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<p>(54) Title: METHODS AND APPARATUS FOR CARRYING OUT CLINICAL, CHEMICAL AND BIOLOGICAL TESTING</p>		
<p>(57) Abstract</p> <p>A method for carrying out a clinical, chemical or biological test, in which a macro-solid phase adsorbent test material is contacted with a sample and later washed or treated with a washing liquid, characterized in that the washing or reagent liquid treatment is carried out by (a) inserting the macro-solid phase test material into an apertured container in which there is located a compressible resilient porous liquid-retaining solid which contains washing or reagent liquid, (b) compressing the porous solid while the test material is in its inserted position to the extent necessary to wash or treat the surface of the test material, (c) releasing the compression to allow the porous solid to reabsorb substantially all the washing or treatment liquid, and (d) removing the washed or treated test solid substantially free of the washing or treatment liquid.</p>		

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Methods and Apparatus for Carrying Out Clinical, Chemical
and Biological Testing

This invention relates to devices and their use in
5 processes of clinical, chemical and biological testing. In
particular, the invention relates to devices for the
application of liquids, especially for example aqueous
washing liquids or reagents, such as water or buffer
solutions, to solid adsorbents or absorbent materials
10 which play a part in such test processes.

One important application of the invention is in the
facilitation of washing processes which have to be applied
to small bodies of adsorbent or absorbent materials during
15 the course of analytical or diagnostic procedures, such as
binding or absorption or adsorption tests, especially
immunoassays using solid immunosorbents.

It is an aim of the invention to enable a small solid
20 body to be washed by an arrangement for exposing it to
washing fluid while containing the washing fluid against
much of the normal risk of liquid spillage that attends
manipulations of this kind, so that a number of such
manipulations can be conveniently carried out by an

operator working at a table or bench without personal or environmental contamination by materials present on the solid body or in the wash fluid. It is recognised that complete security against risk of contamination during such liquid treatments is often very hard to achieve. The present invention aims to provide devices that can reduce such contamination risks significantly, even if it is not possible to eliminate them entirely with simple apparatus. The management of such contamination risks is particularly important in connection with diagnostic tests that involve possibly infectious material such as possibly septic clinical samples, or samples containing viral elements.

Among the prior art devices for handling test materials, GB Specification No. 1 392 912 (Philips) describes a device for use in radioimmunoassay in which a syringe contains an elastic sponge of which the porous surface carries a layer of antibody relevant to the assay. In the use of this device, a sample liquid is aspirated, the sponge is incubated with the sample liquid and then squeezed empty, before determination of its radioactivity. This prior art is not concerned with the problem of disposal of possibly contaminated materials used in test procedures, or with the spent washing liquids used in such procedures.

The prior art also includes a number of laboratory washing arrangements, eg. US 3 897 002 and FR 2 177 651. It is considered that these disclosures also do not concern themselves with the problem mentioned above.

According to the invention there is provided a method for carrying out a clinical, chemical or biological test, in which a macro-solid phase adsorbent test material is contacted with a sample and later washed or treated with a washing liquid or reagent liquid, wherein the washing or

reagent liquid treatment is carried out by (a) inserting the macro-solid phase test material into an apertured container in which there is located a compressible resilient porous liquid-retaining solid which contains washing or reagent liquid, (b) compressing the porous solid while the test material is in its inserted position, to the extent necessary to wash or treat the surface of the test material, (c) releasing the compression to allow the porous solid to reabsorb substantially all the washing or treatment liquid, and (d) removing the washed or treated test material substantially free of washing or treatment liquid.

A washer or liquid applicator device according to the invention comprises:

an apertured liquid container, having an aperture of suitable size to allow insertion of a solid test material which is to be washed or to have liquid applied to it;

a compressible resilient porous liquid-retaining solid, located within the container and (in use) retaining a liquid for washing or application to the said solid material, and

a compression member for compressing the porous liquid-retaining solid, while the solid test material is in its inserted position, to the extent necessary to wash the surface of the test material, the arrangement being such that liquid overflow does not occur upon compression of the porous solid, and that on release of the compressive force on the compression member the liquid can return and be reabsorbed by the porous solid.

Suitable examples of arrangements to prevent liquid overflow are (a) provision of a stop or limit to the extent of compression of the porous material, and/or (b) provision of container wells able to contain all the

liquid released when the porous material is fully compressed, where the arrangement allows this.

5 Suitable examples of the apparatus can have one or a plurality of cavities to receive solid test materials in the form of beads, strips, sticks, or pegs, e.g. in the form of assemblies comprising a plurality of solid test materials held by a common holder or carrier.

10 It is especially suitable for the apparatus to be designed for reasonably close complementarity to the shape and form of whatever test material or assembly of test materials it is desired to wash, and the invention accordingly includes the combinations of wash apparatus
15 and test material as well as the wash apparatus alone.

 The test material to be washed may either be completely enclosed in the apparatus during the washing operation or it may partly protrude, e.g. by a holder,
20 with only a relevant sensitised or reactive part being located within the washer.

 It is preferred for the lining of the cavity or cavities into which the test material is inserted to be
25 substantially rigid and not to be appreciably deformable or compressible, so that the surface of the test material is not appreciably wiped during the washing or liquid-application.

30 The cavities may therefore be lined with or consist of one or more apertured sleeves, e.g. of substantially rigid material, to allow insertion and removal of the test material and also the entry and exit of washing liquid. These can be let into apertures in the foam porous
35 material itself. The cavities can in particular take the form of borings or cavities or sleeves in or of a rigid

solid component of the apparatus, e.g. a lid or top component, that can for example fit within the container and be optionally sealed thereto with for example flexible sheet sealing material.

5

Compression of the porous liquid-retaining material is provided for by the construction of the apparatus in any suitable way, e.g. as follows. The container of the apparatus can have a flexible wall or wall portion
10 allowing the porous material to be squeezed and made to release its retained liquid. In this arrangement it is preferable to provide at least a pair of rigid wall portions or rigid container lining portions between which the porous material is compressed: this helps to provide
15 uniform compression when the apparatus is squeezed manually. An internal stop or stops can usefully be provided to ensure that the compression of the porous material is partial rather than complete.

20 In an alternative and preferred arrangement, compression of the porous material is achieved by pressure on the solid top component of the apparatus carrying the cavities into which the test material is inserted, e.g. downward pressure due to a continuation of motion or
25 exertion of pressure or force in the same direction as that in which the test material is inserted into the apparatus. The top component can for this purpose be a more or less close sliding fit in the container of the apparatus, which can for this purpose be substantially
30 rigid. All parts of the apparatus can be of plastics material, e.g. a thermoformed container and a solid moulded e.g. injection moulded sliding insert carrying the cavity or cavities. The container is in this arrangement preferably given an intermediate stop formation to prevent
35 complete compression of the porous material. Alternatively this stop can be part of the sliding insert,

or a separate, (e.g. substantially incompressible) solid component placed within the container.

The available distance of travel of the movable component(s) in the apparatus dictates the volume of liquid released at a maximum compression in use from the porous material. This volume is preferably matched carefully to the free space around the inserted test material so that the released liquid flows around the surfaces to be washed without overflow from the apparatus. If desired, the foam may contain less than the maximum volume of liquid it is capable of retaining.

Recovery of the apparatus from the compressed condition may occur by intrinsic resilience of the porous material or by a separate spring arrangement if desired.

After use the apparatus can be discarded to an incinerator if need be with little or no risk of environmental contamination en route. If desired, a clip-on lid can be provided.

The washing liquid may be any liquid that it is desired to apply to the test material, e.g. water, buffer, or saline, e.g. phosphate buffered saline to wash immunosorbent plastics surfaces, with or without detergents or other additives according to the purpose of the washing operation, and optionally including colour-forming or coloured reagents capable of indicating to the naked eye that the washing operation has been carried out, or other relevant reagents.

The resilient porous liquid-retaining material is chosen from among those materials that can retain liquid without appreciable dripping or loss in the absence of compression: preferably no such loss occurs at all. If

the porous solid is to contain and release a reagent, then it can be chosen to be effectively inert with respect to that reagent. If it is to be used to contain washing liquid which will be discarded, it can usefully be chosen as to possess sorptive capacity with respect to materials which are likely to be washed off the test objects. Preferably the porous material is a microporous hydrophilic foam material with a large (>c.90%) void volume. Microporous products suitable for this purpose can for example be made as described in GB Patent Specification No. 1 576 228 (Akzo), and certain suitable materials may also be found amongst those prepared according to GB Patent Specifications No. 1 078 055 (Rohm & Haas), No. 1 428 125 (ICI), No. 1 493 356 (ICI), USP 3 225 127 (Bayer), and European Patent application No. 0 060 138 (Unilever). Also suitable is a hydrophilic polyurethane foam with a water-holding capacity of about 30 times its own weight, and fine pores, about 70 to the linear inch, as available commercially under the name Acquell (Trade Mark) from Scott Paper Company, Chester, Pennsylvania, USA.

A non-limitative example of the invention is described below with reference to the accompanying drawings in which Figures 1, 2 and 3 respectively show in diagrammatic form a plan, side part-sectional view and end part-sectional view of a washer or liquid applicator arrangement according to an embodiment of the invention.

The apparatus comprises a thermoformed substantially rigid plastics container 1 with a flat upper flange 2 to which is bonded a sealing metal or metallised plastics or plastics foil strip 3 intended to be broken or torn off before use of the washing apparatus by pulling at end 4 where there is a weakened or perforate end to flange 2. The article can be prepared for use with or without a

liquid content: either a suitable liquid can be included or it can be left to the user to add liquid after opening the device.

5 Contained within container 1 is a volume 5 of microporous compressible resilient hydrophilic form which contains and retains a volume of washing liquid, e.g. purified water or substantially isotonic (about 0.9% w/v) saline buffered at near neutral pH. In this case the foam
10 is 'Acquell' (Trade Mark) polyurethane foam. Such material is effectively inert with respect to the test reagents.

 Occupying nearly all the remaining volume of
15 container 1 is a sliding insert 6 of solid injection-moulded plastics material having a number of cavities such as 7 in it. These cavities are open at the top and at the bottom, receive the test objects to be washed at the upper opening, and allow inflow and outflow
20 of liquid by the bottom opening.

 The pattern of cavities 7 corresponds to the shape of the test articles to be washed, with a little clearance to ensure that as far as possible delicate surfaces are not
25 scraped or rubbed. In this example the test articles to be washed are for example those shown in Figure 3 of published GB Patent Application No. 2 114 738 and described in that specification. Of course, the sliding insert can alternatively be given whatever pattern of
30 cavities is needed to accommodate the objects to be washed and can have if needed some retaining constriction, neck, plug or mesh to stop the objects from dropping right through.

In use the object to be washed can be inserted into the cavities 7 in sliding insert 6 and the insert 6 directly or indirectly pushed down manually until its lower end edges come to rest against shelf-formations 8 in container 1 which act as stops against the further downward movement of insert 6. Foam 5 is compressed by the downward movement and releases part of its liquid content which as free liquid then flows into the cavities 7 in sliding insert 6, and there, without overflowing, contacts and washes the surfaces of the test objects to be washed. On withdrawal, preferably at a moderately slow and defined rate of the test objects or else on stopping the downward pressure, the insert 6 rises back to its original position and the free liquid is drawn back substantially entirely into its original position held in foam 5, from which it does not escape by dripping.

This apparatus enables the washing of possibly infective material, e.g. material possibly contaminated by hepatitis virus, with very low risk of contaminating the user or the environment, because of the good degree of containment and absorption of the washing fluid. Whenever it is arranged that there is no liquid overflow from one cavity 7 to the next the risk of cross-contamination between test objects, i.e. possibly between different samples representing different levels of infective material, is practically eliminated.

This arrangement is especially of use where test objects comprising macro-solid phase specific binding sorbents, e.g. immunosorbents, have to be treated to washing operations in the course of immunoassay procedures. The arrangement can therefore form part of a convenient test kit comprising complementary formed macro-solid phase immunosorbent and ancillary materials to carry out the assays. "Complementary" means only that the

immunosorbents can be inserted conveniently into the cavities. It can be seen that the invention disclosed by the present specification and claims is susceptible to variations and modifications to achieve the functions and purposes described above: and includes all combinations of the features described and illustrated herein.

CLAIMS

1. A method for carrying out a clinical, chemical or biological test, in which a macro-solid phase adsorbent
5 test material is contacted with a sample and later washed or treated with a washing liquid or reagent liquid, characterised in that the washing or reagent liquid treatment is carried out by (a) inserting the macro-solid
10 phase test material into an apertured container in which there is located a compressible resilient porous liquid-retaining solid which contains washing or reagent liquid, (b) compressing the porous solid while the test material is in its inserted position to the extent
15 necessary to wash or treat the surface of the test material, (c) releasing the compression to allow the porous solid to reabsorb substantially all the washing or treatment liquid, and (d) removing the washed or treated
20 test solid substantially free of the washing or treatment liquid.
2. A washer or liquid applicator device suitable to form part of a diagnostic test kit which involves the use of a solid adsorbent test material, which device comprises:
- 25 an apertured liquid container (1), having an aperture of suitable size to allow insertion of a solid test material which is to be washed or to have liquid applied to it;
- 30 a compressible, resilient porous liquid-retaining solid (5), located within the container and (in use) retaining a liquid for washing or application to the said solid material, and
- 35 a compression member (6) for compressing the porous liquid-retaining solid(s), while the solid test material is in its inserted position, to the extent necessary to wash the surface of the test material, the arrangement

being such that liquid overflow does not occur upon compression of the porous solid (5), and that on release of compressive force on the compression member (6) the liquid can return and be reabsorbed by the porous solid (5).

3. A device according to Claim 2, wherein the compression member (6) comprises a sliding insert located within container (1) and possessing aperture(s) (7) to receive the test objects to be washed or treated with reagent liquid.

4. A device according to Claim 3, wherein a stop (8) is provided to limit the movement of compression-member (6).

5. A device according to Claim 1, wherein the compression member (6) comprises a flexible wall of container (1).

6. A test kit comprising the combination of a washer or liquid applicator device according to Claim 2, 3, 4 or 5, with a complementary solid test body or bodies of adsorbent test material, wherein the solid test body or bodies have such a size as to be receivable with clearance into an aperture or apertures (7) of the washer or liquid applicator device.

7. A test kit according to Claim 6, wherein the test body carries immunosorbent sensitisation.

8. A test kit according to Claim 6 or 7, wherein the compression-member (6) comprises a sliding insert having aperture(s) (7) to receive one or a plurality of beads, strips, sticks or pegs of the test body or bodies.

9. Devices and test kits according to any of Claims 2 to 9, wherein the porous solid (5) is a microporous

hydrophilic resilient foam, eg. having at least about 90% void volume.

3
5 10. Methods, devices and test kits according to any preceding claim, characterised by any one of more of the several features of the accompanying description and drawings.

Fig. 1.

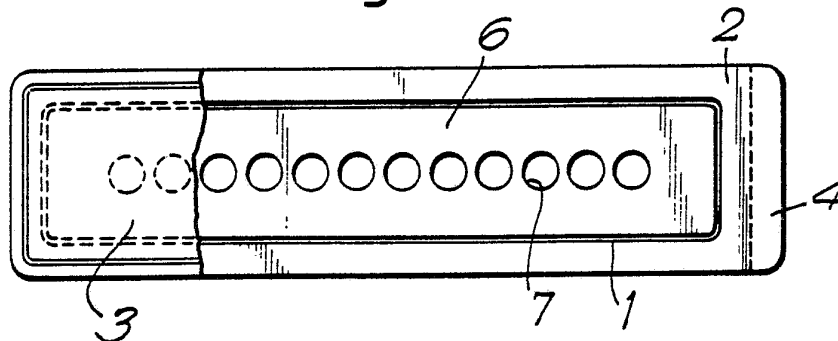


Fig. 2.

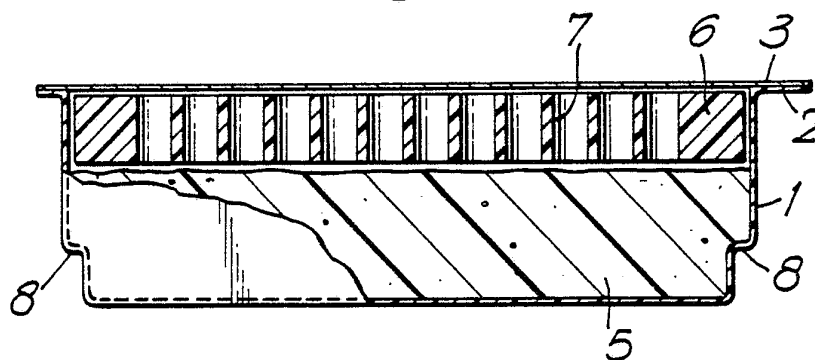
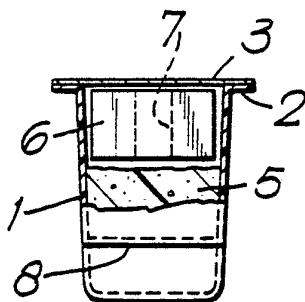


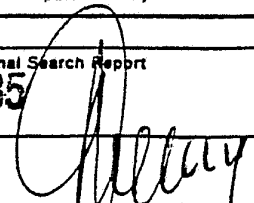
Fig. 3.



INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 85/00239

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) *		
According to International Patent Classification (IPC) or to both National Classification and IPC		
IPC ⁴ : G 01 N 33/53; G 01 N 33/543; B 01 L 11/00		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System ¹	Classification Symbols	
IPC ⁴	G 01 N B 01 L	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category ⁶	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
A	AU, B, 495838 (PHILIPS' GLOEILAMPENFABRIEKEN) 17 October 1974 & GB, A, 1392912 (cited in the applica- tion)	
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A	FR, A, 2536313 (BIOMERIEUX) 25 May 1984	
A	WO, A, 82/03690 (PHARMACIA DIAGNOSTICS) 28 October 1982	
A	DE, B, 1207116 (ABBOTT LABORATORIES) 16 De- cember 1965	
A	US, A, 4087248 (L.E. MILES) 2 May 1978	
A	EP, A, 0060138 (UNILEVER N.V.) 15 September 1982 (cited in the application)	

<p>* Special categories of cited documents: ¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	
24th September 1985	16 OCT. 1985	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	 G.L.M. Kraudenberg	

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON

INTERNATIONAL APPLICATION NO. PCT/GB 85/00239 (SA 9833)

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 09/10/85

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
AU-B- 495838	17/10/74	None	
FR-A- 2536313	25/05/84	None	
WO-A- 8203690	28/10/82	SE-A- 8102316 EP-A, B 0076300	11/10/82 13/04/83
DE-B- 1207116		NL-A- 264183 FR-A- 1315725 US-A- 3206602 US-A- 3376114 US-A- 3372992 CH-A- 404243	
US-A- 4087248	02/05/78	None	
EP-A- 0060138	15/09/82	AU-A- 8126282 JP-A- 57198713 CA-A- 1184553 US-A- 4522953	16/09/82 06/12/82 26/03/85 11/06/85

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