March 14, 1972 A. E. FREEMAN 3,649,464

ASSAY AND CULTURE TRAY

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FIG. 1

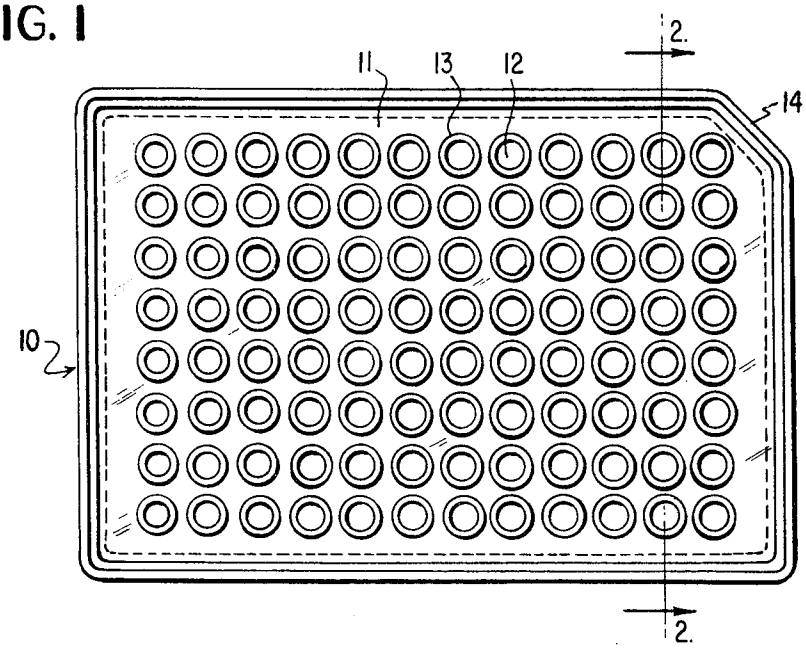
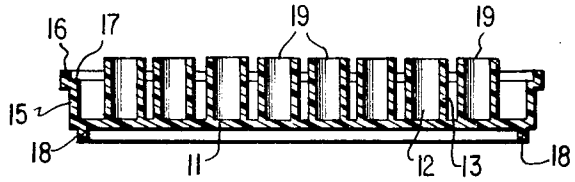



FIG. 2



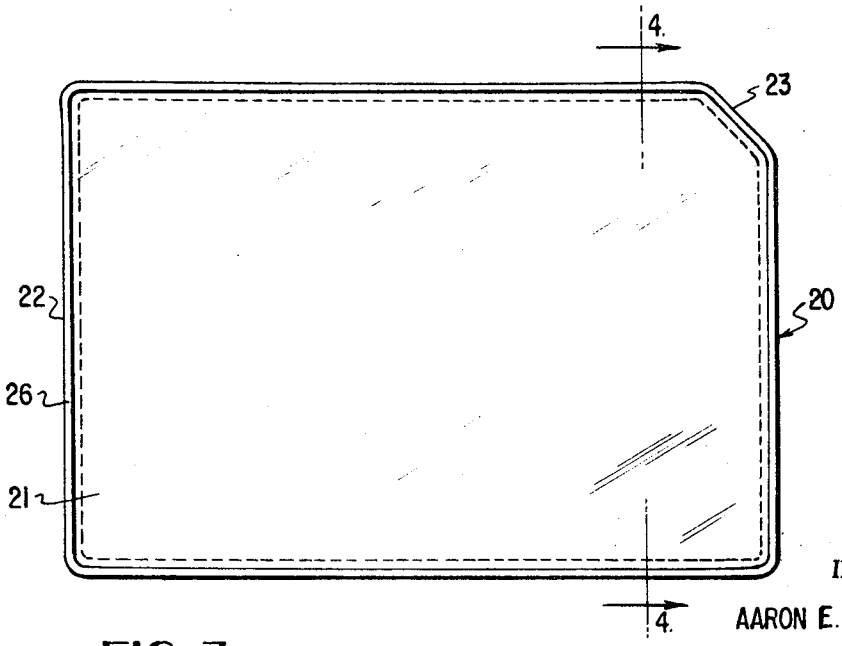




FIG. 3

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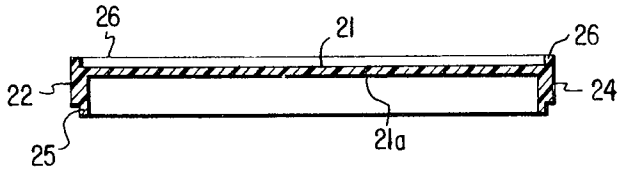
FIG. 4



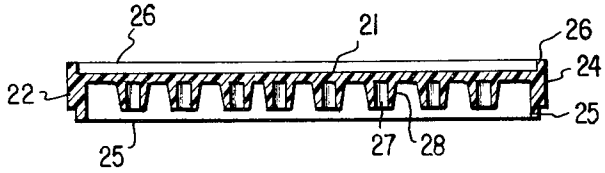




FIG. 5

FIG. 7

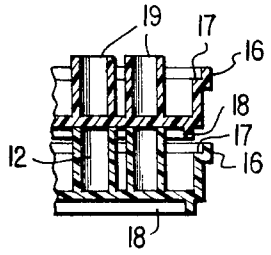






FIG. 6

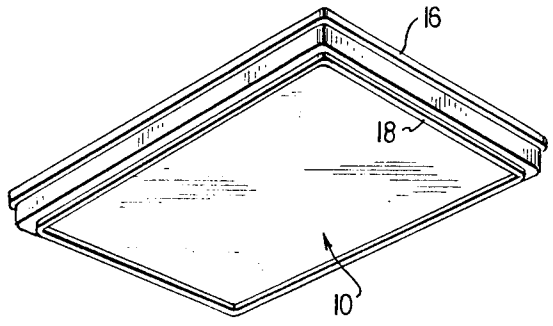



FIG. 9

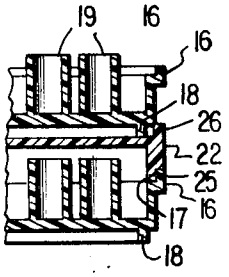



FIG. 8

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United States Patent Office 3,649,464 Patented Mar. 14, 1972



3,649,464

# ASSAY AND CULTURE TRAY

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Filed Dec. 5, 1969, Ser. No. 882,493
Int. Cl. C12k 1/00
U.S. Cl. 195—140 15 Claims

## ABSTRACT OF THE DISCLOSURE

A plate or tray suitable for assay and cell and tissue culture on a miniature scale comprises a transparent base member made of plastic and having extending upward therefrom a plurality of parallel rows of open top cylindrical wells spaced apart from each other a sufficient distance to avoid cross-contamination, an integral peripheral upstanding wall terminating in a flange provided with a seat adapted to receive and sercure a lid having a downwardly extending wall adapted to engage the flange portion of the plate, which lid may include a plurality of parallel rows of downwardly extending well seals positioned to engage the mouth portions of the wells to form closures therefor.

## BACKGROUND OF THE INVENTION

The rapid expansion of cell and tissue culture, particularly in the field of virology, has made necessary the processing of large numbers of individual cultures by macrotechniques, employing standard size Petri dishes and other culture vessels. The need for subsequent virus isolation, titration, and assay tests and the like, has involved the handling and manipulation of large numbers of culture vessels and the transfer of substantial volumes of media with attendant space requirements, and hazards of spillage and contamination.

Efforts have been made by virologists and others engaged in cell and tissue culture to utilize for growth, virus assay, neutralization and toxicity tests and the like, the currently available miniature titration or assay plates. These plates are designed for complement-fixation and other serological tests and have proved to be poorly adaptable and generally inadequate for cell and tissue culture purposes. Such assay or titration plates customarily comprise a one piece molded plastic shell including a plurality of parallel rows of uniformly arranged cups which depend downwardly from a top wall which contains the open upper ends of the cups, tangentially disposed to each other, the closed lower ends being individually formed at the bottoms of the respective cups. When it is attempted to utilize such assay plates for cell and tissue culture purposes, one drawback is the possible cross-contamination of viruses, reagents and cells from one cup or well to another because of the arrangement of the cups whereby the fact that their openings are flush with the top wall surface permits any spillage to flow from one cup into another, which spillage may even result in possible contamination of an entire incubator where the plate is being used in an incubator.

The commercially available miniature titration plates employ a standard type of tape sealing system to cover the well openings and when an effort is made to use such plates for cell or tissue culture purposes, the tape presents the danger of causing cross-contamination through a mechanical action.

Accordingly, there has existed a need for a cell and tissue culture and assay plate, particularly adapted for cell and tissue culture and attendant assays on a miniature scale and which would be free from the drawbacks of other types of plates not designed specifically for cell and tissue culture purposes.



## GENERAL DESCRIPTION OF THE INVENTION

In accordance with the present invention, there is provided a novel cell and tissue culture and assay plate, capable of multiple culturing or assaying on a miniature scale, together with a special lid or cover therefor.

The miniature plate of the invention comprises a transparent integral molded base from which there extend upward a multiplicity of small cups or wells arranged in rows, which are capable of functioning as culture vessels for cell or tissue culture, or as cups for microassay work. The outer walls of the cups or wells protrude upward, and are spaced apart from each other, and are not adjoined by an upper wall surface, thereby eliminating the possibility of spillage flowing from one well to another, by reason of the troughs made between adjacent cups or wells. This serves to prevent cross-contamination when the cups are employed for cell or tissue culture work. The plate is also provided with an upstanding peripheral wall which forms a trough with the bottom of the plate and serves to prevent external spillage.

These and other novel features and advantages of the plate of the invention will be better understood by reference the accompanying drawings, in which:

FIG. 1 is a top plan view of the miniculture plate showing the arrangement of the cups or wells;

FIG. 2 is a section taken through the plate of FIG. 1, taken along the line 2—2 of FIG. 1;

FIG. 3 is a top plan view of a particular form of the lid or cover;

FIG. 4 is a cross-sectional view of the lid of FIG. 3 taken along the line 4—4;

FIG. 5 is a cross-sectional view of another form of the lid or cover provided with well-sealing means;

FIG. 6 is a view in perspective of a type of well sealing means;

FIG. 7 is a cross-sectional view showing the interrelationship of two stacked trays;

FIG. 8 is a cross-sectional view showing the interrelationship of a tray covered with a lid and a second tray superimposed thereon; and

FIG. 9 is a view in perspective of the bottom of a tray showing the peripheral bead thereon.

Referring now to the drawings, FIG. 1 illustrates a presently preferred embodiment of the invention, in which the miniature culture or assay plate is shown generally at 10, and includes a bottom tray 11 from which there extend upward a plurality of rows of cups or wells 12, each having a thin wall 13. These cup walls are spaced apart from each other to form troughs between them and to avoid any danger of cross-contamination of the individual cups or wells by reason of spillage or overflow of the well contents. The cups are of equal depth and diameter. Thus, for example, the typical dimension of a well is a wall height of approximately 10 mm., the wall having an inside diameter of approximately 7.5 mm. The space between adjacent outside wall surfaces is about 1 mm. which will ordinarily suffice to avoid the cross-contamination referred to above. The cups may be of any desired shape, but are preferably cylindrical.

The plate is preferably integrally molded of a suitable transparent plastic material, for example a vinyl resin material, or methyl methacrylate type material, which exhibits high mechanical strength, light weight, is readily cleaned if the plate is to be re-used, and which is sufficiently inexpensive so that the plate (and cover) may be treated as disposable.

In the embodiment shown in FIG. 1, the general dimensions of the plate or tray will typically comprise, for example, an over-all length of about 124 mm., and a width

of about 80 mm. One corner of the plate is provided with a cut-off beveled edge **14**. This permits design of the lid to have the same configuration as the plate itself, and forces the user to replace the lid in its original position, eliminating contamination and other difficulties which might arise from replacing the lid in the wrong position.

In the preferred embodiment shown in FIG. 1, there are 12 rows of cups or wells, each row containing 8 cups, providing a total of 96. However, it will be understood that the number of cups and their arrangement may be varied as circumstances require. The tray **11** may be, for example, about 3 mm. thick.

Referring to FIG. 2, there extends peripherally around the edge of the tray **11** an upstanding wall **15**, which is molded integrally therewith, the main portion of which wall advantageously has an over-all height equal to approximately one-half the height of the cups or wells, i.e. about 5 mm., but this is not critical. The wall terminates in an integral flange **16**, having a seat **17** formed by an extension of the wall which serves to seat and secure the lid **20**, as described below.

For purposes of tray stacking, the tray **11** of the plate is provided with a downwardly extending peripheral bead or lug **18**, which is adapted to fit around and encompass the outer limit of the array of wells **19** so that when one tray is stacked on top of another without the lid **20**, the upper tray is anchored and cannot slide off. The bead **18**, in addition to permitting stacking of the plates, also serves to prevent the bottom of the plate from being scratched when laid on a surface, thus preserving its optical qualities. The arrangement of bead **18** will be more clearly understood by reference to FIG. 9.

The microculture plate of the invention may be provided with a suitable lid or cover, the basic version of which is illustrated in FIGS. 3 and 4. The lid **20** is advantageously made of transparent plastic material, and is integrally molded. It includes a substantially flat wall **21**, which merges into a downwardly extending peripheral wall **22** as shown in FIGS. 4 and 5. The lid is so designed that the wall height is sufficient, when the lid is seated over the miniculture plate **10**, to provide a clearance between the tops **19** of the wells **12** and the lower surface **21***a* of the lid wall **21**. Typically, such clearance may be, for example, about 2 to 3 mm. The lid has a configuration matching that of the plate itself, that is, it is provided with the cut-off or bevel corner **23**, to engage the plate in a single position. In the embodiment shown in FIGS. 3 and 4, the lid wall terminates in a flange portion **24**, as shown in FIG. 4, having an inner lug **25**, to engage the edge of the flange **16** and the seat **17** at the upper end of the plate wall **15**. This minimizes possible contamination.

This tray stacking principle is illustrated more clearly in FIG. 7, showing the inter-relationship of the bead **18** and the wells **19**, with respect to the wall flange portions **16** and **17**, the function of the bead **18** here being to prevent lateral sliding of the upper tray. When trays are thus stacked, the wells can be sealed with the sealing strip illustrated in FIG. 6, and described below.

Extending upward from the lid wall **21** is a peripheral lug **26** which serves to engage the downwardly extending bead **18** of the plate **10**, when a set of plates and lids is stacked. This principle is illustrated in FIG. 8. When the lid is applied to the tray, the outer edge of the lid peripheral wall **22** does not extend beyond the edge of flange **16** of the tray, so that the protruding flange portion **16** of the tray permits grasping and lifting of the tray without the danger of grasping the lid and having the tray drop off.

In a modified version of the lid shown in FIG. 5, there are provided integrally molded well seals **27**, which extend downwardly from the lid wall **21**, in a number matching the number of cups or wells, and positioned so as to engage the mouth portion **19** of the wells by penetrating into the well openings. For this purpose the well seal walls **28** are tapered so that they wedge into the well, providing a positive seal.



The form of well seal shown in FIG. 6 is intended to be used as the sealing means for a given row of wells, or to be used in conjunction with the form of lid shown in FIG. 4. It comprises a strip **30** of a transparent plastic material having integrally molded therein a set of 12 or 8 individual well seals **31** which are adapted to extend into the mouths **19** of the individual wells. The well seals **31** advantageously have tapering walls of the type described in connection with the embodiment of FIG. 5. The strip may be utilized so that the 8 rows of 12 wells can be sealed individually, or conversely, if an 8-seal strip is used, so that the 12 rows of 8 each can be thus sealed. In this way the user can remove the sealing strip from one row at a time without unsealing the remaining 7 or 11 rows of wells. Tab **32** forming one end of strip **30** is provided for this purpose.

What is claimed is:

**1.** A cell and tissue culture and assay plate comprising a transparent substantially planar base member having integrally molded therein and extending upward therefrom a plurality of parallel rows of upstanding open top cups or wells, said wells being spaced apart from each other to form troughs between them and to avoid cross-contamination of the well contents, said base member including a peripheral upstanding wall integral therewith, and means at the upper end of said wall adapted to receive a lid or cover.

**2.** The plate according to claim **1**, in which said plate is made of a transparent plastic material.

**3.** The plate according to claim **1**, in which said wells are arranged in transversely aligned rows containing an equal number of wells.

**4.** The plate according to claim **1**, in which said peripheral wall forms a trough with the bottom of the plate.

**5.** The plate according to claim **1**, in which the height of said peripheral wall is less than the height of said wells.

**6.** The plate according to claim **1**, in which the height of said peripheral wall is approximately one-half the height of said wells and wherein said plate includes a lid secured to said means at the upper end of said wall.

**7.** The plate according to claim **1**, in which said peripheral wall terminates in an integral flange provided with a seal adapted to receive a lid or cover.

**8.** The plate according to claim **1**, which includes a downwardly extending peripheral bead adapted to prevent scratching of the bottom of the plate and to permit stacking upon another plate or upon the lid or cover of a plate.

**9.** The plate according to claim **8**, in which said peripheral bead is adapted to fit around the outer limit of the cups or wells.

**10.** The plate according to claim **1**, which includes, in combination, a lid comprising a transparent substantially planar member including a peripheral downwardly depending wall integral therewith, the lower edge of said wall including a flange portion adapted to seat and secure the lid in the receiving portion of said plate wall, the wall of said lid being of sufficient height to provide a clearance between the bottom surface of the lid and the upper ends of the wells.

**11.** The plate according to claim **6**, in which both the plate and the lid are provided with a matching cut-off corner portion to align said plate and lid in predetermined position.

**12.** The plate according to claim **6**, in which said lid includes a plurality of parallel rows of integral well seals extending downwardly from the inner surface of the lid, said seals being positioned to register with and to engage the mouth portions of the wells to form closures therefor.

**13.** The plate according to claim **6**, in which said lid includes a peripheral upwardly extending bead positioned adjacent the outer edge of the upper surface of the lid, and which is adapted to engage the peripheral bead extending downwardly from the bottom edge of a similar plate, when plate is stacked or superimposed thereon.

14. The plate according to claim 1, in which the mouths of said wells are sealed with a flexible strip sealing member including a plurality of intgeral well seals positioned to register with and to engage the mouth portions of said wells to form closures therefor, said strip including a detaching tab member.

15. The plate according to claim 6, in which the outer edge of the lid peripheral wall does not extend beyond the surface said peripheral plate wall to permit lifting of the plate and lid simply by grasping the plate edge.



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U.S. Cl. X.R.

23—292: 220—21