Dec. 5, 1967 N. M. COOKE ET AL 3,356,462

DISPOSABLE MICROTITRATION PLATE

Original Filed April 5, 1963 3 Sheets-Sheet 1

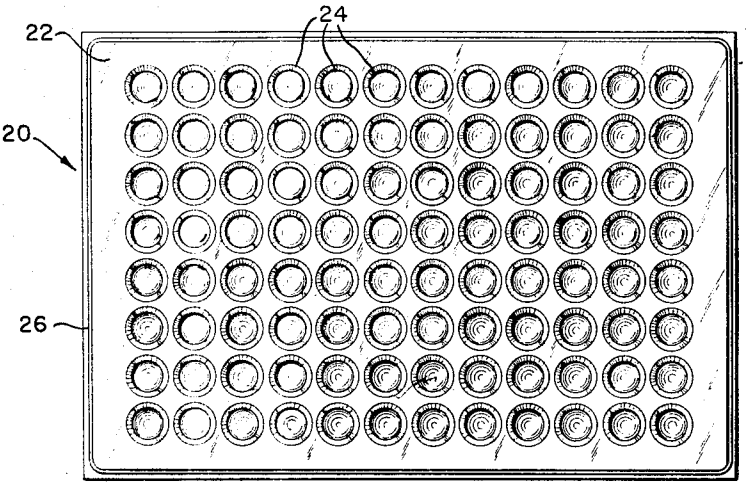


Fig. 1

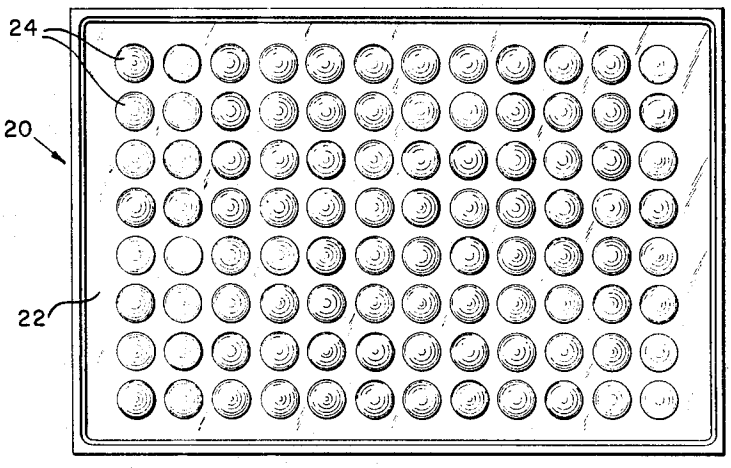


Fig. 2

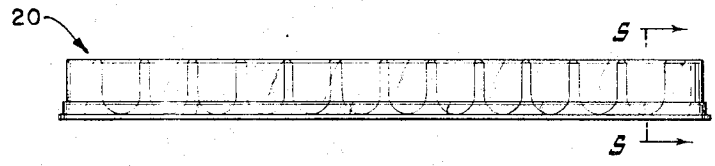


Fig. 3

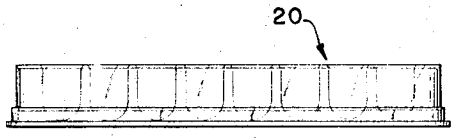


Fig. 4

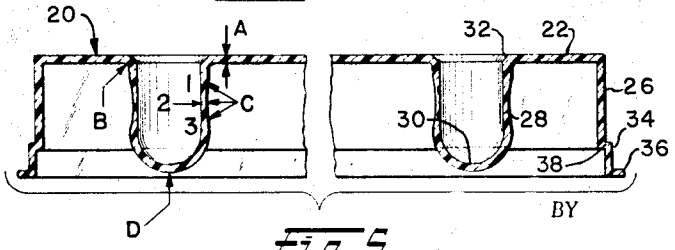


Fig. 5

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DISPOSABLE MICROTITRATION PLATE

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Fig. 6

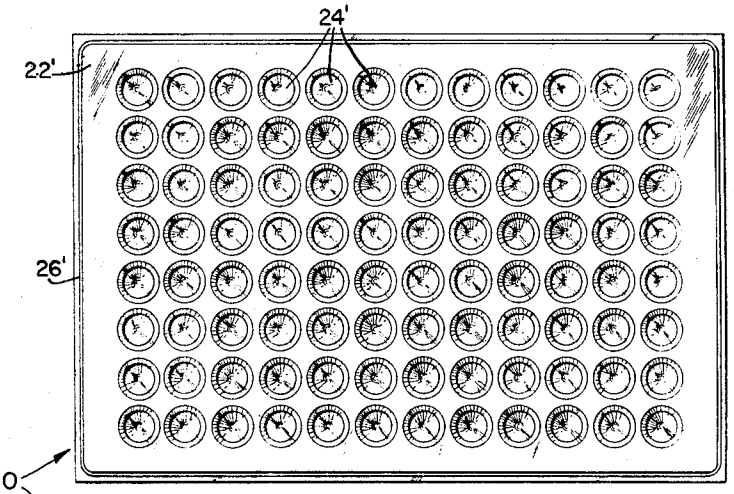


Fig. 7

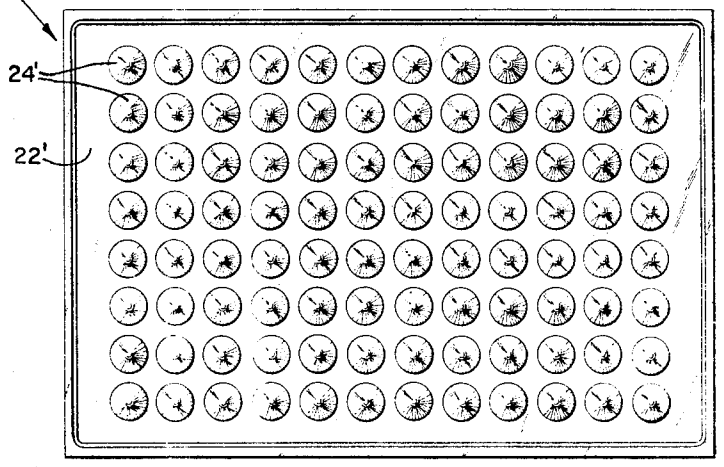


Fig. 8

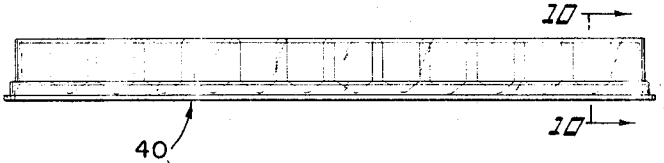


Fig. 9

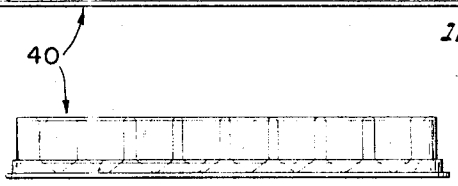
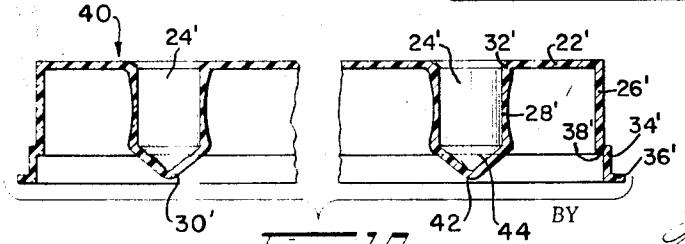


Fig. 10



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DISPOSABLE MICROTITRATION PLATE

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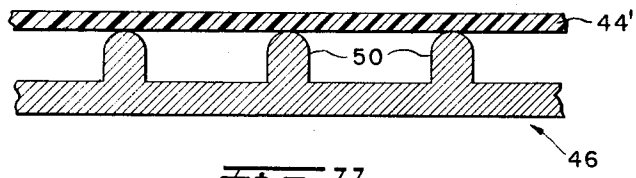


Fig. 11

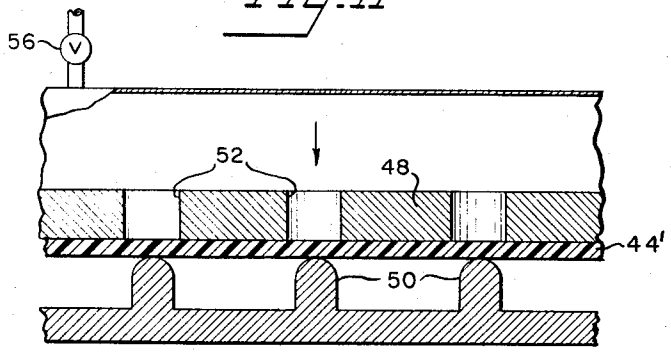


Fig. 12

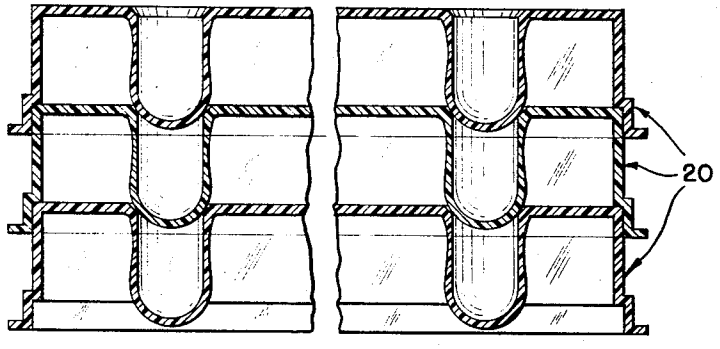


Fig. 13

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United States Patent Office 3,356,462 Patented Dec. 5, 1967

3,356,462

DISPOSABLE MICROTITRATION PLATE

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Continuation of application Ser. No. 271,003, Apr. 5, 1963. This application Aug. 9, 1966, Ser. No. 571,357
5 Claims. (Cl. 23—292)

ABSTRACT OF THE DISCLOSURE

A disposable microtitration plate comprising a molded, one-piece, plastic shell having a planar top wall, a continuous skirt-like side wall, and a plurality of parallel rows of uniformly arranged cups formed in the top wall and depending into the recess defined by the side wall on the underside of the top wall. The side wall is formed with a support flange which spaces the cup bottoms above and out of contact with a planar support surface. The side wall is further formed with a shoulder which provides a support surface for stacking and locating one plate upon the other.

This is a streamlined continuation of our now abandoned application Ser. No. 271,003, filed Apr. 5, 1963, for Laboratory Apparatus.

This invention relates to laboratory apparatus and, more specifically, to disposable plates for use with microtitration apparatus of the type disclosed in copending application No. 135,364, filed Aug. 31, 1961, by Alan A. Duff et al. for Titration Apparatus.

The microtitration apparatus disclosed in the copending application referred to above is especially useful for conducting viral serological investigations and includes a series of Plexiglas plates, each having several rows of recesses which, in the course of a serological investigation, are filled with a minute volume (usually either 0.025 or 0.050 milliliter) of an appropriate diluent.

A number of dilution loops equal to the number of recess rows, each having a liquid-carrying head which usually has a capacity of either 0.025 or 0.050 milliliter, are then filled with a liquid reagent. The filled dilution loops are removed to the Plexiglas plates and inserted into the first diluent filled recess in each row. After rotating the loops to mix the reagent and the diluent, the loops are removed to the adjacent recess in each row and rotated to mix the diluted reagent carried by the loops with the diluent in those recesses. The process is repeated down the rows, progressively decreasing the concentration of the reagent in the recesses. The concentrations thus prepared are then treated or analyzed in accordance with the procedure established for the particular serological investigation being conducted.

The Plexiglas plates disclosed in the copending application referred to above are perfectly satisfactory under most circumstances. However, the Plexiglas plates must be thoroughly cleaned after each test to prevent interference with subsequent test patterns. This is a relatively complex procedure in which the plates are bathed in a sodium hypochlorite or formaldehyde solution for thirty minutes, rinsed thoroughly in running tap water, and placed in a warm detergent wash for thirty minutes. After the detergent wash, the plates are scrubbed with detergent, rinsed in tap water, rinsed in deionized water, and dried. It is also desirable to scrub the plates with a hand brush three times and fill and shake empty three times during each wash and rinse operation.

This cleansing cycle requires too much time and too much attention by trained personnel to be entirely satisfactory for widespread serological investigations as are

conducted during an epidemic, for example, to quickly isolate and identify the efficient cause of the disease.

It is, therefore, an object of the present invention to provide novel disposable microtitration plates, thereby eliminating the above-discussed cleansing cycle.

In conjunction with the foregoing object, it is another object of the present invention to provide microtitration plates which are sufficiently inexpensive that they can be discarded after a single use and which, in addition, permit accurate, rapid viral serological investigations to be made.

Disposable microtitration plates have heretofore been constructed. The prior art plates, however, are too flimsy and are not manufactured to sufficiently close tolerances to ensure consistently accurate test results.

It is, therefore, another object of the present invention to provide novel disposable microtitration plates which are substantially sturdier than any heretofore developed and which are fabricated with close tolerances, enabling accurate test results to be consistently obtained.

Additional objects and further novel features of the present invention will become more fully apparent from the appended claims and as the ensuing detailed description and discussion proceeds in conjunction with the accompanying drawing, in which:

FIGURE 1 is a top plan view of a disposable microtitration plate constructed in accordance with the principles of the present invention;

FIGURE 2 is a bottom view of the microtitration plate of FIGURE 1;

FIGURE 3 is a side view of the microtitration plate of FIGURE 1;

FIGURE 4 is an end view of the microtitration plate of FIGURE 1;

FIGURE 5 is a section through the microtitration plate of FIGURE 1, taken substantially along line 5—5 of FIGURE 3;

FIGURE 6 is a top plan view of a second microtitration plate constructed in accordance with the principles of the present invention;

FIGURE 7 is a bottom view of the microtitration plate of FIGURE 6;

FIGURE 8 is a side view of the microtitration plate of FIGURE 6;

FIGURE 9 is an end view of the microtitration plate of FIGURE 6;

FIGURE 10 is a section through the microtitration plate of FIGURE 6, taken substantially along line 10—10 of FIGURE 8;

FIGURES 11 and 12 illustrate diagrammatically the manner in which the novel microtitration plates provided by the present invention are fabricated; and

FIGURE 13 is a sectional view through a stack of several plates.

Referring now to FIGURES 1–5 of the drawing, the novel, disposable microtitration plate **20** of the present invention includes a top wall **22** onto which plural rows of precisely dimensioned, uniformly spaced cups **24** open, and an integral, depending side wall **26** extending around the periphery of top wall **22** for supporting plate **20** on a horizontal work surface. Disposable microtitration plate **20** is preferably molded from a synthetic plastic material such as Vynex, an extruded rigid vinyl sheet material produced by Nixon-Baldwin Chemicals, Inc. of Nixon, N.J. Vynex has exceptional dimensional stability over a wide humidity range, good chemical resistance, a high degree of transparency, high rigidity, excellent vacuum forming properties, low moisture absorption, and is easily fabricated. Other materials having these properties to a greater or lesser degree than Vynex may, of course, be substituted therefor without exceeding the scope of the broader aspect

of the present invention. In one practical embodiment of the present invention, plates **20** are 5.080 inches long, 3.250 inches wide, and are formed of 0.020 inch thick Vynex sheet.

In the illustrated embodiment, there are twelve rows of cups **24** and eight cups in each row, permitting plates **20** to be used for multiple titrations.

Referring now specifically to FIGURE 5, the cups **24** each have a cylindrical side wall **28**, a hemispherical end wall **30**, and a frusto-conical inlet lip **32**. Inlet lip **32** has an apex angle of approximately 90 degrees to ensure complete drainage into cup **24**. The juncture of inlet lip **32** and side wall **28** must be a sharp corner to prevent the formation of rings of red cells on the lip adjacent its juncture with the side wall as commonly occurred in prior art plates in which this corner was rounded.

Cylindrical side wall **28** and hemispherical end wall **30** each have a diameter of 0.236 inch. Cups **24** are 0.410 inch in depth. For accurate visual comparison of the contents of the several cups **24** of a given plate **20**, it is critical that the depths of cups **24** be equal. A tolerance of plus or minus 0.001 inch is therefore maintained in the commerical embodiment of the present invention.

Referring still to FIGURE 5, the cylindrical side walls **28** of cups **24** vary in thickness between microtitration plate top wall **22** and the lower ends **30** of the cups. This is an important feature of the present invention since by decreasing the side wall thickness, the thickness of the hemispherical end walls **30** is substantially increased in comparison with other arrangements and the cup, as a whole, is much sturdier than those of the prior art devices. Representative plate top wall and cup side and end wall dimensions are as follows:

Measurement:	Dimension in inches
A	0.012
B	0.010
C_1	0.003
C_2	0.002
C_3	0.008
D	0.017

As will be noted, the end wall of the cup is only .003 inch less than the orginal thickness (.020 inch) of the sheet from which the plate is formed despite the .410 inch depth and .236 inch diameter of the cup.

With continued reference to FIGURE 5, integral flanges **34** and **36** are formed on the lower edge of plate side wall **26** and are oriented, respectively, parallel and normal to side wall **26**. Outwardly directed flange **36** supports microtitration plate **20** from the work surface. Flange **34** cooperates with a shoulder **38** extending between flange **34** and side wall **26** to positively locate one disposable microtitration plate **20** relative to another when the plates are stacked as shown in FIGURE 13.

Turning now to FIGURES 6–10, microtitration plate **40** is similar to the microtitration plate **20** described above and like reference characters, but primed, have therefore been employed to designate the corresponding portions of microtitration plate **40**.

The only substantial distinction between microtitration plates **20** and **40** is that the lower end walls **30'** (see especially FIGURE 10) of cups **24'** are conical and terminate in a rounded lowered tip **42**. Rounded tips **42** eliminate the possibility of air bubbles being trapped in the lower ends of cups **24'**. This is extremely important because the reading of the deposit upon the internal surface **44** of the cup end walls **30'** is critical in certain tests.

The inside diameter of cups **24'** is on the order of 0.236 inch and their depth is 0.410 inch. The apex angle of rounded tip **42** is on the order of 118 degrees and the internal radius of the rounded tip is on the order of 0.015 inch.

The provision of plates having both conical and rounded end walls permits the microtitration apparatus described in the copending application referred to above to be used for complement fixation tests, metabolic inhibition tests, and the like, as well as hemagglutination tests and hemagglutination inhibition tests to which prior art devices were limited.

Disposable microtitration plates **20** and **40** will normally be sterilized and packaged in hermetically sealed sterile containers to prevent them from being contaminated.

Turning now to FIGURES 11 and 12, disposable microtitration plate **20** is formed from plastic sheet **44'** in vacuum molding apparatus provided with a male die **46** and a cooperating apertured die **48**. Suitable molding apparatus is well known. For this reason and because its details form no part of the present invention, a detailed description of the molding apparatus is deemed unnecessary.

Formed on male die **46** are a plurality of normally extending projections **50** configured to form cups **24** to the desired shape. The cooperating apertured or female die **48** has through apertures **52** at the cup locations. Male die **46** is fixedly mounted in the molding apparatus and apertured die **48** is mounted for movement toward fixedly mounted die **46** in the direction indicated by the arrow in FIGURE 12.

Male die **46** is heated in any appropriate manner as by forming it of resistive material and connecting it to a source of electrical potential.

Female die **48** is surrounded by an air-tight chamber **54** provided with an outlet **56**.

In the plate forming operation, the plastic sheet **44'** is arranged between the heated male die **46** and the co-operating apertured die **48** and vacuum chamber **54** is evacuated through outlet **56**. Apertured die **48** is then moved toward the fixedly mounted male die **46**. As the plastic sheet **44'** contacts projections **50** of male die **46**, it is heated and softened and forced into the apertures **52** in die **48** by the pressure differential existing between the lower and upper sides of the die. As die **48** continues to move toward die **46**, projections **50** follow the softened sheet into apertures **52**, forming cups **24** to their final configuration.

This novel cooperation of pressure and vacuum acting concomitantly on opposite sides of plastic sheet **44** produces the novel cup side and end wall configurations illustrated in FIGURE 5, substantially increasing the rigidity of cups **24** in comparison to the cups of the prior art devices.

It is to be understood, as will be apparent to one skilled in the art, that the microtitration plate **40** may be formed in a similar manner; that dies **46** and **48** may be appropriately formed to produce the supporting and nesting flanges **34**, **36**, **38**; and that the molding cycle described above may be automatically performed, permitting plates **20** and **40** to be molded at a high rate of speed.

The invention may be embodied in other specific forms without departing from the spirit or essential characteristics thereof. The present embodiments are therefore to be considered in all respects as illustrative and not restrictive, the scope of the invention being indicated by the appended claims rather than by the foregoing description, and all changes which come within the meaning and range of equivalency of the claims are therefore intended to be embraced therein.

What is claimed and desired to be secured by Letters Patent is:

1. A disposable plate for microtitration and like purposes comprising a molded, synthetic plastic shell having a planar top wall supported by a continuous depending marginal flange and having a plurality of parallel equal length transversely aligned rows of uniformly arranged, equal depth, open top cups formed in and depending from said top wall in parallel spaced apart relation and in a uniform pattern, said cups having annular side walls the internal surfaces of which are cylindrical and end walls the internal surfaces of which are surfaces of revolution, the thickness of said end walls of said cups being greater

than the thickness of said top wall and of said side walls of said cups whereby said cup end walls are provided with increased strength, said depending marginal flange being of a height slightly greater than that of the depending cups whereby contact between the external surfaces of said cup end walls and a planar work surface supporting such plate is precluded so long as said planar top wall is not deformed.

2. The disposable microtitration plate as defined in claim 1 wherein said internal surfaces of said cup end walls are conical and coaxial with said cylindrical surfaces, the diameter of the bases of said conical surfaces being equal to the diameter of said cylindrical surfaces.

3. The disposable microtitration plate as defined in claim 1 wherein said internal surfaces of said cup end walls are hemispherical, the centers of said hemispherical surfaces lying on the axes of said cylindrical surfaces and the diameter of said hemispherical surfaces being equal to the diameters of said cylindrical surfaces.

4. The disposable plate defined in claim 1 wherein each of the cup side walls decreases in thickness in directions converging both from said top wall and said cup end wall to a region of minimum thickness intermediate said top wall and said cup end wall, the maximum thickness of the cup side wall above said region being less than the maximum thickness of the cup side wall below said region.

5. A disposable microtitration plate comprising a molded, one-piece, synthetic, plastic shell having a planar top wall, a continuous skirt-like side wall extending around and normally depending from said top wall to delimit a downwardly opening recess beneath said top wall, and a plurality of parallel transversely aligned rows of uniformly arranged, equal depth, open top cups formed in said top wall and depending therefrom into said recess, said cups having annular side walls and end walls, the internal surfaces of said annular side walls being cylindrical, and the internal surfaces of said end walls being surfaces of revolution, the longitudinal axes of said cups being substantially normal to said top wall, said side wall terminating at its end opposite from said top wall in an integral, continuous support flange extending laterally outwardly from said recess in parallel relation with said top wall, said flange having a flat bottom surface which is adapted to be seated on a planar surface for supporting said top wall, the height between a plane containing the bottom surface of said flange and the said top wall being sufficiently greater than the length of said cups that the cups end walls are spaced by said flange above and out of contact with said planar surface, said side wall being formed with upper and lower skirt portions respectively joined to said top wall and to said flange, said lower portion being laterally outwardly offset from said upper portion and being joined thereto to define a continuous, planar shoulder having a downwardly facing surface which is parallel to the upper surface of said top wall, said shoulder providing a support surface which is adapted to seat on the top surface of a plate of like construction to enable like plates to be stacked one upon the other, said lower portion cooperating with said shoulder to positively locate one stacked plate with respect to the other with the cups of an upper plate stacked on a lower plate being disposed in axially aligned, nested relation with the cups of the lower plate.

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MORRIS O. WOLK, *Examiner.*

Disclaimer

3,356,462.—*Nelson M. Cooke*, Great Falls, Va., and *Paul H. Hall*, Clinton, Md. DISPOSABLE MICROTITRATION PLATE. Patent dated Dec. 5, 1967. Disclaimer filed Oct. 8, 1974, by the assignee, *Dynatech Laboratories, Incorporated.*

Hereby enters this disclaimer to claims 1, 2, 3 and 5 of said patent.

[*Official Gazette April 1, 1975.*]