

[54] **MICROCULTURE SLIDE CHAMBER**

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[51] Int. Cl. **C12b 1/00**

[58] Field of Search **195/139, 127**

[56] **References Cited**

UNITED STATES PATENTS

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[57] **ABSTRACT**

A microculture slide chamber for simultaneously growing a plurality of mono-layer cell cultures on a slide includes a matrix which defines a plurality of generally parallel holes extending therethrough so that a plurality of wells for containing the culture bearing fluid are provided when the matrix is in abutment with a slide. Surrounding each hole on one side of the matrix is a gasket that is integral with the matrix and serves to seal the fluid in each well. A pressure plate with mating holes overlies the opposite side of each matrix and spring clips hold the plate, matrix and slide in assembled relation. A cover for the microculture slide chamber is provided.

10 Claims, 2 Drawing Figures

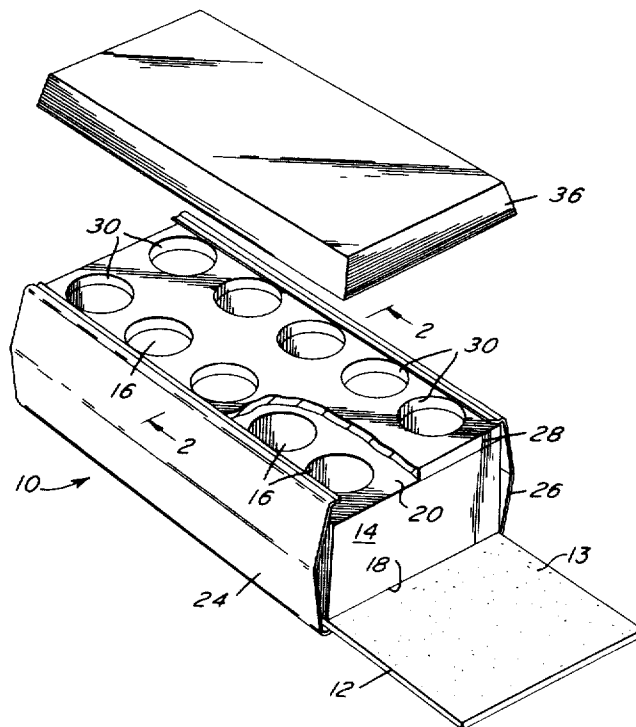


FIG. 1

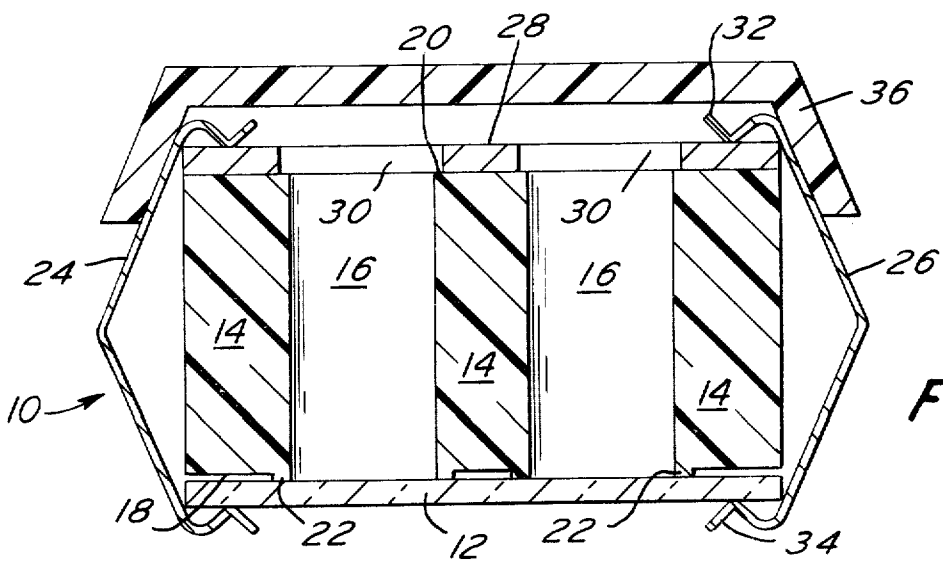
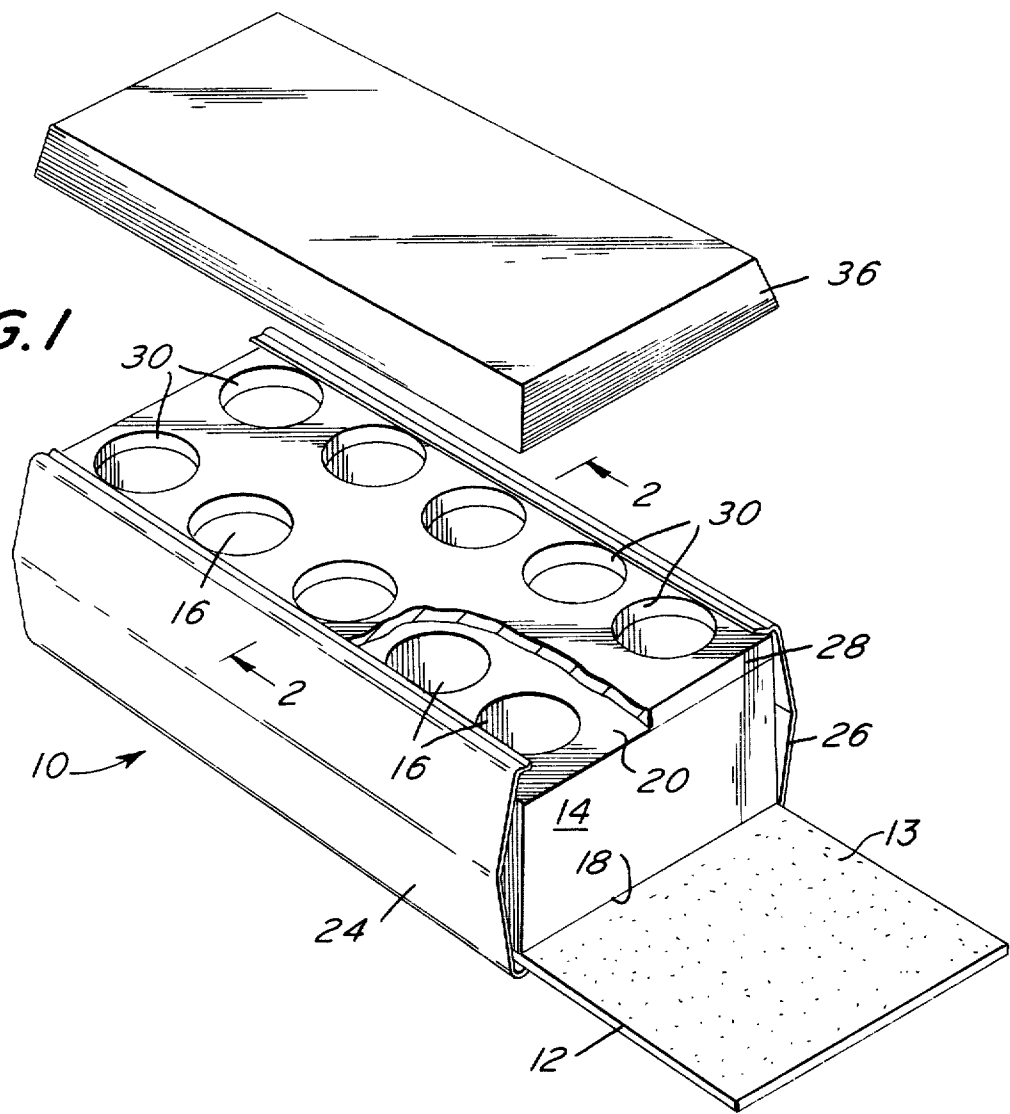


FIG. 2

MICROCULTURE SLIDE CHAMBER

This invention relates to a microculture slide chamber. More particularly, this invention relates to a microculture slide chamber for simultaneously growing a plurality of mono-layer cell cultures on a slide or similar structure.

There are many types of laboratory tests, particularly in the biological sciences, wherein it is desirable to form cell cultures on a slide. Among these are mono-layer cell cultures for which the present invention is particularly suited, although those skilled in the art will recognize that it may have other uses. For various reasons, it is desirable that two or more cell cultures be grown on the same slide. For example, an advantage of growing multiple cell cultures on the same slide is that different viruses can be used to inoculate the same type of cells or, in the alternative, one virus can be used to inoculate different types of cell cultures. There are, of course, other advantages as hereinafter described. The present invention provides a microculture slide chamber which enables such persons to gain these advantages.

Prior attempts have been made to provide microculture slide chambers for growing a plurality of cell cultures on the same slide. Among these is a tissue culture chamber-slide sold by Miles Laboratory, Inc. under Lab-Tek Catalog No. D2270. This device consists of a glass slide with a removable non-toxic gasket and an attached optically clear plastic sample chamber. The chamber-slide has proven to be quite unsatisfactory for several reasons. Among these is that the fluid occasionally leaks from chamber to chamber. Worse still, the separation of the slide from the remaining parts of the device requires the application of pressure to break the gasket seal followed by the removal of the gasket with forcep. In use, the breaking action or the removal of the gasket results in the removal of parts of the culture cells, a wholly unacceptable result.

The present invention overcomes the disadvantages of such prior art devices by providing a readily assemblable and disassemblable microculture slide chamber for simultaneously forming two or more culture cells or the like on a slide. Such cell cultures may be, but need not be, mono-layer cell cultures.

The microculture slide chamber comprising the present invention is designed so that it will have the advantages of consistency from slide to slide, convenience in use, be economical to purchase and maintain, and can be readily stored. The advantage of forming a plurality of cell cultures on a single slide is that there can be consistency in cell staining, consistent histochemistry, and identical manipulation. Such a device is convenient because it provides efficiency in processing and examination of all cells on a single slide and also allows for storing the cells in racks that can be readily identified. Economy is achieved because the microculture slide chamber is recyclable except, of course, for the slide itself.

In accordance with the present invention, the microculture slide chamber comprises a slide on which the cultures are to be grown together with a matrix made of resilient material through which extend a plurality of holes. The matrix is positioned in abutting relation to the slide so that each hole defines a well or chamber within which the culture bearing fluid can be maintained. The side of the matrix which abuts the slide includes gaskets integral therewith and surrounding each

of the holes. The gaskets provide a fluid tight seal for each well thus formed preventing leakage from well to well. Overlying the opposite side of the hole is a plate serving as a pressure plate. The plate has a plurality of holes extending therethrough which holes are arranged on the plate so as to align with the matrix holes. A pair of spring clips engage the side edges of the surface of the slide and plate to retain the same in abutting relation with the matrix. A cover is provided for closing the wells while the cell cultures are being formed.

A microculture slide chamber constructed in accordance with what is described and claimed herein has many uses and applications. Among these are the following:

1. Screening for effects of compounds on cellular morphology, replication, viability and differentiation.
2. Study of the effects of compounds on the cellular uptake of a variety of radio isotopic substrates. This application requires the use of a polymer substrate or slide.
3. Autoradiographic studies permit the localization of radio isotopic tracers in the cells.
4. Viral titrations can be rapidly and easily performed in the chambers.
5. Cytotoxic antibody titrations can be done as well.
6. Lymphocytotoxic assays using either optical or radio-isotopic end points are easily performed.
7. Immunofluorescence methods are especially easy with this invention. The detection of anti-nuclear antibodies (ANA) for testing for lupus erythematosus is very easy. Viral diagnosis could be accomplished in this system by titrating for immunofluorescence of the patient's serum against preinfected cell mono-layers.
8. It is theoretically possible to perform the macrophage inhibition factor assay using this invention.

For the purpose of illustrating the invention, there are shown in the drawings forms which are presently preferred; it being understood, however, that this invention is not limited to the precise arrangements and instrumentalities shown.

FIG. 1 is an exploded perspective view of a microculture slide chamber in accordance with the present invention.

FIG. 2 is a transverse sectional view of the microculture slide chamber showing the same in assembled relation.

Referring now to the drawings in detail, wherein like numerals indicate like elements, there is shown a microculture slide chamber designated generally as 10.

The microculture slide chamber 10 is provided with a slide 12 which may be made of glass, as is conventional. The slide 12 is somewhat longer than the microculture slide chamber 10 so that a frosted portion 13 upon which identifying marks can be made protrudes outward from the cell. Overlying the slide 12 is a matrix 14 best shown in FIG. 1. The matrix 14 is made of a resilient material such as silicone rubber. Of course, other resilient materials may be substituted provided that they are autoclavable. Extending through the matrix 14 are a plurality of holes 16 in generally parallel relation to each other. Although the matrix 14 may take any form, such as circular or even toroidal, it is shown as being generally in the shape of a rectangular parallel-piped having opposed planar surfaces 18 and 20 between which the holes 16 extend. Ten holes 16 are shown extending from surface 18 to surface 20.

However, any number of such holes, as desired, may be provided.

When matrix 14 is brought into abutting relation with the upper surface of slide 12, each of the holes 16 defines a well or chamber for containing the culture bearing fluid. To be certain that the fluid does not leak from well to well, a gasket 22 surrounds each of the holes 16. The gaskets 22 are integrally formed with the matrix 14 and provide a fluid tight seal when the slide 12 is held in abutting relation with the matrix 14 under the force of the spring clips 24 and 26. The advantage of making the gaskets 22 integral with the matrix 14 is that they are simultaneously removed when the matrix is separated from the slide, thus avoiding the danger that their individual removal with forceps would result in damage to the cell cultures.

Overlying the matrix 14 is a pressure plate 28 whose function is to cooperate with the clips 24 and 26 to apply a compression force on the matrix 14 to retain the gaskets 22 in good contact with the slide 12. Plate 28 is preferably made of stainless steel or an autoclavable polymer such as polycarbonate. The plate 28 is dimensioned to have the same width as the matrix 14 just as the matrix 14 has a width approximately equal to the width of the slide 12. Moreover, the plate 28 is provided with holes 30 extending therethrough which holes are positioned in the plate 28 so as to align with the holes 16 in the matrix 14. Thus, the holes 30 permit ready access to the holes 16 and the wells thus defined when the microculture slide chamber is in its assembled condition. If desired, plate 28 may be permanently fixed to matrix 14.

Clips 24 and 26 provide a resilient means for maintaining the microculture slide chamber in its assembled relation. As shown, each of the clips 24 and 26 is made of a tempered spring metal, such as stainless steel, and it is provided with curved dependent edge engaging sections 32 and 34. The edge engaging sections 32 and 34 depend from a medially curved or bent intermediate section such that the distance between the edge sections 32 and 34 is normally less than the thickness of the assembled microculture slide chamber including the slide 12, matrix 14 and plate 28 when each clip is in an unstressed condition. Each of the clips 24 and 26 slides over the edges of the slide 12 and the plate 28 and thereby compresses them toward the matrix 14, thus retaining the microculture slide chamber 10 in its assembled relation without interfering with access to the holes 30. A cover 36 is made of polycarbonate polymer or some other autoclavable material and preferably is light transparent so that the interior of the hole 16 can be observed. Cover 36 is dimensioned to overlie the entire surface of plate 28 and, of course, the matrix 16 thereby protecting the culture fluid when placed in the holes 16.

It should be understood that the number of holes 16 in matrix 14 can be varied as desired. Moreover, the dimensions can also be varied. In one preferred embodiment, the holes 16 are sized to contain culture fluid of 0.4 ml maximum with a recommended amount of approximately 0.2 ml. The slide 12 is preferably of standard dimensions for microscope slides which are approximately 0.9 mm to 1.09 mm in thickness.

In use, the microculture slide chamber is assembled and the appropriate culture bearing fluids are placed in two or more of the holes 16. The cultures are inoculated, the cover 36 is placed on top of the microculture

slide chamber, and the entire device is placed in a CO₂ incubator. As is known, the cells attach to the base of the glass slide 12 to form a monolayer cell culture at the bottom of each of the wells defined by the combination of the slide 12 and the holes 16 in the matrix 14. The cells can be inoculated with viruses, or any of the procedures outlined above can be effected.

Once the monolayer culture has been formed, it is a straightforward procedure to disassemble the microculture slide chamber, fix and stain the cells, thereafter examine them under an appropriate microscope. Cover slips can also be fastened to the cells to make a permanent record of the culture.

The use of the invention is not limited to glass microscope slides. Other types of slides, such as plastic slides to which the cells will adhere, can be used. One such plastic is a polyester sold under the trade name "Melinex" and manufactured by Imperial Chemical Industries, Inc. The advantage of using a plastic is that it can be readily divided, if desired after formation of the cells. This may be advantageous when it is desirable to measure the radioactivity of each cell mono-layer.

The present invention may be embodied in other specific forms without departing from the spirit or essential attributes thereof and, accordingly, reference should be made to the appended claims, rather than to the foregoing specification as indicating the scope of the invention.

I claim:

1. A microculture slide chamber for growing cultures comprising:

a slide on which said cultures are to be grown;
a matrix having a plurality of generally parallel matrix holes extending therethrough, said matrix being made of a resilient material;

said matrix holes when positioned over said slide defining a plurality of wells for containing a culture bearing fluid;

a gasket surrounding the end of each matrix hole adjacent said slide, each said gasket being integral with said matrix, and each said gasket providing a fluid-tight seal between said slide and said matrix for retaining fluid in said wells;

a plate having openings therethrough aligned to permit access to said matrix holes when said plate is in overlying relation to said matrix;

resilient clip means for retaining said microculture slide chamber in assembled relation for growing cultures therein, said assembled relation comprising said slide in abutting relation with the gasket side of said matrix and said plate in abutting and aligned relation with the opposite side of said matrix, and

a cover for said microculture slide chamber.

2. A microculture slide chamber in accordance with claim 1 wherein said clip means comprise first and second resilient clips for engaging the edges of said slide and plate and compressing them into engagement with said matrix.

3. A microculture slide chamber in accordance with claim 1 wherein said matrix is made of a silicone polymer.

4. A microculture slide chamber in accordance with claim 1 wherein said matrix, said clip means, said plate and said cover are made of autoclavable substances.

5. A microculture slide chamber in accordance with claim 4 wherein said cover is made of a polycarbonate polymer.

6. A microculture slide chamber in accordance with claim 4 wherein said clip means is made of a stainless steel.

7. A microculture slide chamber in accordance with claim 4 wherein said plate is made of stainless steel.

8. A microculture slide chamber in accordance with claim 1 wherein said plate is permanently fixed to said matrix.

9. A microculture slide chamber in accordance with claim 1 wherein said slide is made of a polymer material.

10. A microculture slide chamber for growing cultures on a slide comprising:

a matrix having a plurality of generally parallel matrix holes extending therethrough, said matrix being made of a resilient material;

said matrix holes when positioned over a slide defin-

ing a plurality of chambers for containing a culture bearing fluid;

a gasket surrounding one end of each matrix hole on one side of said matrix, each said gasket being integral with said matrix, and each said gasket being capable of providing a fluid-tight seal between a slide and said matrix for retaining fluid in said chambers when a slide is placed against the gasket side of the matrix;

a pressure plate having openings therethrough aligned to permit access to said matrix holes when said plate is in overlying relation to said matrix; and resilient clip means for retaining said microculture slide chamber in assembled relation with a slide for growing cultures on the slide, said assembled relation comprising a slide in abutting relation with the gasket side of said matrix and said plate in abutting and aligned relation with the opposite side of said matrix.

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