to be treated and maintained in the apparatus are animals, such as guinea pigs, it is essential that the same be in a germ-free, non-contaminated condition when inserted in the apparatus. For this purpose, I employ an operating unit 2 best illustrated in Figs. 26 to 30. This unit is provided with ring 18 at its upper center for mounting the transparent plate 22 as illustrated in Fig. 8; and preferably with two pairs of glove claves 45, as illustrated in Fig. 16, on opposite sides of the body or cylinder 10 to permit two operators to work together. The unit is supported upon the usual supporting structure 40, but the upper portion of said structure is preferably enclosed to form a trap. The trap is formed by side and end walls 155 which extend around the frame and fit tightly, and preferably in sealed relation, to the cylinder 10 at their upper edges. A bottom with openings through which the legs 41 extend in a tight sealed fit completes the trap. Panels 156 formed of transparent material are mounted in the side and end walls, and an access door 157 is provided in one of the walls.

An opening 158 is formed in the center of cylinder 10 at the lowermost portion thereof, said opening preferably being of rectangular projected outline. A frame 159 having an upper marginal flange 160 fits tightly in face engagement with the outer surface of cylinder 10 at the margin of opening 158, said frame being secured to said cylinder by securing members 161 and preferably sealed at said joint. A pair of integral depending arms 162 project from frame 159 at one side thereof and extend downwardly below said frame. To the lower ends of these arms 162 are pivoted at 163 links 164 which are connected at 165 to brackets 166 mounted on a closure plate 167. A groove extends around frame 159 at its lower edge and mounts a gasket 168 against which the margin of said closure plate bears. Suitable securing means, such as bolts 169 passing through the plate 167 outwardly of gasket 168 and threaded into frame 159 serve to connect said plate in sealing relation to said frame. A pedestal or support 170 is carried centrally by the upper face of plate 167, and mounts an operating plate 171. An inner frame 172 fits tightly against and is secured to marginal position of cylinder 10 around opening 158. A lap cloth is carried by inner frame 172 and extends across the opening 158 in cylinder 10. The lap cloth is clamped to place at its margin in sealed relation by a rectangular frame 173. The lap cloth is best illustrated in Fig. 30, and comprises two thicknesses of cloth or other suitable flexible material 174 which are provided with registering central slits 175; and between these cloth layers is interposed a sheet 176 of suitable material,

such as "Cellophane" which can withstand application of steam to maintain a seal, and which is normally imperforate. The inner frame 172 also serves as a support to which suitable plates 177 may be secured in substantially flush relation to the lap cloth. Electrical leads 178 pass through the upper portion of cylinder 10, the cylinder aperture therefor preferably mounting suitable fittings 179 through which said leads extend to insure a sealed relation of the cylinder at the point of entry of said leads therein.

The raising unit 1 and transfer unit 4 are each of substantially the construction heretofore described as built around cylinder 10 as a body and provided with standards 40, sealed sight openings, sealed glove claves and other features as hereinbefore described. The transfer unit 4 being employed merely to facilitate transfer of the specimens from one to another of the other units, usually contains no additional equipment.

The raising unit 1, examining unit 3 and such other units as may be required are of the same general construction above described, with the exception that they may be provided with suitable equipment, such as electric leads 180 for lighting and other purposes, and in the event of the examining unit 3, with a microscope 181 mounted in sealed relation to the cylindrical body of the unit and with a grinding or pulverizing machine 182 mounted on a suitable support 183 on the unit and having its operating portion (not shown) extending into the cylindrical body with a sealed connection.

The method of use of the apparatus is as follows: Assuming that it is desired to initiate use of the apparatus for animals, such as guinea pigs, selected units will be interconnected and sterilized. Thus an operating cage 2, and a raising cage 1, may be interconnected by a connecting unit 6, the same constituting a hermetically sealed assembly which can be sterilized by the introduction of steam and then cooled to desired temperature by the water jacket as above described. A pregnant animal, preferably denuded of hair and bathed in an antiseptic solution to insure germ-free condition as far as external or skin conditions are concerned, is placed in the trap of the operating unit through door 157. The animal is then held on operating table 171 in desired position while closure 167 is raised and locked in operative position. The lap cloth 174—176 forms a primary hermetic seal between the cylindrical body of the operating unit and the trap while the animal is being placed on the operating table, and thereafter, upon locking of closure plate 167 in place, said plate forms a secondary hermetic seal. It will be understood, of course, that the trap of the operating unit is cleaned, as by an antiseptic solution, preparatory to placing of the animal therein. When the animal is in proper position and closure 167 is sealed, the intermediate layer 176 of the lap cloth may be slit complementary to slits 175 in outer layers 174 whereby access may be had to the animal. A Caesarian operation may then be performed on the animal to remove the young, as by use of an electric cauter or knife, precautions being taken during the operation as by antiseptic treatment of exposed organs of the animal, to prevent entry of germs into the unit. The newly born animals may then be removed through access or connecting unit 6 to raising chamber 1 containing the necessary equipment for handling, treating and feeding the young after birth.

The closures 103 (Fig. 12) of connecting unit 6 may be sealed after the young are in the raising cage 1, so that operating cage 2 may be disconnected therefrom if desired.

It will be understood that each of the raising and operating units contains the sight opening construction illustrated in Fig. 8 by means of which the operator may see the animal and all other contents of said units during these operations. Likewise it will be understood that these units are provided with the glove clave construction illustrated in Figs. 14 to 18, so that the operator may, by inserting his hands and arms into the rubber gloves 60, reach into the respective units to handle the animals, the necessary instruments, food and the like, without breaking or destroying the hermetically sealed germ-free interior condition of these units. The rubber gloves are flexible, and of a length sufficient to permit the operator to also reach into the connecting unit 6, as to pass the animals therethrough from one primary unit to another and to operate the handles 102 controlling the closures 103 of said connecting unit.

Assuming now that the animal has reached a stage where it can feed itself, and it is desired to transfer the same to a storage unit 5, a hookup as illustrated in Fig. 2 may be made, wherein there are connected to the assembly of raising unit 1 and connecting unit 6, a transfer unit 4 at the end of connecting unit 6, and a storage unit 5 at the end of said transfer unit. During the time the connection of these additional units is mechanically effected by the use of the interconnecting members illustrated in Figs. 13 and 22, at least one of the closures 103 of the connecting unit 6 is maintained in sealed relation. After the mechanical interconnection of the units is effected, steam or other sterilizing media, as antiseptic solution, is used to thoroughly sterilize the newly connected units. When this sterilizing operation is completed, the closures 103 of connecting unit 6 may be opened and the animal passed successively through said connecting unit 6, transfer unit 4, and into storage unit 5. It will be understood that the food and water supply is inserted in the storage chamber 5 before sterilization thereof where steam is the sterilizing medium, so that the same is subjected to the sterilizing action and is insured to be in germ-free condition. After the animal is inserted in storage unit 5, the closure 145 thereof may be applied to seal the same from the remainder of the connected apparatus, whereupon the parts or units may be disconnected for storage of unit 5 in a suitable place having connections for air filter 150. During such storage time the unit 5 may be supported on standard 153—154 (Fig. 24).

It will be seen that the animals can be held in any one storage unit 5 for only a limited period of time, as determined by food and water supply or other conditions, and that the animals must, therefore, be transferred to another storage unit from time to time. For this purpose an assembly as illustrated in Fig. 3 may be employed, comprising a transfer unit 4 mounting storage units 5 at each end thereof. The unit 5 which contains the animal will be maintained in sealed condition while the assembly of parts is effected, and while the empty units are being sterilized. Thereafter the units may be opened into communication by the use of the glove claves to open the respective closures and then handle the animal, as to transfer it to the freshly conditioned storage unit.

It will be obvious from the above that the various units may be assembled in any desired groups or systems to permit transfer of the animals from one to another unit, as from storage to examining cage, without at any time exposing the animal or other specimen to atmosphere or to any contaminating influence. Likewise, the specimen may be maintained in the desired germ-free condition for any desired period of time which may range from a short time to a full life span or even to successive generations. In the latter connection, it will be obvious that where the specimens are animals, they may be brought together for breeding purposes or the like, in which event the new generation may be born in the natural way without necessity for resort to the Caesarian operation technique employing operating unit 2, as heretofore described.

It will be seen that the use of the air filters and air connections 185 permit control of air conditions, such as humidity, which may be of particular value in the event the specimens are plants. Likewise, temperature conditions may be controlled, either through the medium of the water jackets described, with their lines 50, 109, 37, 186, 187 or by heating one or more of the units by external means.

It will be further understood that, while the units may be sterilized by filling with an antiseptic solution and then draining said solution at 184 without admitting air other than by the air-filters, this method is limited by practical considerations to but a few applications because of the advantages of the sterilization by steam. One use of antiseptic sterilization is where it is desired to introduce some particular living material into the system for test of its effect on the specimen uninfluenced by other or foreign matter. Thus it may be desired to introduce a particular kind of micro-organism into the system, in which event the same is sealed in a container, introduced into the desired unit for sterilization, the unit then be sterilized by introduction of the antiseptic solution, and the container of the micro-organisms opened only after the sterilizing operation. It will be obvious that most micro-organisms would be destroyed or killed by the high heat of steam, whereas the use of an antiseptic solution in the above manner will not so destroy the same.

I claim:

1. Apparatus of the character described, comprising a plurality of independent chambers, means interconnecting said chambers in sealed relation to form a sealed assembly, removable closure means interposed between said chambers and controlled by an operator from the exterior of said assembly, and means for sterilizing selected chambers while said assembly is sealed, said closure means being releasable to establish communication between said chambers without exposing the interior of any chamber to atmosphere.

2. Apparatus of the character described, comprising a pair of independent hermetically sealed chambers, a chambered member connecting said chambers, a closure at each end of said member for sealing said member from said chambers, means for selectively supplying steam to said member and chambers and sealed members in each chamber permitting manual access to said closures without destroying the sealed condition of the apparatus.

3. Apparatus of the character described, comprising a plurality of independent chambers, means for connecting said chambers to provide an air-tight joint therebetween, a removable closure between said chambers, and flexible means carried by one chamber for affording access to the interior of said chamber and to said connecting means and closure whereby said closure may be operated interiorly of said chamber, said means having an air-tight seal with said chamber.

4. Apparatus of the character described comprising a sealed chamber having an opening therein, means for affording access to said chamber comprising an imperforate flexible member mounted in sealed relation at the periphery of said opening, said member being formed of material impenetrable by air and a removable closure for said opening disposed interiorly with respect to said access means.

5. Apparatus of the character described, comprising a container, having a pair of openings therein, a sealing closure for one of said openings, closure locking means within said container, a glove of material impervious to air mounted in the other opening in sealing relation at its perimeter, said glove being of a length sufficient to reach to said closure locking means.

6. Apparatus of the character described, comprising a pair of storage chambers, and a transfer chamber having an opening, elongated flexible means sealed at said opening and affording access to the interior of said chambers, means for interconnecting said chambers in a sealed assembly, and sealing closures for the inner ends of said storage chambers and accessible through said elongated flexible means for release to open said chambers into communication.

7. Apparatus of the character described comprising a plurality of chambers, means for interconnecting said chambers in sealed relation, means for opening said chambers into communication, at least one of said chambers having an opening therein, and a glove secured at its open end to the periphery of said opening, said glove being formed of material impenetrable by air and being of a length sufficient to extend into connected chambers.

8. The combination with a chamber having an opening therein, of a glove secured at its open end to the periphery of said opening, a closure for said opening disposed inwardly of said glove, and means for releasably locking said closure.

9. In combination a chamber having an opening therein, a closure for said opening, means for locking said closure, a glove, and means for clamping the edge of said glove at the perimeter of said opening in sealed relation exteriorly of said closure.

10. In combination a chamber having an opening, an open ended member mounted in said opening in sealed relation, a closure at the inner end of said member, and a glove secured at its open end to the periphery of member in outwardly spaced relation to said closure.

11. In combination, a chamber having an opening, an open ended member mounted on said chamber at said opening, a closure for the inner end of said member, means within said member for operating said closure, a glove formed of air-impervious material sealed at its open end to the periphery of said member outwardly of said closure operating means, and a closure at the outer end of said member.

12. In combination, a chamber having an opening therein, an adapter ring secured to said

chamber at the margin of said opening, an open ended member having a sealed perimetral joint with said adapter, a closure for the inner end of said member, and a glove secured at its open end to the inner periphery of said member.

13. In combination, a chamber having an opening therein, an open ended member having a sealed perimetral connection with said chamber at said opening, a releasable closure at the inner end of said member, a glove having a sealed perimetral connection with said member in outwardly spaced relation to said closure, and means for supplying steam to said member intermediate said closure and glove.

14. In combination, a chamber adapted to house a biological specimen and having an opening therein, an open ended water jacketed member having a sealed perimetral connection with said chamber at said opening, a releasable closure at the inner end of said member, a flexible glove sealing the outer end of said member, and means for supplying steam to said member intermediate said glove and closure, said water jacket minimizing heat transfer to said chamber upon steam supply to said member alone.

15. In combination, a chamber adapted to house living matter and having an opening therein, an endless water jacketed member secured to the chamber at the margin of said opening, an open ended water jacketed member having a sealed perimetral connection with said endless member, releasable closures for the ends of said member, and means for supplying steam to said last named member, said water jackets minimizing heat transfer to said chamber when said last named member is supplied with steam and separated from said chamber.

16. In apparatus of the character described, a transfer unit comprising an open ended housing, a releasable closure at each end of said housing, locking means for each closure, and a perimetral flange projecting exteriorly from said housing adjacent one end and spaced from the closure therefor adapted for connection with an open ended support through whose open said housing projects.

17. In biological apparatus, the combination with a chamber having an opening therein, a housing smaller than said chamber projecting through said opening, releasable means forming a sealed connection between said chamber and an intermediate portion of said housing, a closure for each end of said housing, and means within said chamber for operating the inner closure.

18. In biological apparatus, the combination with a chamber having spaced openings, of a glove formed of material impervious to air, means for mounting said glove to seal one of said openings, an open ended housing projecting through the other chamber opening, means forming a sealed joint between said chamber and housing, and a releasable closure at each end of said housing, said glove being of a length to reach said inner closure.

19. The construction defined in claim 18, and means for supplying steam to said housing, said inner closure being releasable to permit steam sterilizing of said chamber.

20. In biological apparatus, a pair of communicating chambers, one of said chambers having an opening, a rubber glove sealing said opening and affording access to the interior of said chamber, a releasable closure for the inner end of the other chamber within reach of said glove, an exteriorly accessible releasable closure for said last named chamber, and means in said last named chamber for sterilizing any material desired to be inserted in said first named chamber.

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The above entitled patent was extended January 8, 1952, under the provisions of the act of June 30, 1950, for 2 years and 328 days from the expiration of the original term thereof.

Commissioner of Patents.