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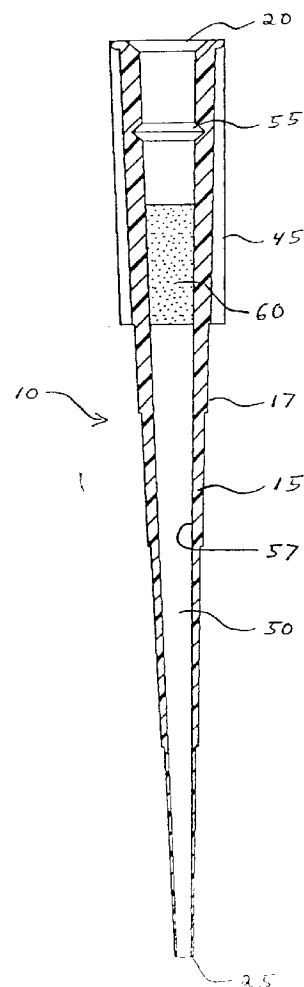
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(54) **Pipette Tip**

(57) A disposable pipette tip (10) having an aerosol absorbing foam as a barrier (60) to fluid flow that does not interfere with air flow through the pipette tip (10). The aerosol absorbing foam is an open cell foam having a web-like structure that permits the flow of air through the foam and passageway but prevents droplets or aerosols from passing through the foam and passageway. The flow of air is sufficient to permit an automated aspirating instrument to detect fluid using air flow changes.

FIG-2



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Description**BACKGROUND OF THE INVENTION**5 **1. Field of the Invention**

The present invention relates to an aerosol barrier for use in a disposable pipette tip and, more particularly, to a disposable pipette tip having an aerosol barrier made from an absorbent open cell foam that provides sufficient air flow through the disposable pipette tip to perform air flow fluid detection but sufficiently blocks droplets and aerosol from flowing through the disposable pipette tip.

10 **2. Background Description**

A pipette is a device commonly used in reagent laboratories as a fluid transfer device to perform addition and mixing of liquid components, i.e., reagents and samples.

Early transfer devices were typically glass pipettes or glass tubes with a hollow interior that allowed liquid to be pulled into their distal end by applying a vacuum at their proximal end. The vacuum was usually applied using the mouth of a laboratory worker or by a suction bulb attached at the proximal end of the glass pipette. Since these types of glass pipettes were often re-used they had to be cleaned extensively to prevent cross-contamination of reagents or samples.

Later, disposable pipette tips were introduced to help laboratories avoid the problems of cross-contamination associated with reusing pipettes. The disposable pipette tips were attached to the distal end of mechanical aspirators, i.e., a pipettor, and were designed to fit on the end of the mechanical aspirator so that the only air path from the mechanical aspirator was out the distal end of the disposable pipette tip. The mechanical aspirator typically used a plunger to push air through the aspirator and out the distal end of the disposable pipette tip, prior to the distal end being inserted into a fluid to be aspirated from a source container. After the distal end was placed in the fluid, the plunger on the mechanical aspirator was released to draw a vacuum into the disposable pipette tip and thereby pull fluid from the source container into the disposable pipette tip. The aspirated fluid contained in the disposable pipette tip could then be dispensed into a target container using the plunger.

After use, disposable pipette tips were commonly ejected from the mechanical aspirator using a tubular or ejector sleeve that pressed against the top of the disposable pipette tip to push the pipette tip off the mechanical aspirator. The operation of ejecting the disposable pipette tip from the mechanical aspirator in this manner has the potential for creating aerosols from liquid residues within the disposable tip within the mechanical aspirator. In addition, aerosols within the mechanical aspirator can also be generated when aspirating fluid into the disposable pipette tip. Aerosols coming from the pipette tip into the mechanical aspirator can potentially contaminate the mechanical aspirator and, therefore, other reagents or samples. One proposed solution to the aerosol problem was to add a porous barrier between the fluid and the mechanical aspirator. Typically a hydrophobic filter plug, made of polyethylene, for example, has been used to prevent fluid and aerosol passage from the distal end of the pipette tip into the mechanical aspirator without impacting aspirations and dispensing of the fluid from the disposable pipette tip.

More recently, robotic aspirating instruments have come to replace manual mechanical aspirators, especially in high throughput, or more labor intensive environments that require more automation. Robotic aspirating instruments have typically consisted of a stainless steel needle that aspirates fluid into its distal end from a target container by applying a vacuum to its proximal end by hydraulic displacement, for example. Of course, such robotic aspirating instruments must be washed periodically to prevent cross-contamination of reagents or samples. Because of this problem, disposable pipette tips have been attached to the robotic aspirating instruments to reduce the risk of cross-contamination. However, when using a robotic aspirating instrument in an automated environment it is critical for the controller of the instrument to detect when its distal end enters the fluid in the target container. This problem has been addressed by providing such robotic aspirating instruments with fluid detection capability to prevent their distal end from being plunged too far into the fluid. Typically, when using a metal or stainless steel needle, fluid detection can be performed by monitoring capacitance in the needle, where a change in capacitance indicates entry of the distal tip into the fluid. However, capacitance flow detection will not work without using more expensive, non-standard disposable plastic pipette tips, typically of conductive plastic. When using a standard nonconductive disposable plastic pipette tip, fluid detection is performed by monitoring air flow, where a change in air flow indicates blockage at the distal end of the pipette tip by fluid.

A problem, however, is encountered when using air flow fluid detection, if the disposable pipette tip contains a barrier to prevent aerosol passage into the robotic aspirating instrument. Aerosol filter barriers used in disposable pipette tips are often submicron hydrophobic plugs that cause large resistance to air flow. Such barriers are too dense to allow sufficient air flow, which causes a detrimental effect on small volume pipetting and does not work at all with

automated robotic aspirating instruments that use air flow fluid detection. Therefore, there is the need for a new kind of barrier to be used in disposable pipette tips that will sufficiently entrap fluid and aerosol from flowing into the robotic aspirating instrument, but provide sufficient air flow for an air flow fluid detection system to operate.

5 **SUMMARY OF THE INVENTION**

The present invention overcomes the problems identified in the background material by providing a barrier for a disposable pipette tip that allows sufficient air flow through the pipette tip into a robotic aspirating instrument for an air flow detection system to operate, but continues to sufficiently entrap fluid and aerosol from flowing through the pipette tip and into the robotic aspirating instrument.

10 A preferred embodiment of a pipette tip according to the present invention includes a cannula having a distal and proximal end, with the proximal end being larger than the distal end and both ends being connected by a passageway. A barrier is mounted within the passageway of the pipette tip near the cannula's proximal end to capture and prevent fluid and aerosol from flowing through the pipette tip and out the proximal end. However, the barrier allows sufficient air flow through the pipette tip to permit air flow liquid detection systems in a robotic aspirating instrument to properly operate. Preferably, the barrier is made from a highly absorbent open cell foam that can sufficiently trap aerosols but not restrict air flow.

15 These and other aspects, features and advantages of the present invention will become apparent from the following detailed description taken in conjunction with the accompanying drawings.

20 **DESCRIPTION OF THE DRAWINGS**

Fig. 1 is a perspective view of a pipette tip according to the present invention;

25 Fig. 2 is a cross-sectional view of the pipette tip shown in Fig. 1;

Fig. 3 is an electron microscope photograph of a foam barrier in the pipette tip shown in Fig. 1; and

30 Fig. 4 is an electron microscope photograph of a prior art barrier used in conventional pipette tips.

DETAILED DESCRIPTION

Fig. 1 is a perspective view of a pipette tip 10, according to the present invention, for use on a manual or robotic aspirating instrument to perform fluid transfer in a laboratory.

35 Pipette tip 10 includes an open cannula 15 having a generally tapering conical shape defined by a cylindrical outer wall 17. Cannula 15 includes an open proximal end 20 and an open distal end 25 with a plurality of optional annular gradations 130, 135 and 140 on outer wall 17 therebetween. Cannula 15 also includes a plurality of ribs 45 projecting from outer wall 17 and extending longitudinally from proximal end 20 towards distal end 25. Ribs 45 are provided to vertically support pipette tip 10, when attaching pipette tip 10 to an aspirating instrument. Vertical axial alignment is critical to robotic attachment of pipette tip 10 to an aspirating instrument, especially if automatic vision aids are not present.

40 Optional gradations 130, 135 and 140 divide cannula 15 into sections 30, 35 and 40 with each gradation 130, 135 and 140 representing a predetermined volume of liquid that may be located between the respective gradation and distal end 25 within cannula 15. These gradations are used by laboratory workers when visually measuring the volume of aspirated liquid during a manual pipetting operation. For example, when the level of the liquid within cannula 15 is aligned with gradation 130 the approximate volume of liquid contained in section 30 of cannula 15 between distal end 25 and gradation 130 is 10 μ l; when the level is aligned with gradation 135 the approximate volume of liquid in sections 30 and 35 is 50 μ l; and when the level is aligned with gradation 140 the approximate volume of liquid in sections 30, 35 and 40 is 100 μ l. Preferably, the total volume of liquid that can be held in this usable portion of pipette tip 10 is approximately 120 μ l. Of course, the above-noted volumes are merely exemplary, the present invention will also work and be very beneficial for pipette tips having larger and smaller volumes with or without gradations.

45 Fig. 2 is a cross-sectional view of pipette tip 10, shown in Fig. 1 along lines 2-2, and shows a passageway 50 with a generally tapering conical shape extending from proximal end 20 to distal end 25. As shown in Fig. 2, passageway 50 is defined by an interior wall 57 having a diameter that decreases from proximal end 20 to distal end 25. A foam barrier 60, according to the present invention, is contained within passageway 50 near proximal end 20 and is preferably mounted in place using a light friction press fit. However, other means, i.e., adhesive, could also be used to mount foam barrier 60 in position.

50 Foam barrier 60 is preferably an open cell aerosol absorbing foam having a web-like or filamentous structure,

similar to that shown in Fig. 3, that permits the flow of air through the foam but prevents droplets or aerosols from passing through the foam. Fig. 3 is an electron microscope photograph of an actual foam barrier 60 for use in pipette tip 10, according to the present invention. Foam barrier 60 having the structure of the present invention properly performs as a barrier to fluid droplets and aerosol that attempt to travel up passageway 50 from distal end 25 towards proximal end 20, during an aspiration process or when pipette tip 10 is ejected from the distal end of the aspirating instrument, and does not overly restrict the air flow necessary to perform automated air flow fluid detection.

During use, pipette tip 10 containing foam barrier 60 is attached to the distal end of the aspirating instrument and held in place by friction on the distal end of the aspirating instrument. When transferring a reagent or sample from a source container to a target container the distal end of the aspirating instrument with pipette tip 10 thereon is moved over the source container and slowly lowered into the fluid to be aspirated. As the disposable pipette tip is being lowered into the fluid the aspirating instrument generates an air flow through pipette tip 10 which is monitored by a controller to detect a change in air flow, when distal end 25 of pipette tip 10 enters the fluid. When a decrease in air flow is sensed, the aspirating instrument can determine that pipette tip 10 has entered the fluid and can begin an aspiration process, wherein a vacuum is applied to proximal end 20 to aspirate fluid through distal end 25 of pipette tip 10 and into passageway 50. The vacuum is applied until a predetermined volume of fluid has been aspirated into passageway 50. Then, the aspirating instrument extracts pipette tip 10 from the fluid source and moves pipette tip 10 to the target container to dispense the aspirated fluid.

When the aspirating instrument has positioned pipette tip 10 over the target container, air pressure is applied to proximal end 20 to dispense a volume of fluid in passageway 50 into the target container. After dispensing the fluid into the target container, when the aspirating instrument extracts pipette tip 10 from the target container and allows residue fluid to form across distal end 25 any sudden pipetting movements can aerosolize this residual fluid. After fluid transfer is complete, the aspirating instrument ejects pipette tip 10 from its distal end into a disposal container which violently displaces a large volume of air from proximal end 20 of passageway 50 in pipette tip 10 causing a momentary vacuum, and high velocity aerosolization of the residual fluid volume contained within distal end 25 of pipette tip 10. However, foam barrier 60 is designed and formed of a material, described below, that captures any such fluid and aerosol to prevent it from flowing into, impacting upon, or being passed by the aspirating instrument.

Cannula 15 can be made from any form of plastic and foam barrier 60 can be made from polyurethane, polyvinylchloride or polyvinylalcohol. Preferably, foam barrier 60 is formed from a melamine-based open cell foam with a density in range of 0.5 to 0.8 pcf, with the most preferred density being 0.7 pcf. Foams having these general properties are available from a number of suppliers for use as a thermal and acoustical insulation. In particular, Willtec™ foam available from illbruck, Inc. in Minneapolis, Minnesota, is a flexible, lightweight melamine-based open cell foam having the preferred density of 0.7 pcf. In addition, Willtec™ foam exhibits chemical resistance to organic solvents as well as to a series of diluted acids and alkali. Other physical properties of Willtec™ foam are:

Physical Properties	Typical Values	Test Methods
Tensile Strength	8.0 psi	ASTM D3574-77
Tear Strength	0.3 lb/in	ASTM D3574-77
Ultimate Elongation	8.0%	ASTM D3574-77
Temperature Stability	-60°C to 150°C permanent 24 hours to 250°C possible	

Willtec™ foam is, of course, merely exemplary of a foam that can be used to form a foam barrier 60 according to the present invention. More importantly, as described above, foam barrier 60 must be made from a foam material that does not overly restrict the flow of air through foam barrier 60, but does prevent droplets or aerosols from passing through foam barrier 60. It has been determined that an open cell foam structure, similar to that shown in Fig. 3, satisfies this criteria and that a closed, ball-like or globular structure, similar to that shown in Fig. 4 does not perform as well. Fig. 4 is an electron microscope photograph of a prior art barrier found in conventional aerosol filtered pipette tips. The barrier shown in Fig. 4 does not provide sufficient air flow to permit air flow fluid detection to be performed by an automated robotic aspirating instrument. If foam like that shown in Fig. 4 is used in a disposable pipette tip on an automated robotic aspirating instrument it would be impossible for the instrument to determine if the pipette tip has entered the reagent or sample using the air flow detection technique.

Conventional manufacturing techniques can be used to manufacture foam barrier 60 from Willtec™ foam. For example, a cork borer is used to punch a "plug" shaped foam barrier 60 from a 0.25 inch thick sheet of Willtec™ foam. The "plug" shaped foam barrier 60 is then inserted through proximal end 20 of pipette tip 10 and pressed to a predetermined position within passageway 50. Of course, this manufacturing technique and the materials and tool used are merely exemplary, various other manufacturing methods and materials could also be used.

In the foregoing discussion, it is to be understood that the above-described embodiment is simply illustrative of a

disposable pipette tip having an aerosol absorbing foam as a barrier to fluid flow that does not interfere with air flow through the pipette tip, in accordance with the present invention. Of course, other suitable variations and modifications could be made to this embodiment and still remain within the scope of the present invention.

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Claims

1. A pipette tip for use on an aspirating instrument comprising:

10 a cannula having an open proximal end and an open distal end with a passageway extending from said open proximal end to said open distal end; and
a barrier located within said passageway, said barrier being formed from an open cell foam capable of preventing an aerosol entering said distal end from passing through said passageway to said proximal end without restricting air flow through said passageway.

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2. A pipette tip according to Claim 1, wherein said foam is an open cell foam having a web-like structure.

3. A pipette tip according to Claim 2, wherein said foam has a density in a range between 0.5 pcf to 0.8 pcf.

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4. A pipette tip according to Claim 3, wherein said density is 0.7 pcf.

5. A pipette tip according to Claim 1, further comprising means for removably attaching said pipette tip to said aspirating instrument.

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6. A pipette tip according to Claim 1, wherein said foam is an absorbing foam.

7. A pipette tip according to Claim 1, wherein said foam is an open cell foam that is not hydrophobic.

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8. A pipette tip according to Claim 1, further comprising means for vertically supporting said pipette tip when robotically attaching said pipette tip to said aspirating instrument.

9. A pipette tip according to Claim 8, wherein said means for vertically supporting said pipette tip when robotically attaching said pipette tip to said aspirating instrument comprises a plurality of ribs projecting from said cannula and extending longitudinally from said proximal end towards said distal end.

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10. A pipette tip according to Claim 1, wherein said foam is made from a melamine-based open cell foam material.

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FIG-1

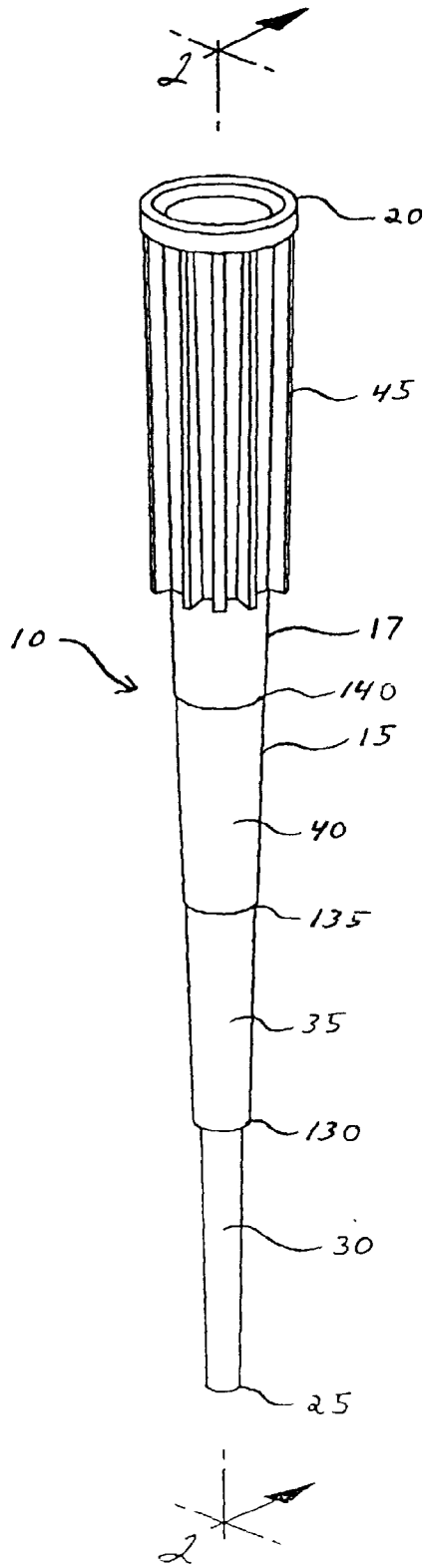


FIG-2

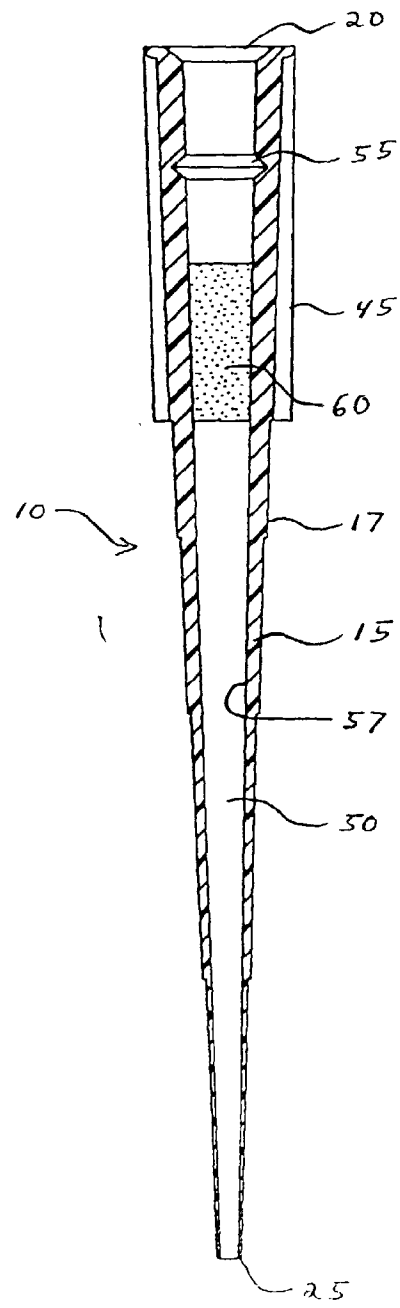


FIG-3

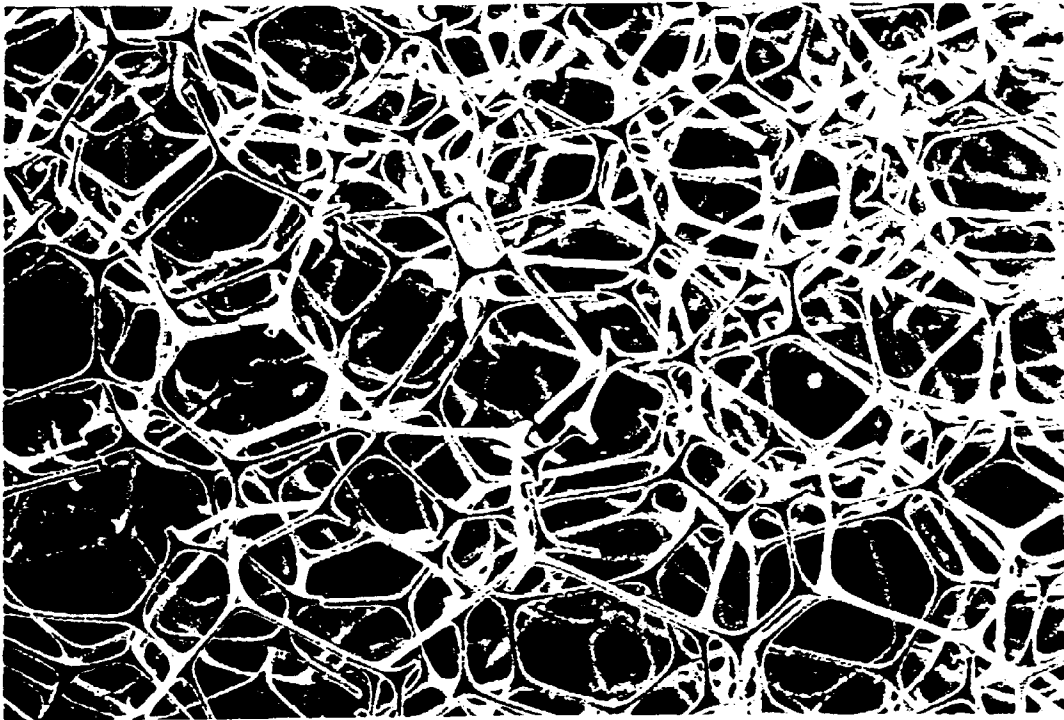
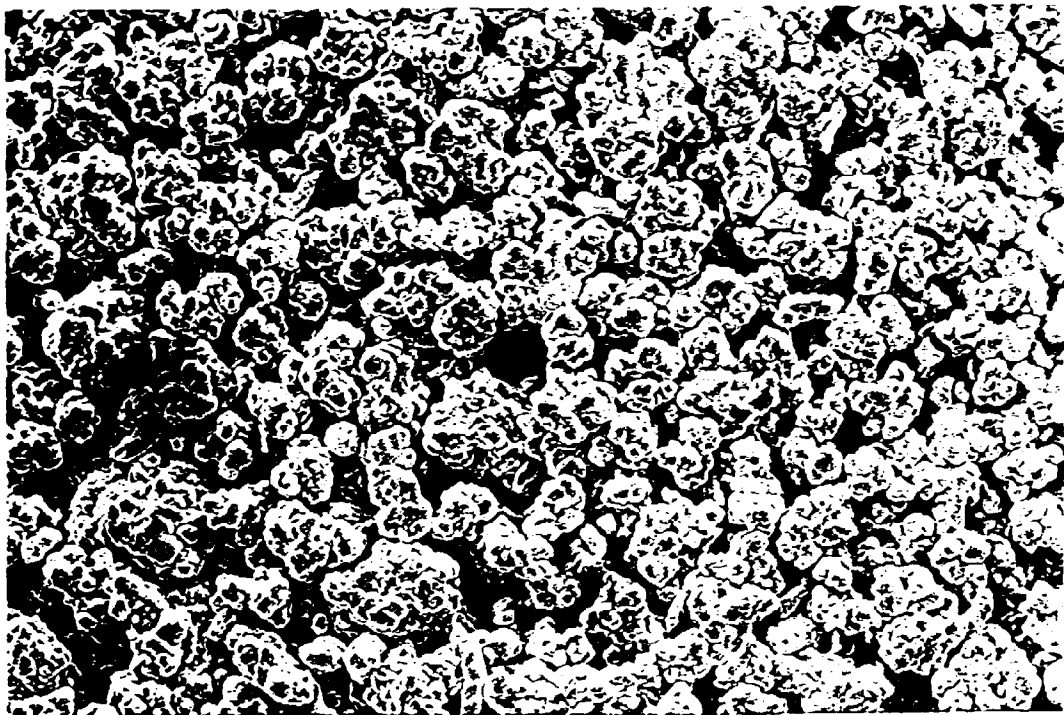


FIG-4 PRIOR ART





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EUROPEAN SEARCH REPORT

Application Number
EP 96 30 1946

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.6)
A	US-A-5 364 595 (SMITH MICHAEL W) 15 November 1994 * the whole document * ---	1,5	B01L3/02
A	US-A-4 119 403 (REX JOHN WALTER) 10 October 1978 * column 3, line 21 - column 4, line 13 * ---	1	
P,A	US-A-5 477 256 (LOYD JOHN C ET AL) 19 December 1995 * abstract * ---	1,6,7,10	
A	US-A-4 267 729 (EDELDMAN ROY T ET AL) 19 May 1981 * column 2, line 29 - line 56 * ---	1,5	
A	US-A-5 156 811 (WHITE DAVID A) 20 October 1992 * abstract * ---	1,5,7	
A	DE-A-21 55 566 (JANSEN HELMUT DR MED) 17 May 1973 * claim 1 * -----	1	TECHNICAL FIELDS SEARCHED (Int.Cl.6)
			B01L
The present search report has been drawn up for all claims			
Place of search THE HAGUE		Date of completion of the search 27 June 1996	Examiner Bindon, C
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons ----- & : member of the same patent family, corresponding document	

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