

- [54] **ROTATING FLASK CULTURE APPARATUS**
[75] Inventor: **Robert P. Adams**, Walden, N.Y.
[73] Assignee: **Cenco Medical Health Supply Corporation**, Chicago, Ill.
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[51] Int. Cl.**C12b 1/00**
[58] Field of Search**195/127, 139, 143; 259/57, 259/81**

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Primary Examiner—Alvin E. Tanenholtz
Assistant Examiner—R. B. Penland
Attorney—Robert E. Wagner

[57] **ABSTRACT**
An apparatus for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens which supports flasks in which such cultures are grown at their neck and bottom only so that such flasks are suspended above the base of the apparatus along the culture growing surface. An apparatus which rotates these flasks with respect to these two points of support by drive wheel means engaging the bottom of the flasks. A culture flask apparatus having releasable spring means exerting a force along the central axis of the stopper disposed in the mouth of the flask which forces the flask toward the drive wheel means at its bottom and having a surface supporting the flask stopper in bearing which prevents the flask stopper from rotating with the flask.

18 Claims, 6 Drawing Figures

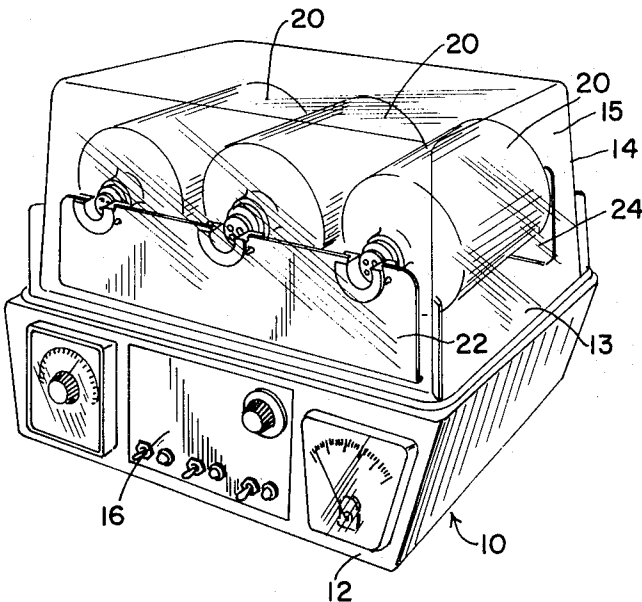


FIG. 1

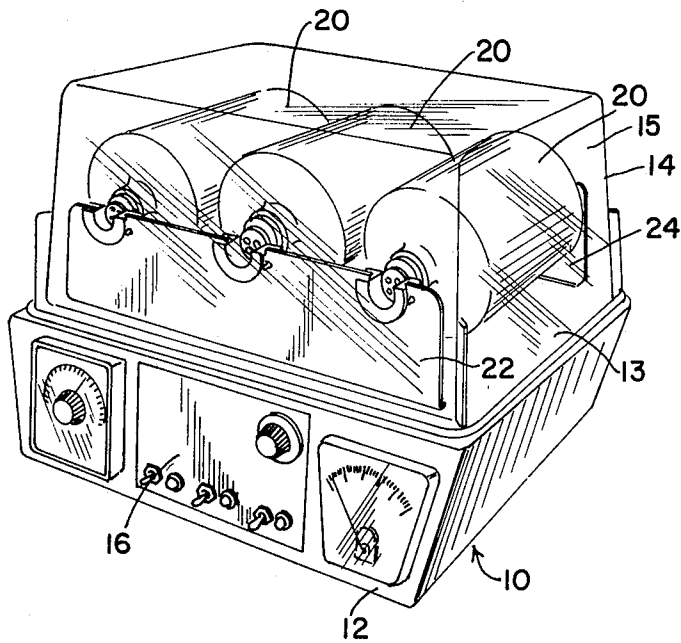


FIG. 4

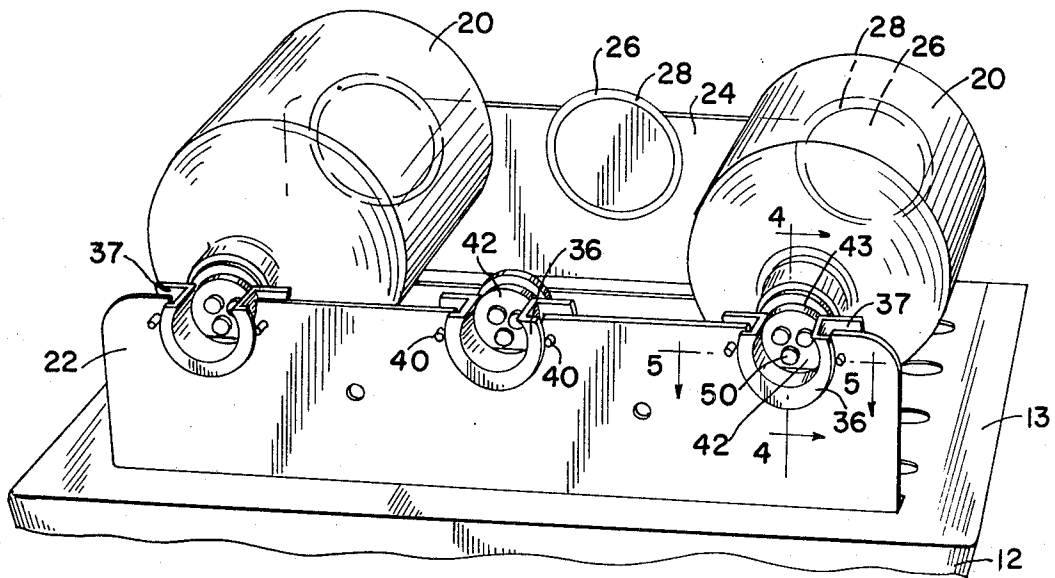
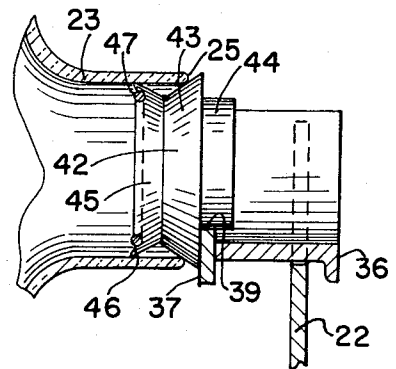


FIG. 2

INVENTOR

ROBERT P. ADAMS

BY

Robert E. Wagner

ATT'Y

FIG. 3.

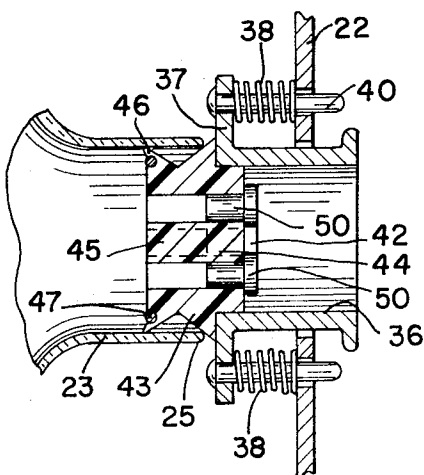
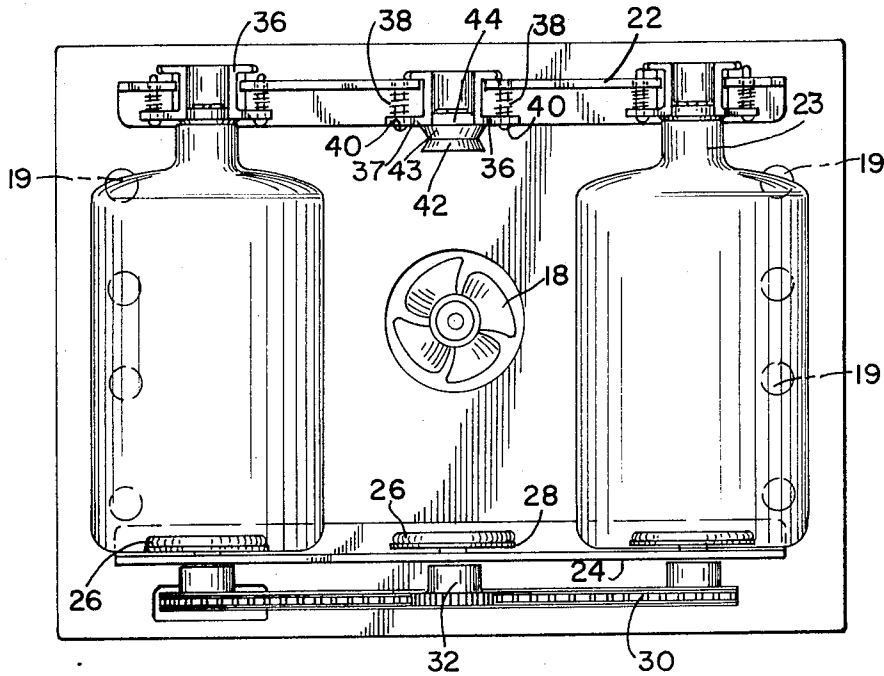


FIG. 5.

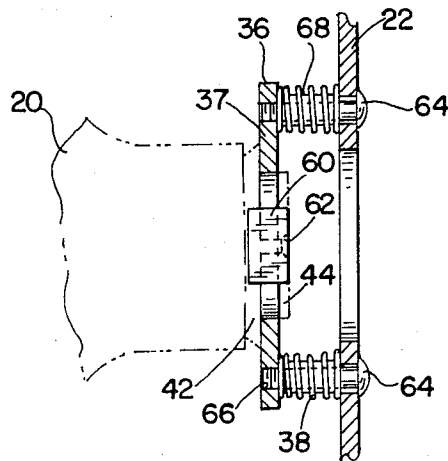


FIG. 6.

INVENTOR

ROBERT P. ADAMS

BY

Robert C. Wagner

ATT'Y

ROTATING FLASK CULTURE APPARATUS

BACKGROUND OF THE INVENTION

This invention relates to apparatus for the cultivation and investigation of cell, virus, vaccine, hormone and antigen growth on the walls of flasks by rotating such flasks.

The production of cells, viruses, vaccines, hormones and antigens in cultures is an essential procedure in both research-oriented and clinical laboratories. It is desirable that growth of these cultures take place at optimum rate. It is also desirable that such cultures, while they are growing, be available for instantaneous inspection and observation and that they be accessible for more complete investigation at any point in their growth. Experience has shown that one of the best mediums for the cultivation of culture growth is a closed vessel made of an inert material such as glass in which the entire vessel surface is exposed to the environment. Such a vessel not only permits exposure of the growing culture to light and the effects of circulating air or water but also satisfies the important requirement of instantaneous observation and investigation.

It has been further discovered that rotation of the flasks in which the culture is being grown by rollers induces more rapid cell growth and yields a higher production of cells and viruses on the interior flask walls. Furthermore, since the flasks are continually rolled at an optimum speed for cell attachment and growth, minimal volumes of culture media are required to provide an abundant yield. The entire interior surface of the flask is exposed by rolling to cell growth, thus increasing the yield.

The prior art cell cultivation apparatus accomplishing this flask rotation is characterized by a series of parallel rollers between which the culture flasks are placed. Each roller rotates at the same speed and in the same direction, causing the culture flasks whose sides are in contact with the rollers to rotate in an opposite direction. However, such roller-type apparatus have been shown to have definite disadvantages.

First, the fact that the rollers pass in contact with each point on the entire outside cylindrical surface of the culture flask during each rotation of the flask causes several problems. The cell layer which is grown on the inside walls of the culture flask is subjected to temperature variations at the point in time when the flask touches the roller since the thermal conductivity and capacity of the roller may be significantly different than that of the surrounding environment. Thus, there is a temperature variable imparted by the rollers to the flasks which is of possibly significant magnitude in the cultivation and growth of the cultures. Furthermore, the conventional rollers impart of coating to the outside of the culture flasks which makes it extremely difficult to observe the cell growth through the glass. This fog requires handling and cleaning operations in order to clear it from the outside of the culture flask to permit observation. Such handling and cleaning operations often cause mechanical and thermal shock to the cells inside the culture flask resulting in variation and mutation in growth.

In addition, perfusion of gas or other media into or out of the flask during rotation is impossible with many conventional roller apparatus since the flask stopper rotates with the flask, thus preventing the insertion of any fixed tubes through the stopper.

DESCRIPTION OF THE INVENTION

This invention comprises a novel apparatus for the cultivation and growth of cells and viruses for the production of vaccines, hormones and antigens within a conventional culture flask which is supported at its neck and its bottom above the base of the apparatus and which is rotated by a drive means engaging its bottom about the central axis of a stopper means inserted into its mouth, which stopper means remains fixed with respect to the apparatus base during the rotation of the culture flask.

This apparatus overcomes the limitations of the conventional roller-type apparatus because it achieves cell cultivation and growth by rotating a culture flask supported above the apparatus base at only the neck and bottom of the flask. Supporting the flask at these two points alone eliminates the constant contact of the outer walls of the culture flask with a roller composed of material of different thermal conductivity or capacity than that of the surrounding environment.

In this apparatus, the culture flask is thus suspended as it rotates. Since its sides only come in contact with a uniform controlled environment which is circulated uniformly about the flask, there is no temperature variable imparted to the sides of the flask which can cause variation or mutation in the growth of the cells in the culture. Additionally, since there is no contact with conventional rollers, no coating is imparted to the outside of the flask, making observation of the cell growth impossible or difficult. This ability to readily observe without excess handling and cleaning further eliminates the possibility of thermal or mechanical shock to the culture caused by the necessity of such handling or cleaning in conventional apparatus.

Furthermore, since the culture flask rotates about the flask stopper, which is held in a fixed position with respect to the apparatus base, it is possible to insert tubes through the stopper, for perfusion of gas or other media into or out of the apparatus during the actual rotation of the flask.

The rotating flask culture apparatus of this invention has a vertical flange member which indirectly supports the neck of the flask above the base of the apparatus. Disposed in the upper portion of this neck support member is a bearing member having a side configuration similar to that of the top cylindrical portion of the culture flask stopper and a flat bearing shoulder supporting the top portion of this stopper in bearing and maintaining it in a fixed position during rotation of the flask. This bearing member is held in spaced relation from the neck support member by releasable spring means attached to a retainer flange portion located at its inward end which, impelled by the spring means, abuts and bears upon a facing flange portion of the flask stopper.

The flask stopper is thus impelled by the flange portion and the attached spring means into the mouth of the culture flask with sufficient force that the entire flask is urged toward the drive wheel means at its opposite end. Since one end of the stopper is disposed in the mouth of the flask and the other is supported by the bearing member, the flask is, in turn, supported above the base of the apparatus.

The stopper has, at its inward end, a flexible lip which, upon insertion of the stopper into the flask mouth, forms a seal to Accomodate moderate pressure

differentials inside the flask, without allowing a sufficient coefficient of friction to be developed between the inside of the flask mouth and the stopper to cause the stopper to rotate with the flask.

The bottom end of the culture flask is indirectly supported and held above the apparatus base by a vertical flange member or bottom supporting wall member. The flask is actually supported on a drive wheel means disposed in the upper portion of the bottom supporting wall and which is received into a recess formed in the bottom of the culture flask and which holds the culture flask in fixed relationship for purposes of rotation by a non-skid ring disposed about its circumference. The drive wheel means itself is rotated by a sprocket means disposed on the opposite side of the bottom supporting wall member and connected to the drive wheel means by a common axis disposed through the wall member. The sprocket means is in turn driven by a belt means powered by a drive motor. This drive motor may be controlled to impart any desired speed of rotation to the culture flask.

Thus, the culture flask is suspended above the apparatus base at two points only and allows for unobstructed circulation of the controlled environment about the exterior of its growing surface.

Accordingly, it is an object of this invention to provide an apparatus for the cultivation and growth of cell cultures by constant, uniform rotation of the flask in which such cultures are to be grown.

It is another object of this invention to provide an apparatus in which rotation of flasks for growth and cultivation of cultures is accomplished without any contact between the exterior of the growing surfaces of the culture flask and the means for rotating these flasks.

It is a further object of this invention to provide an apparatus for the cultivation and growth of cultures in which no possible temperature variation is imparted to the culture flask growing surfaces by the means for rotating such a flask.

It is still another object of this invention to provide an apparatus for the cultivation and growth of cultures which permits ready observation and inspection of the culture growing inside the culture flask without any necessity for handling or cleaning of the flask walls.

It is still a further object of this invention to provide an apparatus for the cultivation and growth of cultures in which perfusion of gas or other media into or out of the culture flask may be accomplished through a non-rotating flask stopper during rotation of the flask.

These and other important objects of this invention will become apparent from the following description taken in conjunction with the drawings illustrating a preferred embodiment wherein:

FIG. 1 is a perspective view of the rotating flask culture apparatus;

FIG. 2 is a fragmentary view of the top of the rotating flask culture apparatus with the middle culture flask removed.

FIG. 3 is a top plan view of the rotating flask culture apparatus;

FIG. 4 is an enlarged vertical cross-sectional view taken generally along line 4—4 in FIG. 2 and showing the neck and mouth portion of the flask, the flask stopper means as a whole in side view, the stopper bearing member and the neck support means;

FIG. 5 is an enlarged horizontal cross-sectional view taken generally along line 5—5 in FIG. 2 and showing the neck and mouth portion of the culture flask, the flask stopper means, the spring impelled bearing member and the neck support means; and,

FIG. 6 is an enlarged horizontal cross-sectional plan view of an alternate embodiment of the flask neck support elements shown in FIG. 5 with the stopper shown in hidden lines.

Referring now to the drawings and, more particularly, to FIG. 1, the rotating flask culture apparatus is shown at 10. This apparatus includes an apparatus base 12 which contains an environmental chamber 15 and drive motor control panel 16 and a drive motor means internally (not shown). The apparatus base 12 also includes a fan means shown at 18 in FIG. 3 and vent openings shown at 19 in FIG. 3 to provide for circulation of air within an enclosed environmental chamber 15.

The apparatus base 12 supports on its top surface 13 a flask neck mounting member 22 and a flask bottom mounting member 24. These members support between them and above the apparatus base top surface 13 one or more culture flasks 20 in which the cultivation and growth of the desired cultures occur. An environmental chamber enclosure or cover 14 encloses the culture flasks 20 about the periphery of the top surface 13 of the apparatus base 12, defining an environmental chamber 15 in which control of the temperature and circulation of air may be maintained by means of the controls on chamber control panel 16.

In FIG. 2 is shown the top surface portion 13 of the apparatus base 12 wherein two culture flasks 20 are positioned between flask neck mounting member 22 and flask bottom mounting member 24 above the top surface 13 for rotation. The neck of the culture flask 20 is supported indirectly by the flask neck mounting member 22 which is a vertical flange fixed at its bottom portion to the top surface 13 of the apparatus base 12 and having disposed in its top portion one or more bearing members 36 having interior configurations similar to that of the top cylindrical portion of the culture flask stopper 42. The bearing member 36 is attached to the flask neck mounting member 22 by means of retainer screws 40 on either side of the member 36. The bearing member 36 has a retainer flange 37 formed at its inward end which abuts and bears on a similar flange portion 43 of the flask stopper 42 by means of a spring means 38, as shown in FIG. 3, which surrounds the retainer screws 40 between the flange portion 37 of the retainer bearing member 36 and the flask neck mounting member 22. The spring means 38 pushes the flange portion 37 of the bearing member 36 against the top surface of flange portion 43 of the flask stopper 42 so that the flask stopper 42 is forced into the mouth and neck 23 of the culture flask 20. The top cylindrical portion 44 of the flask stopper 42 then rests upon the flat bearing shoulder portion 39 of bearing member 36 which supports said flask stopper 42 and, therefore, neck 23 of the culture flask 20 as shown in FIG. 4.

As the spring-impelled bearing member 36 pushes the flask stopper 42 into the mouth and neck 23 of the culture flask 20, it also forces the entire culture flask 20 toward the bottom drive wheel means 26 as shown in

FIGS. 2 and 3. These bottom drive wheel means 26 are mounted on the vertical flask bottom mounting member 24 which is a vertical flange fixed at its bottom portion to the top surface 13 of the apparatus base 12. The drive wheel means 26 are of such configuration that they fit into a recessed portion formed in the bottom of the culture flask 20 as shown in FIG. 3. These drive wheel means 26 engage the bottom of the culture flasks 20 by means of a non-skid rubber ring 28 disposed about their circumference which provides a sufficient coefficient of friction to prevent the culture flask 20 from slipping with respect to the drive wheel means 26 as the drive wheel means 26 rotates.

As shown in FIG 3, the bottom drive wheel means is connected to a drive sprocket or gear 32 disposed on the opposite side of the flask bottom mounting member 24 by means of a common axle (not shown) which is disposed through the bottom mounting member 24. In this embodiment, the sprocket or gear 32 has a series of teeth disposed about its circumference which are engaged by a chain drive or belt means 30 driven by a drive motor means (not shown).

In FIGS. 4 and 5 is shown the unique relationship between the neck and mouth 23 of the culture flask 20 and the flask stopper 42. As seen in FIG. 4, the flask stopper 42 has a cylindrical top portion 44 which is adjacent to and bears upon the interior flat bearing shoulder portion 39 of the bearing member 36. Near the middle of the stopper, there is a frusto-conical shaped, flange portion 43 having a top surface which abuts the flange 37 of the bearing member 36 as the bearing member 36 and said flange 37 are impelled against it by the spring means 38 as seen in FIG. 5. The side surface of the frusto-conical shaped flange portion 43 of the flask stopper 42 abuts the lip 25 of the culture flask 20 in bearing at a single point about its circumference. The bottom portion 45 of the flask stopper 42 has a flexible lip seal 46 formed about its circumference by the insertion of an O-ring 47 within its circumference, the O-ring spreads the outer portion of the bottom portion 45 of the flask stopper 42 and pushes it against the interior walls of the neck and mouth 23 of the culture flask 20 to form the flexible lip seal 46 to accommodate moderate pressure differentials inside the culture flask 20.

The various bearing points of the flask stopper 42 with respect to the neck and mouth 23 of the culture flask 20 and the bearing member 36 are shown in FIGS. 4 and 5. From these figures, it can be seen that the inward force exerted by the spring means 38 located on either side of the bearing member 36 against the flask stopper 42, impelling the flask stopper 42 into the mouth of the culture flask 20, such force being exerted parallel to the central axis of the flask stopper 42 and the conjunction of the cylindrical top portion 44 of flask stopper 42 and the flat shoulder 39 of bearing member 36, causes the flask stopper 42 to remain in a fixed position with respect to the bearing member 36 as the culture flask 20 rotates about the central axis of the flask stopper 42. Thus, the flask stopper 42 provides a bearing surface for the neck of the flask 20 as well as a separate flexible lip seal 46 to accommodate moderate pressure differentials inside the culture flask 20.

The fact that the flask stopper 42 remains in a fixed position during rotation of the flask 20 allows perfusion

of gas or other media into or out of the flask 20 by means of tubes inserted through plugged holes 50 bored in each flask stopper 42 as seen in FIGS. 2 and 5. Since the flask stopper 42 does not turn or rotate with the flask, the tubes may replace the plugs in these holes 50, without the problem of twisting, in order to introduce inert gas and nutrients, or to remove spent nutrients.

In the operation of this rotating flask culture apparatus for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens, a culture flask 20 containing the nutrient media and the culture subject and having a flask stopper 42 disposed in its mouth is placed on the rotating flask culture apparatus 10 by depressing the spring-loaded retainer flange 37 of bearing member 36, placing the top cylindrical portion 44 of the flask stopper 42 onto the flat shoulder portion 39 of bearing member 36 and positioning the recessed portion of the bottom of the culture flask 20 over the drive wheel 26.

When the bottom recessed portion of the culture flask 20 is located over the drive wheel 26, the flange portion 37 of bearing member 36 is released and spring means 38 then impels the retainer flange portion 37 against the top surface of flange portion 43 of the flask stopper 42 with a force sufficient to maintain the stopper 42 in sealed position within the culture flask neck and mouth 23 and to maintain the culture flask bottom in fixed relationship to the drive wheel means 26. The bearing member 36 supports flask stopper 42 and the culture flask 20 at its neck above the apparatus base 12, and the drive wheel 26 supports the culture flask 20 at its bottom above the apparatus base 12. The motor control 16 is then set for the desired speed of rotation, the motor is turned on, and the drive motor means (not shown) moves the chain drive 30 in such a manner that the drive sprockets 32 and the connected drive wheel means 26 are rotated. Since the drive wheel means 26 engages the bottom of the culture flask 20 in fixed relationship by the non-skid ring 28, it therefore imparts a rotation to the culture flask 20.

The one or more culture flasks 20 contained on the rotating flask culture apparatus 10 may be enclosed by the environmental chamber 15 in which the temperature and circulation of air are controlled. Such control is accomplished by the fan means 18 which circulates the air through the environmental chamber 15 with the aid of vents 19 formed in the top surface 13 of the apparatus base 12 as shown in FIG. 3. Water or other fluids may also be used for thermal control.

The culture flasks 20 not only have no contact with the means for rotation or any other portion of the rotating flask culture apparatus 10 along the exterior of any surface of possible culture growth, but also the culture flasks 20 are easily removable from the rotating flask culture apparatus 10 by simply depressing the spring-loaded flange 37 of the bearing means 36 adjacent to the flask stopper 42. In addition, if space availability is limited, this rotating flask culture apparatus 10, because of its unique means of support and spring retention of the culture flask 20 in the apparatus 10, could actually be run upside down or on its side without danger of the culture flasks 20 falling off or the speed of rotation varying.

In FIG. 6 is shown an alternate, somewhat simpler, and often preferred embodiment and construction of the culture flask neck support elements. In this embodiment, bearing member 36 includes a collar-shaped retainer flange 37 having a right angle shaped bearing surface tab or shoulder 60 which is mounted on flange 37 below the top cylindrical portion 44 of flask stopper 42 by bolt 62 inserted through its downwardly extending leg. The other leg of the right angle tab 60 presents a flat bearing surface or shoulder which may be placed adjacent a side portion of the flask stopper 42, to support the stopper 42 and the culture flask 20 above the apparatus base 12. The bearing member 36 is mounted on flask neck mounting member 22 by screws 64 which are threaded for insertion into threaded bores in retainer flange 37.

Prior to insertion in flange 37, the screws 64 are inserted through cylindrical sleeves 68 which are surrounded by spring means 38. Each sleeve 68 abuts the surface of retainer flange 37 at its one end and passes through a mounting hole in flask neck mounting member 22 to abut the head of screw 64 at its opposite end. The sleeve 68 thus maintains the retainer flange 37 in definite spaced relationship to the head of screw 64 while providing sufficient bearing surface within the mounting member 22 to maintain the screw 64, spring means 38, bearing member 36 and mouth and neck 23 of flask 20 in a position substantially parallel to the top surface 13 of apparatus base 12.

The flask 20 may be placed in position for rotation as described above by depressing the flange 37 and spring means 38 and positioning the stopper means 42 within the collar of flange 37 and adjacent bearing surface tab 60. When the bottom of flask 42 is positioned over drive wheel means 26, the spring means 38 is released and the flask 20 is ready for rotation.

Flask stopper 42 may be formed in such a manner that the portion of the flask stopper 42 which is adjacent bearing surface tab 60 has either a flat shoulder itself or is cut out so that the tab 60 may be fitted into it. Such cut out configuration acts as a locking means to prevent any possible rotation of the flask stopper 42 with the culture flask 20.

The culture flasks themselves may be made from any suitable material which is easily shaped, transparent, impervious to fluids and conductive to heat, such as glass, which has been most popular in this type of work.

The flask stoppers may be formed of any suitable materials which are impervious to fluids, slightly compressible, non-toxic, resilient and resistant to wear. The preferable materials for fabricating the stopper are glass-filled Teflon for the body and the points, such as those in contact with the culture flask, subject to wear, and silicone rubber for the O-ring 47. The flask stopper is also equipped with plugs, preferably made of stainless steel, which are inserted into the holes bored for perfusion tubes, until perfusion is desired.

The bearing member may be made from any suitable, smooth surface, easily formed rigid material having non-corrosive, long-wearing properties such as stainless steel or stainless steel alloys.

While the invention has been described in relation to preferred embodiments thereof, it will be apparent to those skilled in the art that the structural details are capable of wide variation without departing from the principles of the invention.

I claim:

1. A rotating flask culture apparatus adapted for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens on flask walls, including flask neck mounting means attached to an apparatus base means said neck mounting means having flask stopper bearing means mounted thereon, said flask stopper bearing means having bearing surface means in contact with flask stopper means disposed in the mouth of said culture flask shaped to prevent rotation of said stopper means with respect to said bearing means and thereby supporting the neck portion of said culture flask above said base means at a point perpendicular to its major axis, and retainer means abutting said flask stopper means movably urged by releasable spring means and impelling said flask stopper means and said culture flask horizontally along the central axis of said stopper means toward rotational drive means engaging said culture flask at its bottom end, said rotational drive means mounted on flask bottom mounting means attached to said base means, said flask bottom mounting means thereby supporting the bottom portion of said culture flask, above and parallel to said base means said rotational drive means rotating said culture flask, supported only at its neck and bottom, about the central axis of said flask stopper means, said flask stopper means being maintained in a fixed position with respect to said flask stopper bearing means, said flask stopper means allowing for rotation of said culture flask while hermetically sealing the inside of said culture flask.

2. The rotating flask culture apparatus of claim 1 wherein said flask neck mounting means includes a vertical flange member attached at its bottom to said apparatus base means and having at its top openings disposed therein to accept said flask stopper bearing means for mounting thereon and maintaining said flask stopper bearing means in fixed relationship thereto.

3. The rotating flask culture apparatus of claim 1 wherein said flask stopper bearing means includes bearing surface means of even surface adjacent said flask stopper means about at least part of its circumference, said bearing surface means supporting said flask stopper means and the neck of the culture flask into which said stopper means is inserted above the surface of said apparatus base means, said flask stopper bearing means having a retainer means comprising a retainer flange portion abutting and bearing on said flask stopper means, spring means interposed between said flange portion and said flask neck mounting means, said spring means impelling said flange portion against said flask stopper means, said flange portion thereby exerting a force parallel to the central axis of said flask stopper means on said flask stopper means, said force being effective to maintain said stopper means in the mouth of said culture flask, and to maintain said culture flask in a position above the surface of said apparatus base means.

4. The rotating flask culture apparatus of claim 1 wherein said flask stopper means includes a plug of impervious, compressible, corrosion-resistant material having a bottom portion for inserting into said culture flask mouth, a top cylindrical portion which rests in bearing on said bearing surface means of said bearing means, a flange portion abutting said retainer means of said flask stopper bearing means, and a side portion,

said bottom portion being slightly smaller in dimension than the mouth of said culture flask, but having a ring means imbedded slightly inside its circumference causing an outwardly projecting lip to bear upon the inside surface of said culture flask mouth, thereby providing a pressure seal, said side portion of said flask stopper means being tapered inward toward its middle from both the bottom portion and the flange portion of said flask stopper means such that the rim of the mouth of said culture flask bears upon an outwardly projecting surface of said side portion at an acute angle, said rim moving with respect to said outwardly projecting surface of said side portion of said stopper means when said culture flask is rotated.

5 The rotating flask culture apparatus of claim 1 wherein said flask bottom mounting means comprises a vertical flange member attached at its lower portion to said apparatus base means and having in its upper portion openings disposed to accept said rotational drive means.

6 The rotating flask culture apparatus of claim 1 wherein said rotational drive means includes drive motor means connected by belt means to sprocket means mounted for rotation on axes disposed through openings in the upper portion of said flask bottom mounting means, said power drive motor means causing said sprocket means to be rotated on said axes, said axes of said sprocket means being fixed to drive wheel means on the opposite side of said flask bottom mounting means, said drive wheel means being held in fixed relationship to said sprocket means thereby and being rotatable with said sprocket means on said axes, said drive wheel means being insertable into a recess in the bottom of said culture flasks, said recess having substantially similar dimensions to that of said drive wheel means and accommodating said drive wheel means therein, said drive wheel means engaging the bottom of said culture flasks by non-skid means disposed about the circumference of said drive wheel means, said drive wheel means holding said culture flasks in fixed relationship thereby, said culture flasks being rotated by said drive wheel means as said drive wheel means rotates on said axes in conjunction with said sprocket means being rotated by said belt means driven by said drive motor means.

7 In rotating flask culture apparatus adapted for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens on flask walls, the improvement comprising, spring impelled flask stopper bearing means mounted on flask neck mounting means, said flask stopper bearing means having a flat bearing surface means in contact with a cylindrical top portion of a flask stopper means said flat bearing surface means thereby supporting the neck portion of said culture flask above the apparatus base means at a point perpendicular to the central axis of said flask stopper means while precluding rotation of said flask stopper means with respect to said flask stopper bearing means, the bottom portion of said flask stopper means being disposed in the mouth of said culture flask, and having a lip created by a ring means disposed about the circumference of said flask stopper means, said lip bearing against the inside surface of said flask mouth about its entire circumference thereby creating a hermetic seal within said flask mouth, said

culture flask being supported at its bottom end by a drive wheel means insertable into a recess in the bottom of said culture flask, said drive wheel means engaging the bottom of said culture flask by non-skid means disposed about the circumference of said drive wheel means, said drive wheel means supported above said apparatus base means by a flask bottom mounting means, said drive wheel means rotatable on an axis disposed through said flask bottom mounting means and connected to sprocket means on the opposite side of said flask bottom mounting means, said sprocket means being rotated by belt means driven by drive motor means, said drive wheel means thereby imparting rotation to said culture flask, causing said culture flask supported above said base means at its neck and its bottom to rotate about the central axis of said flask stopper means.

8 The improvement defined in claim 7 wherein said flask stopper bearing means includes flat bearing surface means adjacent said flask stopper means about at least a part of its circumference, said flat bearing surface means supporting said flask stopper means and the neck of the culture flask into which said stopper means is inserted above the surface of said apparatus base means, and maintaining said flask stopper means in fixed position with respect to said flask stopper bearing means, said flask stopper bearing means having retainer means comprising a retainer flange portion abutting and bearing on a flange portion of said flask stopper means exterior to the mouth of said culture flask, spring means interposed between said retainer flange portion and said flask neck mounting means, said spring means impelling said retainer flange portion against said flange portion of said flask stopper means, said retainer flange portion thereby exerting a force parallel to the central axis of said flask stopper means on said flask stopper means, said force being effective to maintain said stopper means in the mouth of said culture flask, and to maintain said culture flask in a position above the surface of said apparatus base means.

9 In a rotating flask culture apparatus adapted for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens on flask walls, the combination including:

Vertical neck mounting means and vertical bottom mounting means supporting culture flasks above the surface of the apparatus base means;

Flask stopper bearing means mounted on said vertical neck mounting means and having flat bearing surface means supporting flask stopper means about at least a part of its circumference and maintaining said flask stopper means in a fixed relationship with respect to said flask stopper bearing means, and spring impelled retainer means abutting said flask stopper means exterior to said culture flask and holding said culture flask parallel to said apparatus base means, while urging said culture flask toward said vertical bottom mounting means, said flask stopper means having a ring means imbedded about the circumference of its interior portion disposed within said culture flask mouth, said ring means impelling a circumferential lip portion of said flask stopper means against the inside mouth of said culture flask to create a hermetic seal;

drive wheel means mounted on said bottom mounting means and insertable into a recess in the bottom of said culture flask, said drive wheel means engaging said culture flask by a non-skid surface means disposed about the circumference of said drive wheel means said drive wheel means rotatable on an axis disposed through said bottom mounting means and connected to sprocket means, said drive wheel means thereby rotating said culture flask while supporting the bottom of said flask above said apparatus base means.

10. A rotating flask culture apparatus adapted for the cultivation and investigation of cell and virus growth for the production of vaccines, hormones and antigens on flask walls comprising at least one culture flask supported only at its opposite ends above the base means of said apparatus, rotating means rotatable about a central axis and supporting said culture flask at one end thereof and capable of imparting a rotation to said culture flask, stationary mounting means supporting said culture flask above said base means at the opposite end thereof and allowing rotation of said culture flask with respect thereto, perfusion means allowing the passage of fluid into or out of said culture flask, and environmental enclosure means allowing said culture flask to be surrounded by circulating fluid of uniform temperature thereby effectively maintaining a controlled environment about said culture flask.

11. The rotating flask culture apparatus of claim 10 wherein said stationary mounting means includes a vertical flange member attached at its bottom to said base means.

12. The rotating flask culture apparatus of claim 11 wherein said vertical flange member is located at the neck and mouth end of said culture flask and includes top openings disposed therein to accept flask stopper bearing means for mounting thereon and to maintain said flask stopper bearing means in fixed relationship

thereto, said flask stopper bearing means supporting in bearing a flask stopper means insertable into said mouth and neck of said culture flask.

13. The rotating culture flask apparatus of claim 10 wherein said rotating means rotatable about a central axis includes means for engaging said culture flask at one end thereof, said means mounted on a vertical flange member attached at its lower portion to said base means of said apparatus, said means connected to a drive motor means by which it is rotated about said central axis.

14. The rotating flask culture apparatus of claim 13 wherein said rotating means is located near the bottom end of said culture flask.

15. The rotating flask culture apparatus of claim 10 wherein said environmental enclosure means includes cover means disposed over the culture flask positioned on said apparatus, said cover means thereby defining an environmental chamber about said culture flask within which air of uniform temperature may be circulated about said culture flask by fan and vent means.

16. The rotating culture flask apparatus of claim 10 wherein said environmental enclosure means includes container means having said culture flask disposed therein and being capable of containing at uniform temperature a quantity of water for circulation about said culture flask.

17. The rotating culture flask apparatus of claim 10 having a culture flask constructed of a material suitable for the growing of cultures, said culture flask including a neck and mouth formed at one end thereof and a bottom formed at the opposite end, said bottom having recessed portion.

18. The rotating culture flask apparatus of claim 17 wherein said bottom of said culture flask has a recessed portion of sufficient dimension to receive said rotating means therein.

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