

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
23 June 2011 (23.06.2011)

(10) International Publication Number  
**WO 2011/075075 A1**

- (51) International Patent Classification:  
*B01L 3/02* (2006.01)
- (21) International Application Number:  
PCT/SE2010/051435
- (22) International Filing Date:  
20 December 2010 (20.12.2010)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
0950991-0 18 December 2009 (18.12.2009) SE
- (71) Applicant (for all designated States except US): **ZAFENA AB** [SE/SE]; Sjöbacka Fallhagen 1, S-590 76 Vreta Kloster (SE).
- (72) Inventors; and  
(75) Inventors/Applicants (for US only): **RÅNBYS, Mats, Gustaf** [SE/SE]; Sjöbacka Fallhagen 1, S-590 76 Vreta Kloster (SE). **ERICSSON, Carl, Stefan, Thorsten** [SE/SE]; Algatan 21, S-565 33 Mullsjö (SE).
- (74) Agent: **AWAPATENT AB**; Att: Sofia Sander Jakobsson, Junkersgatan 1, S-582 35 Linköping (SE).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO,

[Continued on next page]

(54) Title: MICROPIPETTE

(57) Abstract: Disclosed is a micropipette provided with a capillary tube adapted for collecting a well-defined volume of liquid by capillary action, a gas displacement mechanism, and a tubular body to which ends the capillary tube and the gas displacement mechanism are connected, respectively. The inner surfaces of the capillary tube and the tubular body have different capillary capacity. The micropipette may be used for collecting and discharging well-defined volumes of liquid and for mixing a first collected volume of liquid in a second volume of liquid, which may be larger than the first volume of liquid.

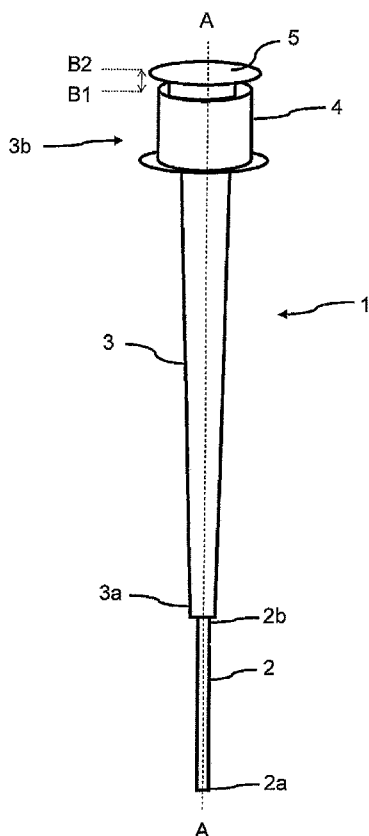


Fig. 1

WO 2011/075075 A1



DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**(84) Designated States** (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG,

**Published:**

— with international search report (Art. 21(3))

MICROPIPETTETechnical field

The present invention relates to a micropipette for collecting and discharging well-defined volumes of liquid. The micropipette is provided with a capillary tube, a gas displacement mechanism, and a tubular body to which  
5 ends the capillary tube and the gas displacement mechanism are connected, respectively. The invention also relates to methods in which the micropipette is used, in a kit (set of parts) comprising the micropipette, and an assembly for use in the micropipette. The invention further relates to a micropipette suitable for mixing of liquids.

10

Background

Pipettes provided with capillary tubes that automatically are filled with liquids when placed in such liquids are useful when, for example, collecting blood samples at high-hygiene requiring sites such as a finger puncture.

15

In US 3,952,599 a pipette is shown where the bore of the capillary tube has two adjacent zones, a hydrophilic first zone and a second zone, which is made hydrophobic by coating of the bore with for example bees wax, paraffin wax or dilute lacquers of hydrophobic plastics. When the hydrophilic end of the tube is placed into contact with a liquid it is filled until the liquid reaches  
20 the interface between the two zones. The content of the capillary tube may then be added into a container with a second liquid by connecting the hydrophilic end of the capillary tube to the container, and repeatedly squeezing the container to mix the two liquids. Coating of the second zone of the hydrophilic bore, making it hydrophobic, is quite complicated and it is  
25 difficult to get a distinct interface between the two adjacent zones. As a consequence the volume collected by the capillary tube may be less well-defined and may also vary between different pipettes.

Microcaps® marketed by Drummond is a micropipette which is composed of a capillary tube connected to a second tube having a much

larger diameter than the diameter of the capillary tube. One end of the capillary tube is inserted through a central hole in a rubber plug and this rubber plug is in turn plugged into one end of the second tube, creating a tight seal between the two tubes. The second tube is further provided with a squeeze bulb at its second end. With this micropipette a well-defined liquid volume is collected and discharged by the capillary tube. If the discharge of the collected liquid is in a larger volume of a second liquid, the inside of the capillary may be rinsed with the mixture by cautious manipulation of the squeeze bulb. If mixing of the two liquids is desired, then there is only one obvious and practical, but less attractive, way to do this by use of the Microcap, and this is by more forcibly squeezing the squeeze bulb to force gas or air to bubble through the mixture-

A disadvantage with Microcaps® is that it requires considerable skill for successful use. Upon incautious manipulation of the squeeze bulb to discharge the collected liquid into a larger volume of second liquid, and subsequent rinsing of the inside of the capillary tube with the mixture, there is an ever present risk that some, or most, of the mixture is sucked up through the capillary and be trapped at the bottom of the in second tube. This, apart from resulting in loss of sample and disruption of the ongoing activity, will require that the second tube with its rubber plug is either replaced or is dismantled and carefully cleaned

In US 6,531,098 a pipette device formed from a single, continuous tube of hydrophilic and elastomeric material is shown. It has an elongate capillary section with a fluid port formed at one end of the tube, a bulbous section with sealed end at the other end of the tube, and a central channel extending along the entire length of the tube. A vent means, a small hole, is provided on the capillary section. The location of the vent hole relative the fluid port defines the volume that may be collected by the capillary tube. This pipette device may allow for mixing of the collected volume in a second volume by either drawing the mixture up into the sealed bulbous section of the device and discharging it, or by stirring the mixture by rotating the device between fingertips while the capillary end of the device is submerged in the mixture. As a consequence of the manufacturing process there is a pair of opposed fins

fixed to and projecting radially-outwardly from the capillary section. These fins may aid the mixing during the stirring of the mixture.

A disadvantage with this pipette device stems from the pair of fins, which forms creases and crevices on the outside of the capillary portion that will trap unintended volumes of the collected liquid in a way that resists attempts of removal, and thus compromises the precision and accuracy of the pipette.

Another disadvantage with this pipette is inherent to the position and function of the vent hole. Liquid in the capillary section will come in contact with the vent hole and there will be a risk of leakage of liquid through the vent hole to the outside of the device.

Thus, there is a need for an alternative or improved micropipette which can be used for collecting and discharging a well-defined volume of liquid, and in particular wherein the pipette also can be used for mixing of the collected volume in a second volume of liquid.

Further, in the mentioned mixing, it is usually desirable to discharge as little gas, most often air, as possible into the mixture, as gas bubbles may adhere to the walls of the container containing the mixture and interfere with optical analysis of the mixture, or in other ways be of nuisance. Furthermore, air or gas bubbles introduced into the mixture may induce the formation of additional air bubbles that cause additional problems. The latter is the case when one or both of the two liquids are rich in carbonic acid, as is for example the case when one, or both, of the liquids is anti-coagulated blood. Therefore it is desirable to have a micropipette with which as little gas as possible is discharged together with collected liquid.

### Summary

It is an object of the present invention to provide an alternative or improved micropipette and use thereof for collecting and discharging a well-defined first volume of liquid, which pipette can be used for mixing of the collected liquid volume in a second volume of liquid that may be larger than the first volume.

The object is wholly or partially achieved by a micropipette, methods using the micropipette, a kit comprising the micropipette and an assembly for

use in the micropipette as defined by the respective independent claims. Embodiments are set forth in the appended dependent claims, in the following description and in the drawings.

According to a first aspect of the present invention, there is provided a  
5 micropipette comprising a capillary tube adapted for collecting a well-defined volume of liquid by capillary action, the capillary tube having a central, axial channel. The micropipette further comprises a gas displacement mechanism, and a tubular body provided with a central, axial channel. The tubular body has a first end and a second end, where the first end is connected to one end  
10 of the capillary tube forming a tubular body-capillary tube assembly with a through channel comprising the axial channels of the capillary tube and the tubular body. The second end of the tubular body is connected to the gas displacement mechanism. A portion of the tubular body that is in a remote location from the first end of the tubular body is provided with vent means, or  
15 the gas displacement mechanism is provided with vent means. The inner surface of the central, axial channel of the tubular body has a different capillary capacity than the inner surface of the capillary tube. Furthermore, the one end of the capillary tube has a first distance between a central axis of the capillary tube and the outer wall of the capillary tube in a direction  
20 perpendicular to the central axis of the capillary tube. The first end of the tubular body has a second distance between the central axis of the tubular body and the inner channel wall of the tubular body in a direction perpendicular to the central axis of the tubular body. The difference between the second distance and the first distance is from around 0 to around 5 times  
25 the wall thickness of the capillary tube. The micropipette may be used to collect blood at a high-hygiene requiring site such as the site of a finger puncture. Liquid could also be collected from a reservoir containing liquids such as blood, serum, plasma, or a chemical solution or mixture.

The micropipette provides the possibility of collecting and displacing a  
30 well-defined volume of liquid, both by capillary force and by the use of the gas displacement mechanism.

The connection of the two separate parts, the tubular body and the capillary tube in the tubular body-capillary tube assembly, is essentially liquid and air tight.

The engagement between the capillary tube and the tubular body in  
5 the assembly may be arranged by inserting an end of the capillary tube directly into the first end of the tubular body or through the use of an adaptor part. A durable connection between the two parts may be obtained by the presence of frictional forces between the capillary tube and tubular body, the presence of a form-fit connection between the two parts, the use of an  
10 adhesive substance and/or by melting of the two parts together.

With a form-fit connection is meant that the capillary tube is tightly engaged in a form-fit manner directly to the tubular body. wherein the inner dimensions of the central, axial channel portion fits in a form-fit manner with the outer dimensions of the end portion of the capillary tube. Thus, this may  
15 also involve a connection by frictional forces.

The consequences of having a difference between the second distance and the first distance from around 0 to around 5 times the wall thickness of the capillary tube is that there is provided a way of, at least for the lower range of distance differences: from around 0 to around 1, from around 0 to  
20 around 2 and from around 0 to around 3, having a substantially smooth transition between the inner surface of the capillary tube and the inner surface of the central, axial channel of the tubular body. By "substantially smooth transition" here means that the transition leaves no or few crevices or recesses for liquid to be retained in the micropipette when larger volumes  
25 than the capillary volume are collected and discharged with the pipette. Such crevices or recesses, if present, should not retain a substantial amount of liquid during use.

Wall thicknesses of the capillary tube may range from about 0.1 mm to about 0.5 mm or about 0.2 to about 0.5 mm, e.g. about 0.25 mm or about  
30 0.35 mm.

Embodiments of transitions will be discussed in more detail in the detailed description section below.

The definition of capillary capacity in this context is a spontaneous movement of a liquid in a thin tube, an end-to-end capillary. In order for the tube to spontaneously fill with liquid, the following requirements on the tube have to be met: firstly, the tube has to be made of a material which has high wettability characteristics throughout its length relative the liquid to be collected; and secondly, the inner diameter of the tube should be small. By contacting one end of such a tube with a liquid, large surface tension forces will draw the liquid into the tube and pull the liquid column up until there is a sufficient mass of liquid in the tube for gravitational forces to overcome the intermolecular forces. A capillary tube with a narrow inner channel will draw a liquid column that is higher than a tube with a wide inner channel.

The height,  $h$ , of a liquid column is given by the formula:

$$h = \frac{2\gamma \cos\theta}{\rho g r}$$

where:

- $\gamma$  is the liquid-air surface tension (energy/area)
- $\theta$  is the contact angle
- $\rho$  is the density of liquid (mass/volume)
- $g$  is acceleration due to gravity (length/time<sup>2</sup>)
- $r$  is the radius of the tube (length)

When the tube has filled and been removed from the source of liquid, a meniscus has formed in each end of the capillary tube restraining the liquid from pouring out of the tube.

By “vent means” here means that the tubular body or the displacement mechanism is provided with means that provide the possibility of a sealable opening between the central, axial channel of the tubular body and the surrounding, which is differently located than the opening provided via the capillary tube. This provides the possibility of a gas flow from the

surroundings via the free end of the capillary, through the capillary tube and the central, axial channel of the tubular body and through the vent means to the surroundings. This in turn means that liquid may be collected by capillary forces into the capillary tube. The gas is in most instances air.

5           This also further provides the possibility of a gas flow from the free end of the capillary, through the capillary tube and the central, axial channel of the tubular body and through the vent means to the surroundings, or vice versa. This in turn means that liquid may be collected by capillary forces into the capillary tube. The gas is in most instances air.

10           In its simplest form the vent means is a through an opening in the gas displacement mechanism, a canal that leads from the inside of the device to the surroundings. For example, the gas displacement mechanism may be provided with a central channel for passing the gas from the inside of the pipette to the surroundings when liquid is being collected by the capillary  
15 tube. Upon activation of the gas displacement mechanism, the vent means may, for example, be sealed by a user's finger or thumb, and a volume of gas is displaced in the direction towards the free end of the capillary tube and collected liquid is consequently discharged from the pipette. Upon  
20 deactivation of the gas displacement mechanism, the displaced volume of gas may be replaced with a volume of gas or, if the free end of the capillary tube is submerged in liquid, with a volume of liquid which is collected into the micropipette by filling the capillary or also the lower parts of the tubular body .

25           The vent means may also be arranged at the tubular body, and then with some distance from the first end of the tubular body, i.e. at a remote location relative the first end of the tubular body. This means that the vent means should not be in direct contact with, or closely located to, the capillary tube so as to secure the function of the micropipette for collecting and displacing well-defined volumes of liquids.

30           By providing the inner surface of the central, axial channel of the tubular body and the inner surface of the capillary tube with different capillary capacities, there is provided a way of collecting a well defined volume of liquid by collecting the liquid only in the well defined space of the interior of the capillary.

By providing the inner surface of the central, axial channel of the tubular body and the inner surface of the capillary tube with different capillary capacities, there is provided a way of automatically collecting liquids of interest. The inner surface of the tubular body should then have a lower  
5 capillary capacity for the liquid to be collected than the inner surface of the central, axial channel of the capillary tube.

The fact that the inner surface of the central, axial channel of the tubular body has lower capillary capacity for a liquid to be collected than the inner surface of the capillary tube results in that the capillary tube, when  
10 connected to the tubular body, stops collecting liquid when the capillary tube is filled and the liquid column has reached the transition between the inner surface of the capillary tube and the inner surface of the central, axial channel of the tubular body. This difference in capillary capacity enables collection of well-defined capillary volumes. If the inner surfaces of the two parts have  
15 similar capillary capacity characteristics, liquid collected by the capillary tube might spill over from the capillary tube into the tubular body and no well-defined liquid volume would be collected.

In one embodiment, the central, axial channel of the tubular body may be provided with a tapered section along its elongation, the tapering being in  
20 a direction towards the first end of the tubular body. This means that for a smaller or larger section of the circular central, axial channel, the inner diameter of the channel decreases in an axial direction towards the capillary tube.

Tapering of the central, axial channel of the tubular body minimizes  
25 retention of liquid in the micropipette when a larger volume than the capillary volume has been collected and is to be discharged.

A material of the tubular body may be a material having a lower capillary capacity for a hydrophilic or hydrophobic liquid than a material of the capillary tube.

30 In one embodiment, the capillary capacity of the capillary tube may originate from providing the capillary tube with hydrophilic inner surface.

In a further embodiment, the inner surface of the central, axial channel of the tubular body may be hydrophobic.

With a hydrophilic surface is here meant a surface having a strong affinity for water and a hydrophobic surface is a surface having low affinity for water.

The materials may be the main materials forming any of the tubes, and  
5 which materials may provide the inner surfaces of the tubes with the mentioned hydrophilic or hydrophobic properties.

In one embodiment, the capillary tube and the tubular body of the micropipette may comprise polymeric materials.

The capillary tube and the tubular body may be made of different  
10 polymeric materials.

A micropipette may for example be produced from a capillary tube made of nylon, such as Pebax® 7033 (extruded polyether block amide) and a tubular body made of a polyolefin, such as polypropen (Ashland RF830MO).

15 Further examples of materials and material combinations which may be used for such a micropipette will be discussed in more detail in the detailed description section below.

A micropipette made of polymeric materials is suitable for single-use and thus is disposable after use. The gas displacement mechanism may,  
20 however, be reused several times with different capillary tube – tubular body assemblies. The materials chosen for the different parts of the micropipette should preferably be disposable, and thus also inexpensive.

The inner surfaces may be made more hydrophilic or hydrophobic by some kind of surface treatment, such as surface coating. Such a coating may  
25 be covalently or non-covalently attached to the inner surface. The inner surface may be supplied with a polymeric coating that includes a functional group attached to the inner surface and capable of polymerizing with an organic compound in an organic solvent. In prior art US 3,952,599 bees wax, paraffin or dilute lacquers of hydrophobic plastics are used to render a  
30 hydrophilic surface more hydrophobic. Also these may be used here and applied as described in US 3,952,599.

According to one embodiment, the capillary tube may be transparent. The transparency facilitates visual control of the collection/discharging of liquid in/from the capillary tube.

In a further embodiment the tubular body may be transparent. The  
5 transparency facilitates visual control of the collection/discharging of liquid in/from the tubular body.

A micropipette provided with both a transparent capillary tube and a transparent tubular body would even more enhance the visual control of the process of filling and discharging the micropipette.

10 In yet another embodiment, the material of the capillary tube and/or the material of the tubular body may be coloured.

This colouring is made without losing of transparency of the coloured material.

Transparent capillary tubes and tubular bodies also facilitate the  
15 assembly of the two parts.

Connecting a translucently coloured capillary tube to a transparent tubular body may facilitate the assembly of the capillary tube and the tubular body, making the transition between the two parts more clearly visible. Alternatively, connecting a translucently coloured tubular body to a  
20 transparent capillary tube may also facilitate the assembly of the capillary tube and the tubular body, making the transition between the two parts more clearly visible. Or both parts could be translucently coloured with different colours, more clearly visualizing the transition between the two parts.

The maximum liquid volume that may be collectable by the capillary  
25 tube is in the range of 0.25  $\mu\text{l}$  to 200  $\mu\text{l}$ , preferably less than or equal to 50  $\mu\text{l}$ , less than or equal to 20  $\mu\text{l}$ , less than or equal to 15  $\mu\text{l}$ , or less than or equal to 10  $\mu\text{l}$ .

The inner geometry of the capillary tube determines the volume which may be collectable by the capillary tube. The diameter of a substantially  
30 circular inner channel of the capillary tube may range from 0.1 mm to 2.5 mm and hence the length of the tube may also be varied to obtain tubes with different fill-volumes.

In one embodiment the maximum liquid volume that may be collectable by the tubular body is larger than or equal to 1.5, 2, 5, 10, 20, 30, 40, 50 or 100 times the maximum liquid volume collectable by the capillary tube.

5 A capillary tube dimensioned to collect a maximum liquid volume larger than the maximum capillary volume may be useful when applying the micropipette for mixing applications, such as mixing a collected capillary volume in a larger second volume, but also for rinsing of the inside surface of the capillary tube to assure a quantitative discharge.

10 In one embodiment, the gas displacement mechanism may be an ordinary squeeze bulb, which upon compression displaces a volume of gas in a direction towards a free end of the capillary tube, and the displaced gas volume is being arranged to discharge a volume of liquid from the free end of the capillary tube.

15 In another embodiment, the gas displacement mechanism may be movable between two distinct end positions, namely one activated first end position and one deactivated second end position. The gas displacement mechanism may be arranged to be activated by a movement from the second end position towards the first end position, and a well-defined volume of gas may be displaced in a direction towards a free end of the capillary tube. The  
20 displaced gas may be arranged to discharge a well-defined volume of liquid from the free end of the capillary tube.

By distinct end positions is here meant two positions which the user of the micropipette by tactical sensations readily recognizes. The distinct  
25 recognition of the end positions is important in some embodiments of the invention used for mixing two liquids since a user's finger or thumb may be required to continuously occlude or seal the vent means during repeated activations and deactivations of the gas displacement device.

The well-defined volume of gas displaced from the gas displacement mechanism is repeatable. Upon movement towards the deactivated second  
30 end position a well-defined gas volume, replaced gas volume, or in the case when the free end of the capillary tube is in contact with a liquid, a well-defined volume of liquid, will enter the micropipette.

According to one alternative embodiment said gas displacement mechanism may comprise a first plunger which is movable between two distinct end positions: one activated first end position and one deactivated second end position, wherein said gas displacement mechanism may be arranged to be activated by a movement of said first plunger from said second end position towards said first end position, whereby a well-defined volume of gas may be displaced in a direction towards a central channel arranged in a first plunger of the gas displacement mechanism.

This means that the micropipette encompasses a vent means that is not occluded, closed or sealed until a first activation of the gas displacement is completed, or nearly completed. By this, the activation of the gas displacement mechanism will result in at least some of the displaced gas escaping through the vent means and not moving in the tubular body toward the capillary and discharging collected liquid and gas through the free end of the capillary. In cases where the invention is used to mix a well-defined volume of a first liquid collected in the capillary with a second volume of liquid, the described delayed closure or sealing of the vent means will result in the discharge of less gas through the mixture, and thus alleviated problems caused by gas being bubbled through the mixture. After the vent means has been closed or sealed, repeated deactivation and activation of the gas displacement mechanism can, as in previous disclosures of the invention, result in the mixing of a first well-defined volume of liquid collected in the capillary with a second volume of liquid, but with a difference. Little or no gas will be discharged through the mixture, and not as otherwise, a volume of gas about equal to the difference between the volume of gas displaced by activation of the gas displacement mechanism and the volume of liquid collected in the capillary. The advantage of providing a way for gas, in most instances air, to be discharged through the vent means during the first activation of the gas displacement mechanism is that an unnecessary transfer of air to the mixture may be avoided when a first collected liquid is discharged into a second liquid. This is advantageous in a number of applications where the analyzing apparatus is sensitive to the presence of air bubbles or where the presence of air, in itself, may compromise the mixture.

According to this embodiment, the gas displacement mechanism may further comprise a second plunger, which is arranged to be moveable in the central channel and between two distinct end positions, one deactivated first end position and one activated second end position, wherein said second  
5 plunger may be arranged to be activated by a movement of said second plunger from said first end position towards said second end position wherein the activation of the second plunger seals the central channel.

Since the second plunger seals the central channel no gas may pass through the channel and into the tubular body of the micropipette, thereby  
10 reducing the amounts of unwanted gas to be introduced into the mixture. Also, as the second plunger more permanently seals the central channel, the need is abolished for the user to retain his or hers finger on the vent means throughout the repeated activations and deactivations of the gas displacement mechanism required for good mixing .Gas that is introduced  
15 into the mixture, may in some instances, cause problems, and often more gas causes more problems, e.g. in instances when the mixture is to be subjected to optical analysis and bubbles of the discharged air disturb the light path.

Further according to this embodiment, the second plunger may be arranged to be activated following the activation of the first plunger, and  
20 further wherein the gas displacement mechanism may be arranged to be deactivated when the first plunger is moved from said activated end position to said deactivated end position and wherein the second plunger may remain in the activated position.

As the second plunger of the gas displacement mechanism remains in  
25 the activated position this may allow for a second liquid to be drawn up into the micropipette, and more specifically into the tubular body. This will occur when the entire gas displacement mechanism is deactivated, since the volume of gas, displaced and discharged through the vent means, during the initial activation of the first plunger may be replaced by liquid entering through  
30 the free end of the capillary tube. By the entire gas displacement mechanism is meant the entity composed of first and second plunger together. By deactivation of the entire gas displacement mechanism is meant that the first

plunger is moved from the activated position to the deactivated position, and that the second plunger preferably is in the activated position.

The assignment of avoiding transfer of gas into the mixture when a first collected liquid is discharged into a second liquid may alternatively be tackled  
5 by constructing an air displacement mechanism that upon activation works in two phases, a first phase resulting in an enlargement of the interior volume of the mechanism and a second phase resulting in a reduction of the interior volume back towards its original volume. The deactivation of such a gas displacement mechanism is similarly by two phases, first an enlargement and  
10 then a reduction of the interior volume.

The gas displacement mechanism may be made of resilient material. Alternatively, it may partially be made of resilient material. Use of resilient material that is deformed by low stress forces makes the gas displacement mechanism easy to handle and minimizes repetitive strain injuries in the hand  
15 of the user. The resilient material may be an elastomer.

The elastomer may be rubber.

Such elastic materials are suitable for a gas displacement mechanism which is to be used several times.

A gas displacement mechanism may for example be produced from an  
20 extruded thermoplastic elastomer such as Dryflex® 600502 with admix of a slip additive such as a silicon oil. Silicon oil is used to make the surface of the gas displacement mechanism more slippery, and thus reduce the friction between the mechanism and the tubular body.

The gas displacement mechanism may be removably attached to the  
25 tubular body.

This provides that the gas displacement mechanism may be reused, This means that the gas displacement mechanism is meant to be used more than once and together with new tubular body-capillary tube assemblies, the latter normally only meant as a one-time-use article. The number of times the  
30 gas displacement mechanism may be reused without losing its distinctiveness may range from 5 to 50 times, preferably more than 10 times. The number of times the gas displacement mechanism may be reused without losing its

distinctiveness may further range from 50 to 1000 times, preferably more than 100 times.

The gas displacement mechanism may be attached to the tubular body via snap-lock members.

5           The volume of displaceable gas from the gas displacement mechanism may be larger than the maximum collectable volume of the capillary tube, and in the range of 0.5  $\mu\text{l}$  to 250  $\mu\text{l}$ , preferably more than or equal to 10  $\mu\text{l}$ , more than or equal to 25  $\mu\text{l}$ , more than or equal to 50  $\mu\text{l}$ , more than or equal to 100  $\mu\text{l}$ , more than or equal to 150  $\mu\text{l}$ , more than or equal to 200  $\mu\text{l}$ , more than or  
10 equal to 250  $\mu\text{l}$  or more than or equal to 300  $\mu\text{l}$ .

A micropipette where the volume of displaced gas is larger than the maximum volume collectable by the capillary tube may be useful when larger volumes than the capillary volume are to be collected and discharged. This is of importance when wanting to mix the capillary volume in a larger second  
15 volume and for rinsing applications. The collected capillary volume may be discharged in a reservoir containing a second liquid of larger volume than the capillary volume. By collecting and discharging a volume of this mixture, a volume larger than the capillary volume, a homogenous mixture will be the result. The micropipette will also have been rinsed during this mixing  
20 procedure ensuring that most of the collected capillary volume has been transferred to or dissolved the mixture.

The volume of the displaced gas is defined by the restrictions of the movements of the gas displacement mechanism. Examples of different embodiments of the gas displacement mechanism will follow in the detailed  
25 description section.

In an alternative embodiment, the volume of displaceable gas from the gas displacement mechanism may be smaller than the maximum collectable volume of the capillary tube.

Such a micropipette provides a possibility of collecting and dispensing  
30 essentially exact volumes of sample liquids, where the dischargeable liquid volume is smaller than the volume of liquid collected by the capillary tube. Furthermore, there is provided a solution to a partial problem with at least some of the prior art pipettes, wherein air bubbles are deposited during the

dispensing action. When discharging a smaller volume than the collected volume into for example a measuring chamber of an analytical instrument the deposition of air bubbles may in this way be kept to a minimum.

According to a second aspect, there is provided a method for collecting  
5 and discharging a well-defined volume of liquid making use of the micropipette defined above, the method comprising the steps of:

- a) collecting a well-defined volume of the liquid by contacting the free end of the capillary tube to the liquid,
- b) activating the gas displacement mechanism to discharge the  
10 volume of the liquid.

According to a third aspect, there is provided a method for collecting and discharging a well-defined volume of a first liquid into a larger volume of a second liquid and mixing the two liquids making use of the micropipette  
15 defined above, the method comprising the steps of:

- a) collecting a well-defined volume of the first liquid by contacting the free end of the capillary tube to the first liquid,
- b) activating the gas displacement mechanism to discharge the volume of the first liquid into a reservoir with the second liquid,
- 20 c) deactivating the gas displacement mechanism by replacing the displaced gas volume with liquid for mixing of the first and the second liquids, wherein a volume of a mixture of the two liquids, larger than the volume of the first liquid, is collected through the capillary tube into the tubular body,
- 25 d) activating the air displacement mechanism to discharge a mixture of the first and second liquids into the reservoir, and
- e) optionally, repeating step c) and d).

When performing the mixing operation, the capillary tube is immersed  
30 in the mixture upon deactivation of the gas displacement mechanism. The volume of displaced/replaced gas may be smaller but commensurable in volume to that of the mixture. The activation/deactivation of the gas

displacement mechanism may be repeated a few number of times, for example 2 to 10 times, to get a homogenous mixture.

By this method it is provided a simple and accurate method of mixing a sample with another liquid such as a reagent.

5           According to a fourth aspect there is provided a method for collecting a well-defined volume of a first liquid and mixing said first liquid with a second liquid, making use of said micropipette defined in the first aspect above, comprising the steps of:

- 10           a) collecting a well-defined volume of said first liquid by contacting said free end of said capillary tube to said first liquid;
- b) activating said first plunger to discharge a well-defined volume of gas contained in the tubular body, in a direction through said central channel;
- c) activating said second plunger to seal the central channel;
- 15           d) contacting the free end of said capillary tube with a second liquid;
- e) deactivating said gas displacement mechanism, thereby replacing said displaced gas volume with a second volume of said second liquid, for mixing of said first and second volumes of said first and said second liquids, wherein a volume of a mixture of said first and second liquids, larger than said volume of said first liquid, is  
20           collected through said capillary tube into said tubular body;
- f) activating said first plunger of said gas displacement mechanism a second time, wherein the second plunger remains in the activated position, to discharge a mixture of said first and second liquids into  
25           said reservoir , and
- g) optionally, repeating step e) and f).

In practice, the first plunger is activated by applying pressure to the second plunger, the forces necessary to activate this second plunger are of a magnitude that is not reached until the first plunger is activated and the gas  
30           has been displaced through the vent means. Then, as the pressure on the second plunger increases this plunger is activated to obstruct, or close, or occlude, or seal, the vent means. As the pressure on the second plunger decreases, the gas displacement mechanism is deactivated, i.e. the first

plunger returns to its original position, whereas the first plunger remains in its activated position and continues to obstruct the vent means. The return of the first plunger to its original position, i.e. to a state of deactivated gas displacement mechanism, the inside volume of the pipette device increases  
5 resulting in a pressure drop, a drop that is neutralized by an influx of mixture through the free end of the capillary tube and into the tubular body. Repeated activation and deactivation of the gas displacement mechanism will then repeatedly expel and impel mixture out of and into the tubular body to accomplish a thorough mixing of the mixture.

10 The method described may allow for an easy way of mixing two liquids with a reduced risk of gas bubbles being present in the mixture, since the gas present in the tubular body is discharged through the vent means when the first plunger is activated the first time and the second plunger then is activated to seal the central channel or vent means. The method further provides a way  
15 to firstly collect a well-defined first liquid and mix this with a second essentially well-defined volume of liquid; this could e.g. be used in order to discharge a volume of blood sample into a volume of reagent and mix to homogeneity to two volumes as steps in the analysis of the blood.

According to a fifth aspect, there is provided a tubular body-capillary  
20 tube assembly for use in a micropipette as described above and where the tubular body-capillary tube assembly comprises the features as defined above.

According to a sixth aspect, there is provided a kit for diagnostic  
25 determination of analytes or analyte processes in near-patient medical or veterinary diagnostic or research laboratories, the kit comprising a micropipette as described above, reagents and disposable reaction containers.

Examples of the analyte or analyte process is prothrombin time (PT),  
activated partial thromboplastin time (APTT), thrombin time (TT), fibrin D-  
30 dimer fragments, coagulation factor VIII (FVIII), coagulation factor XI (FXI), coagulation factor IX (FIX), glucose, glycosylated haemoglobin (HbA1c) or C-reactive protein (CRP).

In patent EP1636595 a method of determining prothrombin time (PT) is shown and in US patent application 2008318259 a method for determining different analytes/analyte processes such as PT, fibrin degradation products (D-dimer), activated partial prothrombin time (APTT), C-reactive protein (CRP) and glucose are shown, wherein the present micropipette and kit may be of use.

#### Brief description of the drawings

These and other aspects of the present invention will now be described in more detail, with reference to the appended drawings showing some embodiments of the invention.

Fig. 1 shows an embodiment of the micropipette and its different interconnected parts.

Fig. 2 is a cross-section of an embodiment of the connection between the tubular body and the capillary tube.

Fig. 3 is a cross-section of an embodiment of the connection between the tubular body and the capillary tube.

Fig. 4 is a cross-section of an embodiment of the connection between the tubular body and the capillary tube.

Fig. 5 is a cross-section of an embodiment of the connection between the tubular body and the capillary tube.

Fig. 6 is an enlarged cross-section of an embodiment of the gas displacement mechanism.

Fig. 7 is an enlarged cross-section of an embodiment of the gas displacement mechanism.

Fig. 8 is a perspective view of an embodiment of the gas displacement mechanism with a cut out section.

Fig. 9 is a perspective view of an embodiment of the gas displacement mechanism with a cut out section.

Fig. 10 is a perspective view of an embodiment of a second plunger.

Figs 11a and 11b are cross-sections of an embodiment of the gas displacement mechanism.

Fig. 12 is a cross-section of an embodiment of the gas displacement mechanism.

Figs 13a and 13b are cross-sections of of an embodiment of the gas displacement mechanism.

5

#### Detailed description

An embodiment of the capillary micropipette 1 is shown in Fig. 1. The micropipette 1 is composed of a self-filling capillary tube 2 having a free end 2a through which liquid is collected and discharged, and a connecting end 2b  
10 for connection to a tubular body 3. The tubular body 3 is provided with a central, axial channel (not shown) in the axial direction A-A and is connected to the capillary tube 3 with its first end 3a. The inner volume of the tubular body 3 is larger than the inner volume of the capillary tube 2. The second end of the tubular body 3b is terminated with a section forming a housing 4 with  
15 enlarged diameter. A gas displacement mechanism 5 is connected to the second end of the tubular body 3b and placed in the housing 4. The gas displacement mechanism 5, here shown as a plunger, is movable between a first end position (in Fig. 1 shown as the position B1 of an upper portion of the plunger) and one deactivated second end position (in Fig. 1 shown as the  
20 position B2 of the upper portion of the plunger). By movement from the second end position B2 towards the first end position B1, the gas displacement mechanism 5 is activated. The micropipette is also provided with vent means (not shown) located at the tubular body 3 or at the gas displacement mechanism 5. If the vent means (not shown) is sealed, this  
25 activation displaces a well-defined volume of gas in the direction towards the free end of the capillary tube 2a of the micropipette 1. The gas is in most instances air.

The vent means may here be a through opening in the tubular body 3 wall or in the gas displacement mechanism 5, providing a gas connection  
30 between the surrounding and the central, axial channel of the tubular body 3. This provides the possibility of a gas flow from the surroundings, via the free end of the capillary tube 2a, through the capillary tube 2 and the central, axial channel of the tubular body 3 and through the vent means to the

surroundings. This in turn means that liquid may be collected by capillary forces into the capillary tube 2. Also provided is the possibility to regulate the collection and displacement of liquid by the gas displacement mechanism. The through opening may easily be blocked by a user's finger, and thereby  
5 providing a simple way of regulating the displacement and collection of liquid.

Any other vent means suitable for this purpose that is known to the person skilled in the art may be used.

By providing the inner surface 7 of the central, axial channel of the tubular body 3 and the inner surface 8 of the capillary tube 8 with different  
10 capillary capacities, there is provided a way of automatically collecting liquids of interest. The inner surface 7 of the tubular body 3 should then have a lower capillary capacity for the liquid to be collected than the inner surface 8 of the central, axial channel of the capillary tube 3. This difference in capillary capacity enables collection of well-defined capillary volumes. If the inner  
15 surfaces 7, 8 of the two parts 2, 3 have similar capillary capacity characteristics, liquid collected by the capillary tube 2 might spill over from the capillary tube 2 into the tubular body 3 and no well-defined liquid volume would be collected. The difference in capillary capacity may be achieved by producing the capillary tube 2 and the tubular body 3 in materials with  
20 different hydrophilicity/hydrophobicity, or by rendering the inner surfaces 7, 8 of the central, axial channel of the tubular body 3 and the capillary body 2 hydrophilic/hydrophobic, by for example surface coating.

For example, a micropipette may be produced from a capillary tube 2 made of nylon, such as Pebax® 7033 (extruded polyether block amide) and  
25 a tubular body 3 made of a polyolefin, such as polypropen (Ashland RF830MO).

This material choice admits the inner surface 8 of the capillary tube 2 to be more hydrophilic than the inner surface 7 of the central, axial channel of the tubular body 3.

30 Other materials which may be used for the capillary tube 2 may be glass, thermoplastic materials or thermosetting materials such as silicates, nylons, polyurethanes, polycarbonates and epoxy-resins.

The hydrophilic or hydrophobic inner surface 7, 8 of the capillary tube 2 and the central, axial channel of the tubular body 3 may also be due to the use of, as the main material for the tube, polymeric materials such as polycarbonate, polystyrene, polyethylene, polypropene or polymethyl  
5 methacrylate.

The person skilled in the art will appreciate how to produce such a micropipette 1. The tubular body 3 may be injection-moulded and the capillary tube 2 may be extruded as a never-ending tube and cut into pieces. Thereafter the two parts may be assembled as illustrated in the Figures and  
10 also as described under the summary of the invention. The person skilled in the art will also appreciate how to provide the materials that the tubular body 3 and the capillary tube 2 are made of with colour. The materials may be coloured with tints or hues of colour so as not to disturb the transparency of the parts.

15 The gas displacement mechanism shown in the Figures may, for example, be produced from an extruded thermoplastic elastomer such as Dryflex® 600502 with admix of a slip additive such as a silicon oil. Silicon oil is used to make the surface of the gas displacement mechanism more slippery, and thus reduce the friction between the mechanism and the tubular  
20 body. Prior to extrusion, the granulated elastomer may be mixed with the slip additive to, for example, a degree of 3%,

As an alternative, the gas displacement mechanism may also be an ordinary squeeze bulb as mentioned above under summary of the invention.

25 The dimensions of the different parts of the micropipette as illustrated in the Figures may be as described above. For example, the capillary tube may be dimension to collect 10  $\mu$ l and a diameter of 0.8 mm. The collectable volume of the tubular body may differ depending on use (see above under summary of the invention).

30 The following illustrates an example of how the embodiment of Fig. 1 may be used. Before activation of the gas displacement mechanism 5, the free end of the capillary tube 2a is brought into contact with a liquid and through capillary action a well-defined volume of liquid is collected by the capillary tube 2. The displacement of a volume of gas upon sealing of the

vent means and activation of the gas displacement mechanism 5 causes a well-defined volume of liquid to be discharged from the free end of the capillary tube 2a. By movement from the first end position B1 towards the second end position B2, a well-defined volume of gas (replaced volume) will be drawn into the micropipette 1, or if the free end of the capillary tube 2a is in contact with a liquid, a well-defined liquid volume will be collected by the micropipette 1.

The gas displacement mechanism 5 shown in this figure, Fig. 1, is only an embodiment of such a mechanism. More embodiments will be discussed later in this description. Nevertheless, for all embodiments and aspects of the invention, the gas displacement mechanism 5 may be removably attached to the tubular body 3. This provides the possibility of reusing the gas displacement mechanism 5.

The whole length of the tubular body 3, or more importantly the central, axial channel of the tubular body 3, is in this embodiment tapered towards its first end 3a. In another embodiment, only a portion of the central, axial channel of the tubular body 3 is tapered in a direction towards the first end 3a. A tapered or partly tapered central, axial channel of the tubular body 3 minimizes retention of liquid in the micropipette 1 when a larger volume than the capillary volume is collected and discharged. It is also possible with embodiments in which the central, axial channel of the tubular body 3 is not tapered at all.

The volume of displaced gas from the gas displacement mechanism 5 is defined by restrictions of the movements of this mechanism 5. Depending on the volume of gas displaced by the movement of the gas displacement mechanism 5 from the second end position B2 to the first end position B1, the capillary micropipette 1 may be used for different applications.

In a first application, only a smaller but well-defined portion of a well-defined volume of liquid collected by the capillary tube 2 is discharged, leaving a remainder of the collected volume in the micropipette 1. In this application the gas displacement mechanism 5 is dimensioned to displace a volume of gas which is smaller than the volume of liquid collected by the capillary tube 2. Furthermore, there is provided a solution to a partial problem

with at least some of the prior art pipettes, wherein air bubbles are deposited during the dispensing action. When discharging a smaller volume than the collected volume into for example a measuring chamber of an analytical instrument the deposition of air bubbles may in this way be kept to a  
5 minimum.

In a second application, a well-defined volume of a first liquid is collected through capillary action by contacting the free end of the capillary tube 2a to the first liquid. Thereafter, the gas displacement mechanism 5 is activated and the well-defined volume of the first liquid is discharged into a  
10 reservoir a second liquid of a larger volume than the well-defined volume of the first liquid. The displaced volume of gas is larger than the volume of the collected first liquid, whereby most of the first liquid volume together with a volume of displaced gas is discharged from the micropipette 1 into the second liquid. The gas displacement mechanism 5 is then deactivated and a volume  
15 of a mixture of the two liquids, larger than the first liquid volume, is collected through the capillary tube 2 into the tubular body 3. The gas displacement mechanism 5 is then activated again to discharge a mixture of the first and second liquids into the reservoir. By repeating the activating/deactivating steps a few times, a homogenous mixture of the first and second liquid is  
20 obtained.

The capillary tube 2 and the tubular body 3 may form an assembly by inserting the connecting end 2b of the capillary tube 2 directly into the first end 3a of the tubular body 3 or by connecting the two parts 2, 3 via an adaptor part. A durable connection between the two parts 2, 3 may be  
25 obtained by the presence of frictional forces between the capillary tube 2 and tubular body 3, the presence of a form-fit connection between the two parts 2, 3, the use of an adhesive substance or by melting of the two parts 2, 3 together. With a form-fit connection is meant that the capillary tube fits tightly in a form-fit manner directly to the tubular body. wherein the inner dimensions  
30 of the central, axial channel portion fits in a form-fit manner with the outer dimensions of the end portion of the capillary tube.

Different embodiments of the connection between the first end 3a of the tubular body 3 and the connecting end 2b of the capillary tube 2 are shown in Fig. 2-Fig. 5.

In Fig. 2 a transition between the tubular body 3 and the capillary tube  
5 2 is shown in cross-section. A recess in the inner wall at the first end 3a of the tubular body 3 provides an inner diameter at the first end 3a that corresponds to the outer diameter of the connecting end of the capillary tube 2b, thereby providing the possibility of form-fit connection between the tubes 2, 3. The recess has a width C which matches the wall thickness of the capillary tube D  
10 at its end 2b. Thus, an inner diameter near the first end 3a of the tubular body 3 has substantially the same diameter as the inner diameter of the capillary tube 2.

The capillary tube 2 is inserted with its connecting end 2b into the first end of the tubular body 3a until it abuts with its connecting end 2b against the  
15 bottom of the recess 6. This embodiment shows an essentially smooth transition between the inner surface 7 of the central, axial channel of the tubular body 3 and the inner surface 8 of the capillary tube 2. A minimal air split might exist in the transition area between the connecting end of the capillary tube 2b and the bottom of the recess 6 of the tubular body 3. If  
20 desired, such an air split could be sealed with some kind of sealing compound.

In Figure 2, the first and second distances E;F as discussed under the summary of the invention are shown. The distances E;F are not shown in respective Figures, but may easily be appreciated for any embodiment. The  
25 requirements on the distances are as mentioned under the summary of the invention.

In an alternative embodiment of a transition between the tubular body 3 and the capillary tube 2, shown in cross-section in Fig. 3, a small air split 9 is present in the transition area between the inner surface 7 of the central, axial  
30 channel of the tubular body 3 and the inner surface 8 of the capillary tube 2. This air split 9 enhances the transition between the inner surfaces 7, 8 and aids in stopping fluid from the capillary tube 2 to spill over in the tubular body 3 when the capillary tube 2 automatically has filled.

In yet an alternative embodiment shown in Fig. 3, the bottom of the recess 6 of the tubular body 3 may be provided with a protuberance 10, which protuberance 10 may be circular or of any other feasible shape, onto which the capillary tube 2 abuts with its connecting end 2b when inserted in the tubular body 3. This protuberance 10 is of smaller diameter than the width of the recess C is, leaving an air split which is smaller than in the previous embodiment (also shown in Fig. 3). The material of this protuberance 10 may be the same material as the tubular body 3 is made of. It could also be made of other materials that either exhibit lower capillary capacity than the inner surface 8 of the capillary tube 2 or has been made more hydrophobic than the inner surface 8 of the capillary tube 2. This is made so in order not for liquid to spill over from the capillary tube 2 to the tubular body 3 upon self-filling of the capillary tube 2.

In a further embodiment, Fig. 4, a shoulder 11 is provided on the inside wall of the tubular body 3 a certain distance from its first end 3a, to which shoulder 11 the connecting end of the capillary tube 2b abuts when inserted into the tubular body 3. This shoulder 11 is of the same magnitude or smaller than the thickness of the capillary tube wall D. The same discussion as was presented above for the protuberance 10 holds for the material choice of this shoulder 11. In a further embodiment also shown in Fig. 4, the shoulder 11 is only provided on a part of the inside wall of the tubular body 3. Alternatively, the inner surface of the tubular body 3 may be used without a shoulder 11. When no shoulder is provided, some kind of indication means could be provided on the capillary to indicate where to stop the insertion of the capillary tube 2 into the tubular body 3, showing when the two tubes 2, 3 have been correctly assembled. Indication means could also be of use for the embodiment without protuberance in Fig. 3. Such an indication means could for example be a visible marking on the tubular body 3.

In Fig. 5, yet a further embodiment of the connection between the capillary tube 2 and the tubular body 3 is shown. Here the tubular body 3 is provided with a first tapered section 3c, the tapering being in the direction towards the first end 3a of the tubular body 3. When approaching the first end

3a, the tubular body 3 changes geometry and becomes tapered towards the second end 3b of the tubular body 3, resulting in a second tapered section 3d.

The material of at least one of the capillary tube 2 and the tubular body 3 is resilient, This together with the geometry of the tubular body 3 with its first  
5 and second tapered sections 3c, 3d allows for the connection between the two parts 2, 3 to be accomplished by forcing the capillary tube 2 into the tubular body so that the resilient material is compressed, resulting in a  
smoothened transition and a tight fit between the two parts 2, 3.

In order for the capillary tube 2 to stop collect liquid when connected to  
10 the tubular body 3, the tubular body 3 is of lower capillary capacity than the capillary tube 2. Also, the air split that is present in some of the embodiments functions to stop the micropipette from collecting more liquid when the capillary tube 2 has been filled. For collecting a hydrophilic liquid, the difference in capillary capacity may be provided by making the capillary tube  
15 2 hydrophilic and the tubular body 3 hydrophobic.

The use of transparent capillary tubes 2 and tubular bodies 3 facilitates the assembly of the two parts 2, 3 and visualizes filling/discharging of liquid from the capillary tube 2 /tubular body 3. By using translucently coloured parts 2, 3 the transition between the two parts 2, 3 may be further enhanced.

20 The gas displacement mechanism 5 may be an ordinary squeeze bulb, such as the one used for the prior art micropipette sold under the trademark Microcaps® marketed by Drummond.

The gas displacement mechanism 5 could also have the appearance shown in the embodiments in Fig. 6 and Fig. 7.

25 The mechanism 5 in Fig. 6 is provided with a movable plunger 12 with a central channel 13 for air ventilation. Further, the movable plunger 12 is provided with a resilient arc-formed wall 14. This wall 14 extends from the underside of the plunger 12 towards the bottom 15 of the housing 4 of the second end 3b of the tubular body 3 connecting to the bottom 15 of the  
30 housing 4. The wall has a cambered surface facing the housing 4. Upon movement of the plunger 12 from an second end position B2 towards a first end position B1, during blocking of the outer end of the central channel 13 by, for example, a user's finger, the resilient wall 14 becomes compressed

towards the bottom of the housing 15. This compression, activation, forces a volume of gas, decided by the dimensions of the gas displacement mechanism 5, towards the free end of the capillary tube 2a of the micropipette 1. When the plunger 12 thereafter is allowed to move in the opposite direction  
5 from the first end position B1 towards the second end position B2, deactivation of the gas displacement mechanism 5 takes place to replace the displaced air volume either with gas or with liquid. If the micropipette 1 upon activation of the gas displacement mechanism 5 contains liquid, this volume of liquid will be discharged from the pipette 1 by the displacement of gas  
10 towards the free end of the capillary 2a.

Furthermore, the plunger 12 is removably attached to the housing 4 via a snap lock arrangement 16, 17 between the plunger 12 and the housing 4.

In Fig. 7, the wall 14 extending from the underside of the plunger 12 towards the bottom 15 of the housing 4 of the second end 3b of the tubular  
15 body 3 and connecting to the bottom 15 of the housing 4 is, as best seen in the figure, differently dimensioned than in the embodiment of Fig. 6. The wall 14 in Fig. 7 is provided with a folded section 18 adjacent to the underside of the plunger 12. Also here, there is a snap lock arrangement 16, 17 for removably attaching the plunger 12 to the housing 4.

20 The location of the end positions B1, B2 of the air displacement mechanism 5 are not restricted to be in the axial direction A-A of the tubular body 3 as shown in the embodiments in Fig. 6 and 7. The end positions B1, B2 of the air displacement mechanism 5 could equally well be arranged in any, for the purpose of displacing a well-defined volume of gas in the direction  
25 towards the free end of the capillary tube 2a, suitable configuration.

The gas displacement mechanism 5 may be activated and deactivated in repeated cycles, where upon activation a well-defined volume of air is displaced and upon deactivation, the same volume of air is replaced.

30 The gas displacement mechanism 5 may further have the appearance as shown in Fig. 8 and Fig. 9. The gas displacement mechanism may be identical to the gas displacement mechanism disclosed in and described for Fig.6 and the micropipette may be identical to the one described for any one of the preceding figures. The gas displacement mechanism may have a second

moveable plunger 22 arranged to be moveable in the central channel or vent means 13. The second plunger is moveable between a first deactivated end position C1 (as shown in Fig. 8) and a second activated end position C2 (as shown in Fig. 9), although not shown in Figs 8 and 9 the first plunger 12 is also moveable between a deactivated end position and an activated end position as described above. The movement from the first end position to the second end position, i.e. the activation of the second plunger, causes the central channel 13 to be sealed or closed, thereby preventing gas, e.g. air to enter into, or be discharged from the tubular body 3 of the micropipette. Thus an "activated" second plunger in all instances described below means that the central channel or vent means is sealed.

As further shown in Fig. 10 the second plunger 22 may comprise a first part 23 and a second part 25. The first portion 23 may be arranged to be moveable in the central channel, and may have an end portion 26 designed to prevent the second plunger from falling out of the central channel, that is having a diameter which is larger than the free end opening 41 of the central channel, alternatively the end portion has a diameter that is adapted to fit tightly within the central channel.

According to one embodiment as shown in Fig. 10 the end portion of the first part 23 of the second plunger is an elongated enlargement of the diameter of the first part, wherein a groove 24 may be arranged. The groove may be arranged such that when the second plunger has been activated the entire length thereof may be contained within the central channel, and preferably also ending at a distance from the open end of the central channel, thereby allowing for an efficient sealing of the central channel 13 by the activated second plunger 22. At least one groove 24 may be arranged along at least a portion of the first part 23.

The first part 23 may further comprise a circumferential or annular lip or flange 27.

The free end opening 41 of the central channel 13 may be adapted to receive the entire first part of the second plunger 22, i.e. have a diameter that allows for the first part to be inserted into and subsequently contained within

the central channel, but at the same time preventing the second plunger from falling out of the central channel.

The central channel may be provided with a lip or flange 37 that abuts the lip or flange 27 of the second plunger when this is in the deactivated  
5 position (Fig. 8), and thus prevents the second plunger from being accidentally activated, that is pushed into the central channel.

The enlarged diameter of the end portion 26 may be adapted to fit within the central channel 13 and thus allow for a smooth closure or sealing of the central channel or the vent means 13. The elongated groove 24 arranged  
10 in the first part 23, is arranged to allow for gas, such as air to escape from the tubular body 3 when the first plunger 12 is activated the first time. Following the activation of the first plunger 12 the second plunger may be activated, and thus pushed into the central channel or the vent means 13. Through the  
15 activation of the second plunger the groove 24 is pushed below the free end opening 41 of the vent means 13 and the flange 27 is pushed below the flange 37, such that no further gas is able to escape or be sucked into the tubular body 3.

According to yet one alternative embodiment the second part 25 of the plunger 22 may be arranged in connection with a septum or bellows 35 as  
20 shown in Figs 11a and 11b. The septum or bellows 35 may be arranged such that it substantially covers the top portion 32 of the first plunger 12 and have an stilted arch shaped cross section, where the arch comprises a semi-circular rounded portion 39 and where the legs or stilts 38 have a height which essentially defines the maximum distance that the septum or bellows may be  
25 depressed. The septum 35 may further be provided with means 40 for allowing gas to escape when the first plunger is activated.

In order to activate the first plunger the user pushes or depresses the septum from a first deactivated position C1 to an activated second position C2, e.g. in a snap action. The second plunger 22 is thus held in the activated  
30 position by the forces created by this snap action.

The stilts or legs 38 of the arched septum also prevents the second plunger 22 to be inadvertently activated, since the septum must be pushed

beyond the stilts, thereby ensuring that gas is able to escape from the tubular body during the the first activation of the first plunger 12.

The septum thus provides for a stable deactivated position and a metastable activated position of the second plunger. This allows for a smooth  
5 closure or sealing of the central channel 13, thereby further reducing the risk of any unwanted gas to pass into the tubular body 3.

The arrangement as shown in Fig 11a and 11b is to be conceived as arranged on the first moveable plunger 12, which is not shown in the figures.

One alternative of the gas displacement mechanism 5 having a septum  
10 arrangement is to provide the septum with a pin or peg 42, which may be formed in one piece with the septum or bellows as shown in Figs 12, 13a and 13b, the septum or bellows may have the same configuration and function as described above for Figs 11a and 11b. The peg or pin may have a tapered cross section at its base portion which is in connection with the septum, such  
15 that the peg or pin is essentially funnel-shaped.

As an example a pressure of approximately 350 pond is required to push the first plunger 12, or bellows 14, from a deactivated position to an activated position and an additional 150 pond to push the septum or bellows  
20 35, having the pin or peg 42 from a deactivated position C1 into an activated position C2, (as shown in Fig. 13b) thereby closing or sealing the central channel or vent means 13.

The central channel or vent means may be shaped and adapted to receive the peg or pin. The force of the users finger on top of the arched septum 39 is sufficient to keep the septum in an activated position.

25 A weld 45 may be arranged on the outside of the legs or stilts 38.

The second plunger 22 or the septum carrying the peg or pin may also easily be restored to its deactivated position either by simply releasing the pressure on the septum or by squeezing lightly on the sides of the septum, whereby the septum snaps back.

30 In the following when the activation of the second plunger is described, this can either refer to the second plunger with or without the septum, and also to the septum provided with a peg or pin 42.

The micropipette may be operated as described in the following. Before activation of the gas displacement mechanism 5, the free end of the capillary tube 2a is brought into contact with a liquid and a first well-defined volume of liquid is collected by the capillary tube 2. The user may then

5 activate the first plunger 12, while the second plunger remains in its first end position C1, whereby it is possible for a well-defined volume of gas to be displaced through the central channel or vent means 13. When the first plunger 12 has reached its second end position B2 the user may activate the second plunger 22, thereby sealing the central channel 13 and thus

10 preventing any further gas to enter or leave the tubular body.

As the central channel 13 has been permanently sealed by the activation of the second plunger 22, i.e. the second plunger is in its activated second end position C2, no gas may neither be pushed out of the tubular body of the micropipette nor be sucked into the tubular body in the

15 subsequent operation of the micropipette.

The user may subsequently contact the free end 2a with a reservoir containing a second liquid, and then deactivate the entire gas displacement mechanism. As the vent means, i.e. central channel has been sealed, a second well-defined volume of liquid, the volume of which corresponds to the

20 volume of gas discharged through the central channel when activating the first plunger 12 the first time, may be collected by the micropipette and drawn up through the free end 2a, together with the first well-defined volume of liquid, which moves from the capillary tube into the tubular body of the micropipette. That means that after the deactivation of the gas displacement

25 mechanism the micropipette may contain a third well-defined volume of liquid, i.e. a mixture and a sum of the first volume collected by capillary action and the second volume collected when deactivating the gas displacement mechanism the first time.

Subsequently the first and second amounts of liquid may then be

30 discharged from the micropipette by a repeated activation of the gas displacement mechanism, and then collected into the micropipette upon repeated deactivation of the gas displacement mechanism. This repeated activation and deactivation of the mechanism thereby allows for an efficient

and simple way of mixing at least two liquids, e.g. a blood sample with a reagent in connection with blood analysis.

The user may re-open the central channel 13, and e.g. enable a re-use of the gas displacement mechanism, by pulling the first and second plungers  
5 apart.

The first and the second plunger may be made of the same or different materials.

One alternative embodiment (not shown in the figures) is to provide the above described activation of the gas displacement mechanism in a two  
10 phase procedure, a first phase in which the inside volume of the first plunger (12) of the gas displacement mechanism expands followed by a second phase in which the inside volume contracts. Mixing of the first and second liquids is then accomplished by subsequent deactivation of only the second phase of the first plunger and repeated cycles of second phase activation and  
15 second phase deactivation.

The person skilled in the art realizes that the present invention by no means is limited to the preferred embodiments described above. On the contrary, many modifications and variations are possible within the scope of the appended claims. For example, the position of the liquid level when the  
20 capillary tube 3 is full could be visualized by visual indication means, such as a mark on the outside of the tubular body 3.

According to one embodiment there is provided a micropipette consisting of:

a capillary tube 2 adapted for collecting a well-defined volume of liquid  
25 by capillary action, the capillary tube 2 having a central, axial channel,

a gas displacement mechanism 5,

a tubular body 3 provided with a central, axial channel, the tubular body 3 having a first end 3a and a second end 3b, wherein the first end 3a is connected to one end 2a of the capillary tube 2, forming a tubular body-  
30 capillary tube 3, 2 assembly with through channel comprising the axial channels of the capillary tube 2 and the tubular body 3, and the second end 3b of the tubular body 3 is connected to the gas displacement mechanism 5, and

wherein a portion of the tubular body 3 that is in a remote location from the first end 3a of the tubular body 3 is provided with vent means, or the gas displacement mechanism 5 is provided with vent means,

5 where the inner surface 7 of the central, axial channel of the tubular body 3 has a different capillary capacity than the inner surface 8 of the capillary tube 2, and

10 where the one end 2b of the capillary tube 2 has a first distance between a central axis of the capillary tube 2 and the outer wall of the capillary tube 2 in a direction perpendicular to the central axis of the capillary tube 2,

where the first end 3a of the tubular body 3 has a second distance between the central axis of the tubular body 3 and the inner channel wall of the tubular body 3 in a direction perpendicular to the central axis of the tubular body 3,

15 where a difference between the second distance and the first distance is from around 0 to around 5 times the wall thickness D of the capillary tube 2.

## CLAIMS

1. A micropipette (1) comprising:  
a capillary tube (2) adapted for collecting a well-defined volume of  
5 liquid by capillary action, said capillary tube having a central, axial channel;  
a gas displacement mechanism (5);  
a tubular body (3) provided with a central, axial channel, said tubular  
body (3) having a first end (3a) and a second end (3b), wherein said first end  
(3a) is connected to one end (2b) of said capillary tube (2), forming a tubular  
10 body-capillary tube (3, 2) assembly with through channel comprising said  
axial channels of said capillary tube (2) and said tubular body (3), and said  
second end (3b) of said tubular body (3) is connected to said gas  
displacement mechanism (5), and  
wherein a portion of said tubular body (3) that is in a remote location  
15 from said first end (3a) of said tubular body (3) is provided with vent means,  
or said gas displacement mechanism (5) is provided with vent means, c h a r  
a c t e r i z e d in that the inner surface (7) of said central, axial channel of  
said tubular body (3) has a different capillary capacity than the inner surface  
(8) of said capillary tube (2); and  
20 wherein  
said one end (2b) of said capillary tube (2) has a first distance (E)  
between a central axis (A-A) of said capillary tube (2) and the outer wall of  
said capillary tube (2) in a direction perpendicular to said central axis of said  
capillary tube (2):  
25 wherein said first end (3a) of said tubular body (3) has a second  
distance (F) between said central axis (A-A) of said tubular body (3) and the  
inner channel wall of said tubular body (3) in a direction perpendicular to said  
central axis of said tubular body (3);  
wherein a difference between said second distance (F) and said first  
30 distance (E) is from around 0 to around 5 times the wall thickness (D) of said  
capillary tube (2).

2. A micropipette (1) comprising:

a capillary tube (2) adapted for collecting a first well-defined volume of liquid by capillary action, said capillary tube having a central, axial channel;

a gas displacement mechanism (5);

5 a tubular body (3) provided with a central, axial channel, said tubular body (3) having a first end (3a) and a second end (3b), wherein said first end (3a) is connected to one end (2b) of said capillary tube (2), forming a tubular body-capillary tube (3, 2) assembly with through channel comprising said axial channels of said capillary tube (2) and said tubular body (3), and said  
10 second end (3b) of said tubular body (3) is connected to said gas displacement mechanism (5), and

wherein the gas displacement mechanism (5) is adapted to be activated by a movement between a first end position (B1) and a second position (B2), and

15 wherein a portion of said tubular body (3) that is in a remote location from said first end (3a) of said tubular body (3) is provided with vent means, or said gas displacement mechanism (5) is provided with vent means, wherein

the inner surface (7) of said central, axial channel of said tubular body  
20 (3) has a different capillary capacity than the inner surface (8) of said capillary tube (2);

c h a r a c t e r i s e d in that

said one end (2b) of said capillary tube (2) has a first distance (E)  
25 between a central axis (A-A) of said capillary tube (2) and the outer wall of said capillary tube (2) in a direction perpendicular to said central axis of said capillary tube (2):

wherein said first end (3a) of said tubular body (3) has a second distance (F) between said central axis (A-A) of said tubular body (3) and the  
30 inner channel wall of said tubular body (3) in a direction perpendicular to said central axis of said tubular body (3);

wherein a difference between said second distance (F) and said first distance (E) is from around 0 to around 5 times the wall thickness (D) of said capillary tube (2), and  
that in the activation of the gas displacement mechanism (5) a well-defined  
5 volume of gas that is larger than the volume of the collected first liquid is displaced.

3. The micropipette (1) according to any one of claims 1-2, wherein said central, axial channel of said tubular body (3) along a section of its  
10 elongation is provided with a tapered portion, the tapering being in a direction towards said first end (3a) of said tubular body (3).

4. The micropipette (1) according to any one of the preceding claims, wherein a material of said tubular body (3) is a material having a lower capillary  
15 capacity for a hydrophilic or hydrophobic liquid than a material of said capillary tube (2).

5. The micropipette (1) according to claim 4, wherein said inner surface (8)  
of said capillary tube (2) is hydrophilic.  
20

6. The micropipette (1) according to claim 5, wherein said inner surface (7)  
of said central, axial channel of said tubular body (3) is hydrophobic.

7. The micropipette (1) according to any one of the preceding claims,  
25 wherein said capillary tube and said tubular body comprises polymeric materials.

8. The micropipette (1) according to any one of the preceding claims,  
wherein said capillary tube (2) and/or said tubular body (3) is transparent.

30 9. The micropipette (1) according to claim 8, wherein said material of said capillary tube (2) and/or said material of said tubular body (3) is coloured.

10. The micropipette (1) according to any one of the preceding claims, wherein the maximum liquid volume that is collectable by said capillary tube (2) is in the range of 0.25  $\mu\text{l}$  to 200  $\mu\text{l}$ , preferably less than or equal to 50  $\mu\text{l}$ , less than or equal to 20  $\mu\text{l}$ , less than or equal to 15  $\mu\text{l}$ , or less than or equal to  
5 10  $\mu\text{l}$ .

11. The micropipette (1) according to any one of the preceding claims, wherein the maximum liquid volume that is collectable by said tubular body (3) is larger than or equal to 1.5, 2, 5, 10, 20, 30, 40, 50 or 100 times said  
10 maximum liquid volume that is collectable by said capillary tube (2).

12. The micropipette (1) according to any one of the preceding claims, wherein said gas displacement mechanism (5) is an ordinary squeeze bulb, which upon compression displaces a volume of gas in a direction towards a  
15 free end (2a) of said capillary tube (2), said displaced gas volume being arranged to discharge a volume of liquid from said free end (2a) of said capillary tube (2).

13. A micropipette (1) according to any one of the preceding claims 1 to  
20 12, wherein said gas displacement mechanism (5) is movable between two distinct end positions (B2, B1): one activated first end position (B1) and one deactivated second end position (B2), wherein said gas displacement mechanism (5) is arranged to be activated by a movement from said second end position (B2) towards said first end position (B1), wherein a well-defined  
25 volume of gas is displaced in a direction towards the free end (2a) of said capillary tube (2), said displaced gas being arranged to discharge a well-defined volume of liquid from said free end (2a) of said capillary tube (2).

14. A micropipette (1) according to any one of claims 1 to 12, wherein said  
30 gas displacement mechanism (5) comprises a first plunger (12) which is movable between two distinct end positions (B2, B1): one activated first end position (B1) and one deactivated second end position (B2), wherein said gas displacement mechanism (5) is arranged to be activated by a movement of

said first plunger (12) from said second end position (B2) towards said first end position (B1), whereby a well-defined volume of gas is displaced in a direction towards a central channel(13) arranged in a first plunger (12) of the gas displacement mechanism (5).

5

15. A micropipette (1) according to claim 14, wherein the gas displacement mechanism (5) further comprises a second plunger (22), which is arranged to be moveable in the central channel (13) and between two distinct end positions (C1, C2), one deactivated first end position (C1) and one activated second end position (C2), wherein said second plunger (22) is arranged to be activated by a movement of said second plunger from said first end position (C1) towards said second end position (C2) wherein the activation of the second plunger seals the central channel (13).

16. The micropipette (1) according to claim 15, wherein the second plunger (22) is arranged to be activated following the activation of the first plunger (12), and further wherein the gas displacement mechanism (5) is arranged to be deactivated when the first plunger (12) is moved from said activated end position (B1) to said deactivated end position (B2) and wherein the second plunger (22) remains in the activated position.

17. A micropipette (1) according to any one of the preceding claims, wherein said gas displacement mechanism (5) is made of or partially made of resilient material.

25

18. A micropipette (1) according to claim 17, wherein said resilient material is an elastomer, preferably wherein the elastomer is rubber.

19. A micropipette (1) according to any one of the preceding claims wherein said gas displacement mechanism (5) is removably attached to the tubular body (3).

30

20. A micropipette (1) according to any one of the preceding claims,

wherein the volume of displaceable gas from said gas displacement mechanism (5) is larger than the maximum collectable volume of said capillary tube (2) and in the range of 0.5  $\mu$ l to 500  $\mu$ l, preferably more than or equal to 10  $\mu$ l, more than or equal to 25  $\mu$ l, more than or equal to 50  $\mu$ l, more than or equal to 100  $\mu$ l, more than or equal to 150  $\mu$ l, more than or equal to 200  $\mu$ l, more than or equal to 250  $\mu$ l or more than or equal to 300  $\mu$ l.

21. A micropipette (1) according to any one of the preceding claims 1-19, wherein the volume of displaceable gas from said gas displacement mechanism (5) is smaller than the maximum collectable volume of said capillary tube (2).

22. A method for collecting and discharging a well-defined volume of a liquid making use of said micropipette (1) defined in any one of claims 1 to 20, comprising the steps of:

- f) collecting a well-defined volume of said liquid by contacting said free end (2a) of said capillary tube (2) to said liquid;
- g) activating said gas displacement mechanism (5) to discharge said volume of said liquid.

20

23. A method for collecting and discharging a well-defined volume of a first liquid into a larger volume of a second liquid and mixing said two liquids, making use of said micropipette (1) defined in any one of claims 1 to 20, comprising the steps of:

- h) collecting a well-defined volume of said first liquid by contacting said free end (2a) of said capillary tube (2) to said first liquid;
- i) activating said gas displacement mechanism (5) to discharge said volume of said first liquid into a reservoir with said second liquid;
- j) deactivating said gas displacement mechanism (5) by replacing said displaced gas volume with liquid for mixing of said first and said second liquids, wherein a volume of a mixture of said two liquids, larger than said volume of said first liquid, is collected through said capillary tube (2) into said tubular body (3);

30

- k) activating said air displacement mechanism (5) to discharge a mixture of said first and second liquids into said reservoir, and
- l) optionally, repeating step c) and d).

- 5           24. A method for collecting a well-defined volume of a first liquid and mixing said first liquid with a second liquid, making use of said micropipette (1) defined in any one of claims 14-16, comprising the steps of:
- h) collecting a well-defined volume of said first liquid by contacting said free end (2a) of said capillary tube (2) to said first liquid;
  - 10           i) activating said first plunger (12) to discharge a well-defined volume of gas contained in the tubular body, in a direction through said central channel (13);
  - j) activating said second plunger (22) to seal the central channel (13);
  - k) contacting the free end (2a) of said capillary tube (2) with a second  
15           liquid;
  - l) deactivating said gas displacement mechanism (5), thereby replacing said displaced gas volume with a second volume of said second liquid, for mixing of said first and second volumes of said first and said second liquids, wherein a volume of a mixture of said  
20           first and second liquids, larger than said volume of said first liquid, is collected through said capillary tube (2) into said tubular body (3);
  - m) activating said first plunger (12) of said gas displacement mechanism (5) a second time, wherein the second plunger (22) remains in the activated position, to discharge a mixture of said first  
25           and second liquids into said reservoir, and
  - n) optionally, repeating step e) and f).

25. A tubular body-capillary tube (3, 2) assembly for use in a micropipette as claimed in any one of the preceding claims 1 to 21, wherein the tubular  
30           body-capillary tube (3, 2) assembly comprises the features as defined in any one of claims 1 to 11.

26. A kit for diagnostic determination of analytes or analyte

processes in near-patient medical or veterinary diagnostic or research laboratories, comprising a micropipette (1) as claimed in any one of claims 1 to 21, reagents and disposable reaction containers.

5

10

15

20

1/10

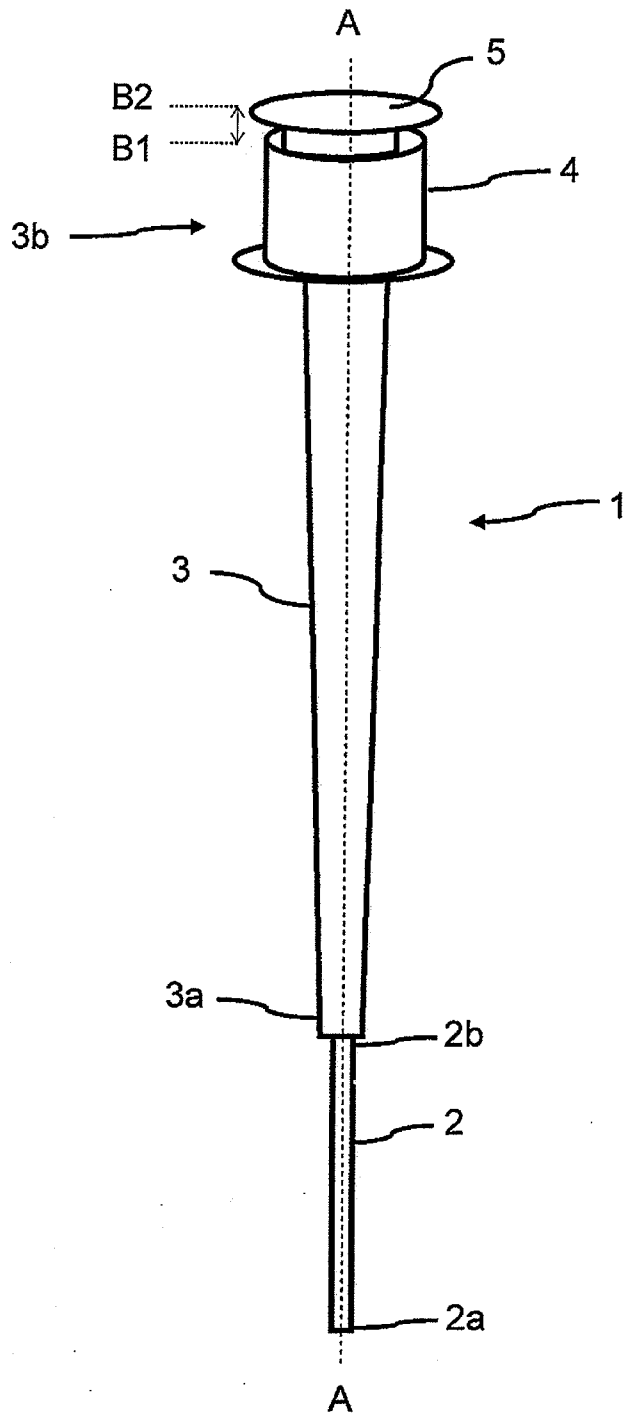


Fig. 1

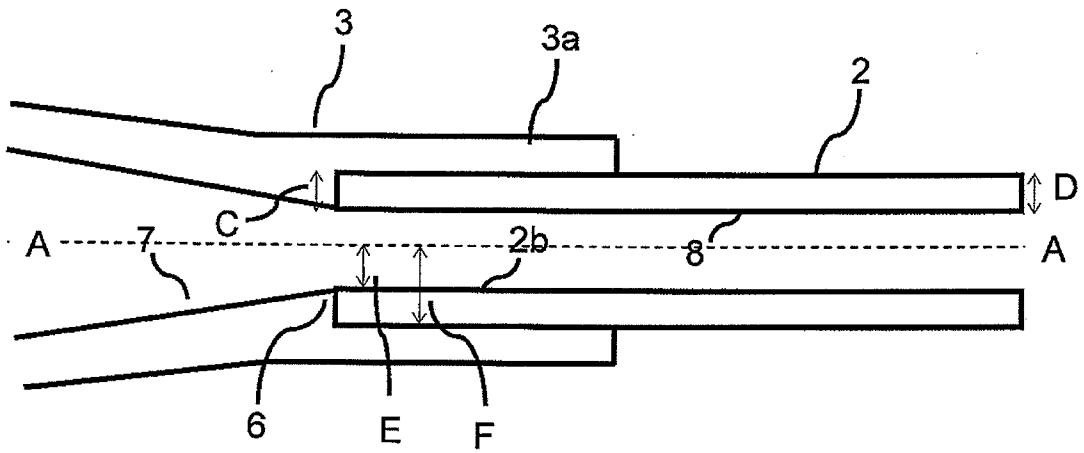


Fig. 2

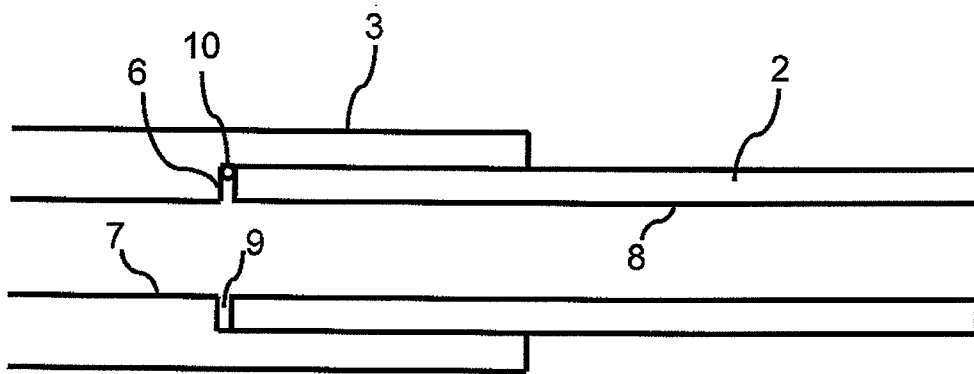


Fig. 3

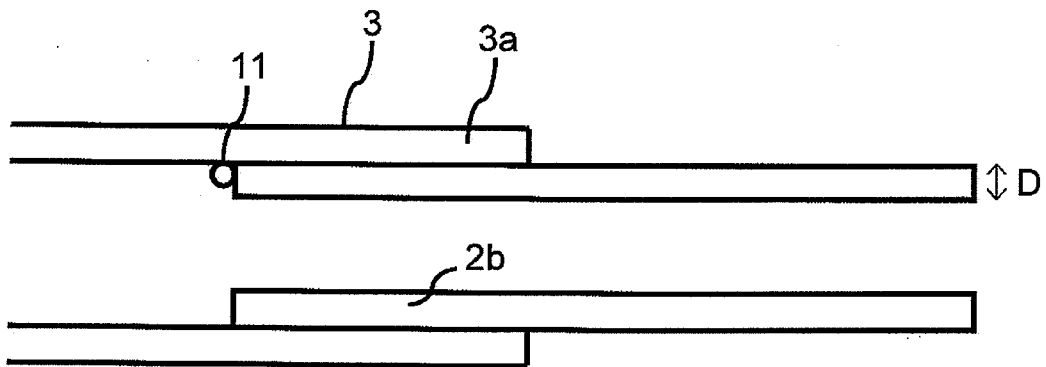


Fig. 4

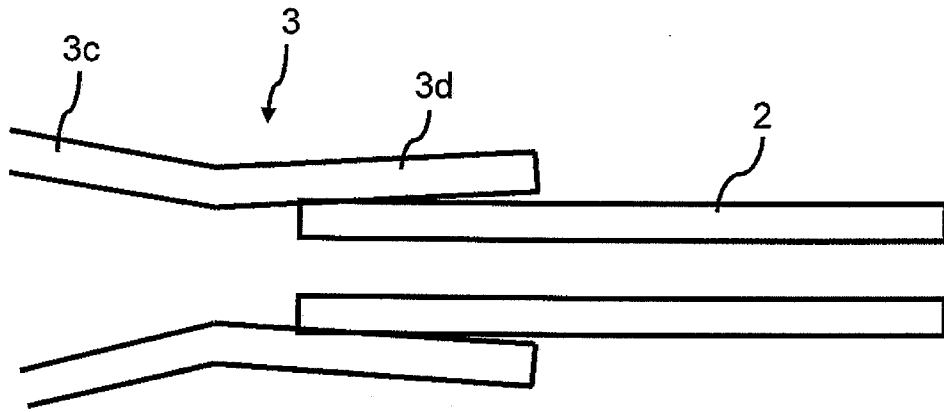


Fig. 5

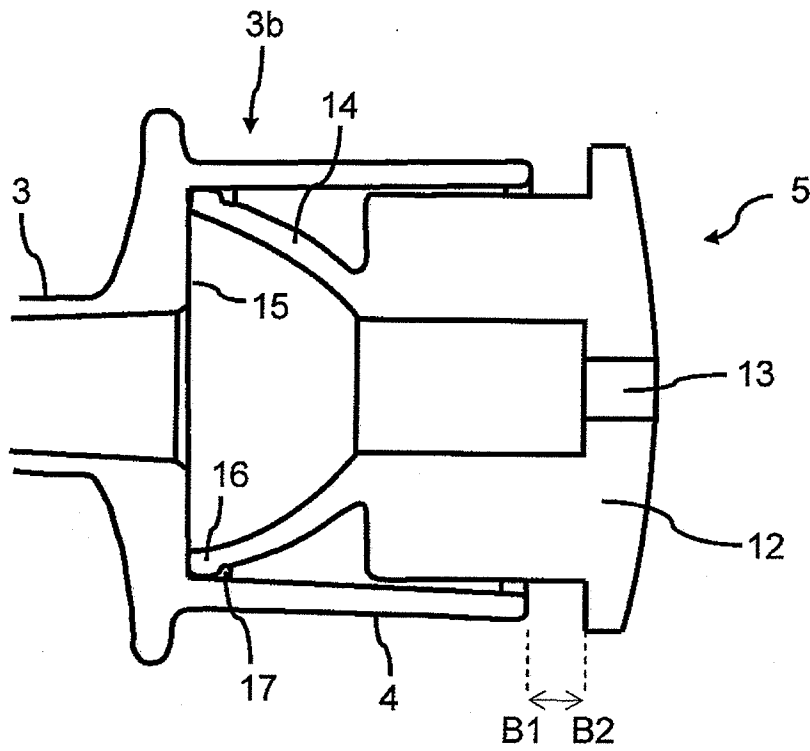


Fig. 6

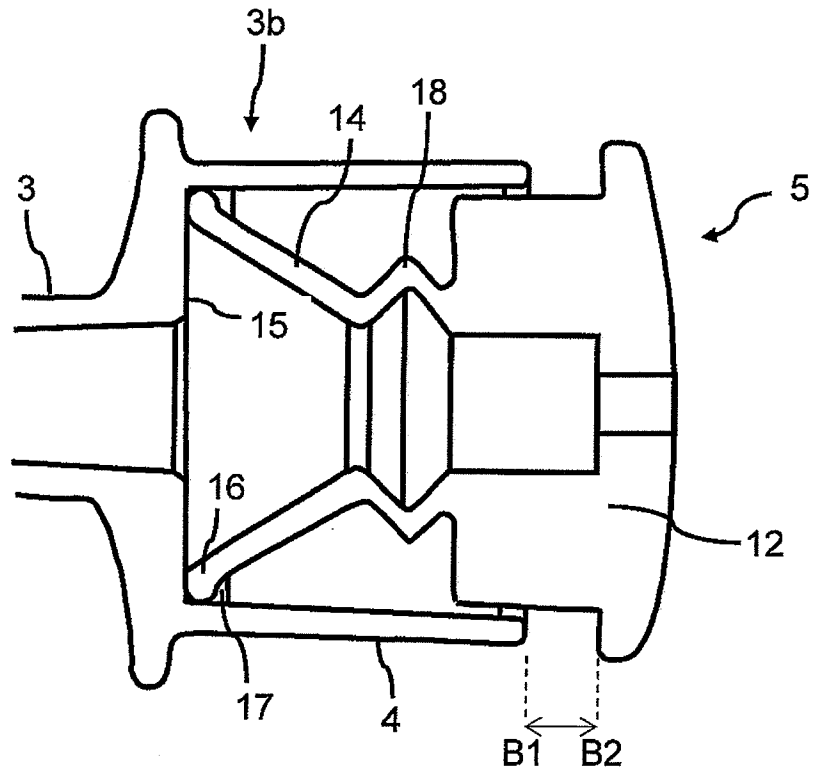


Fig. 7

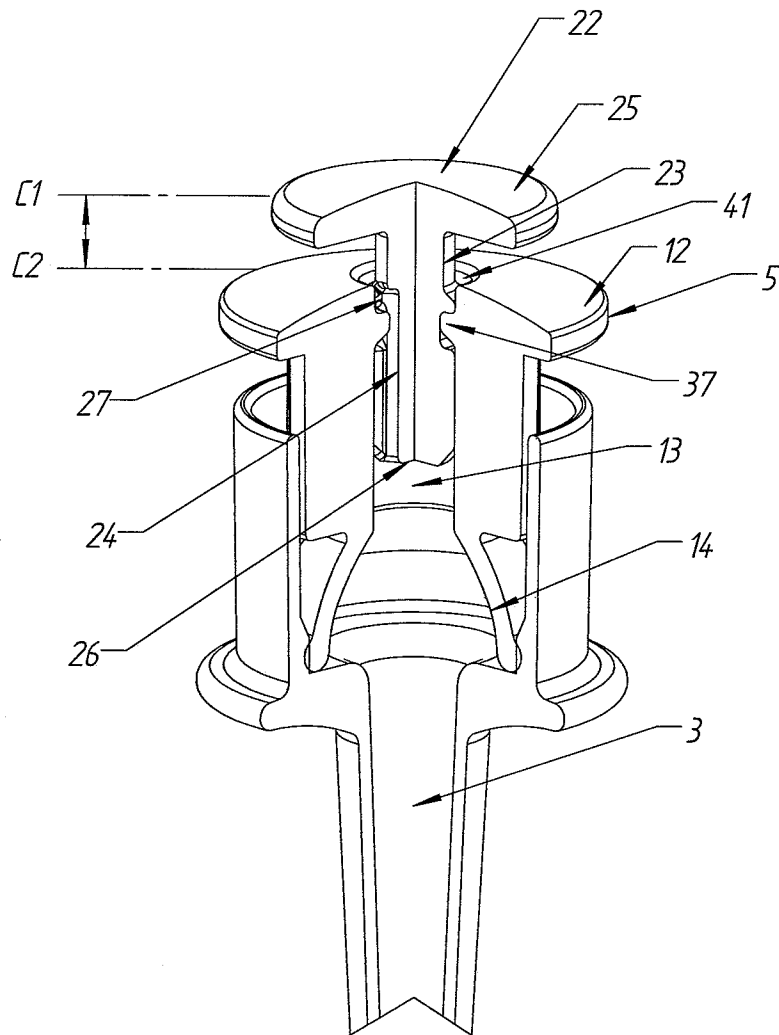


Fig. 8

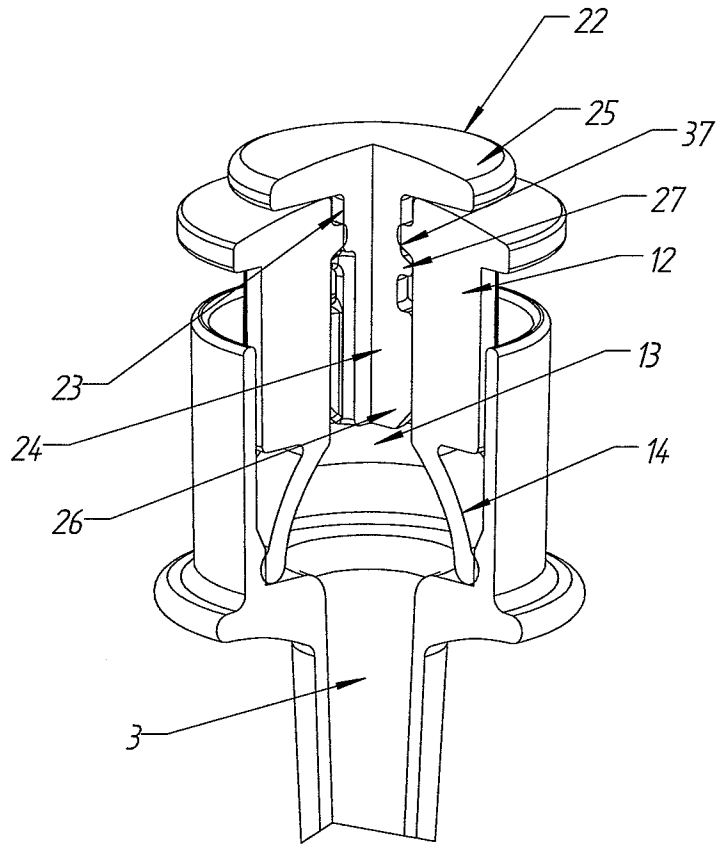


Fig. 9

7/10

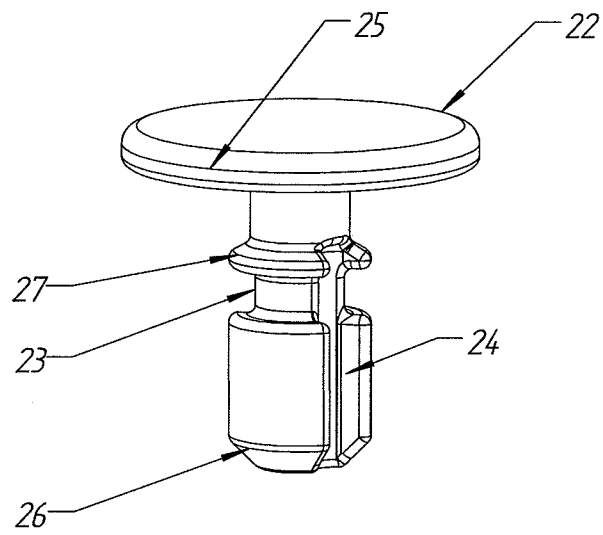


Fig. 10

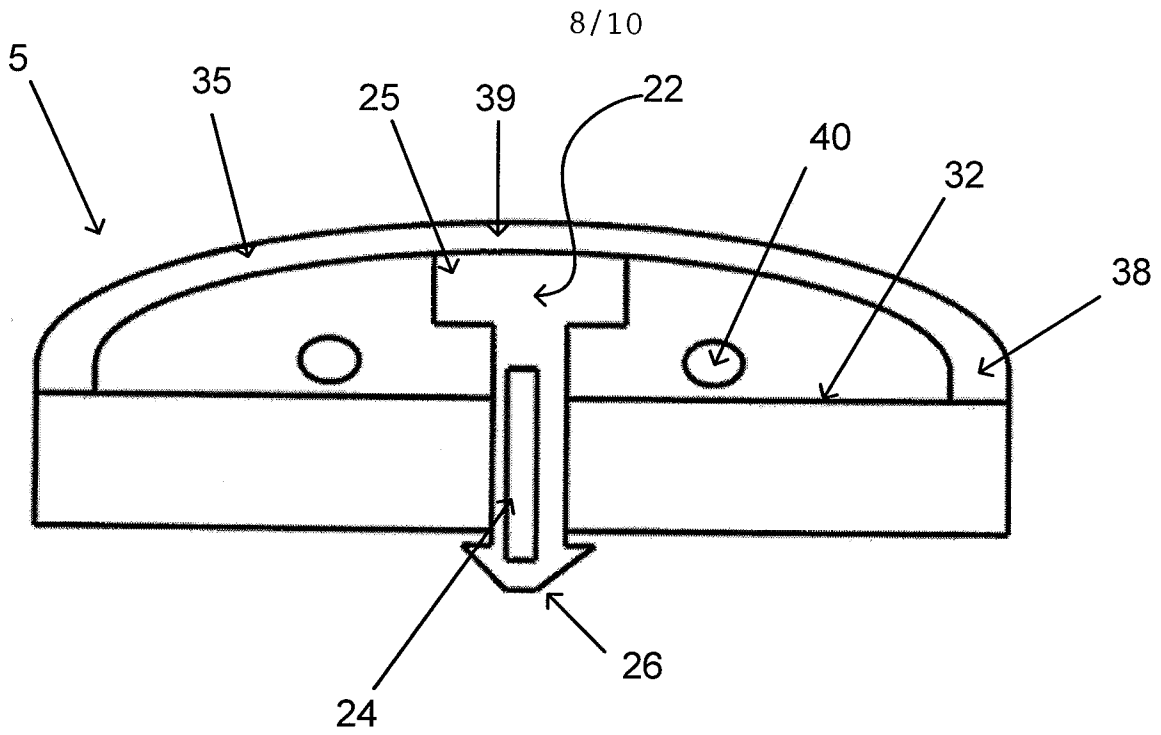


Fig. 11a

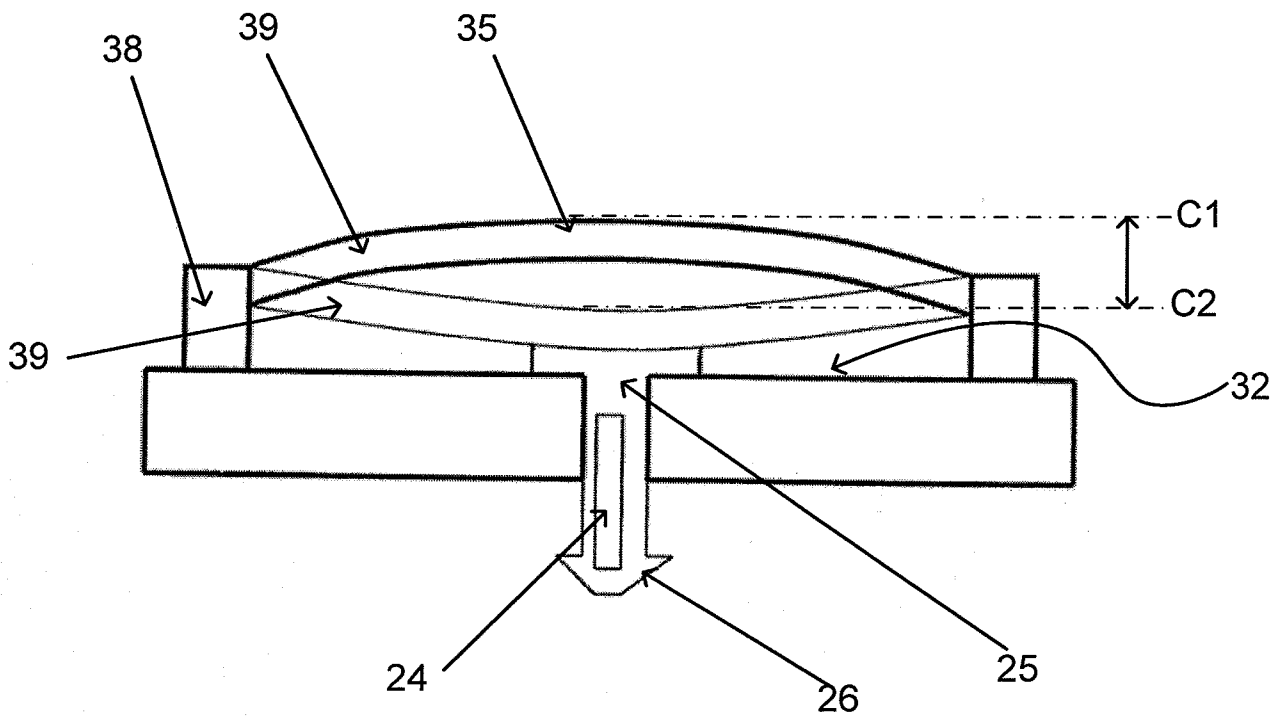


Fig. 11b

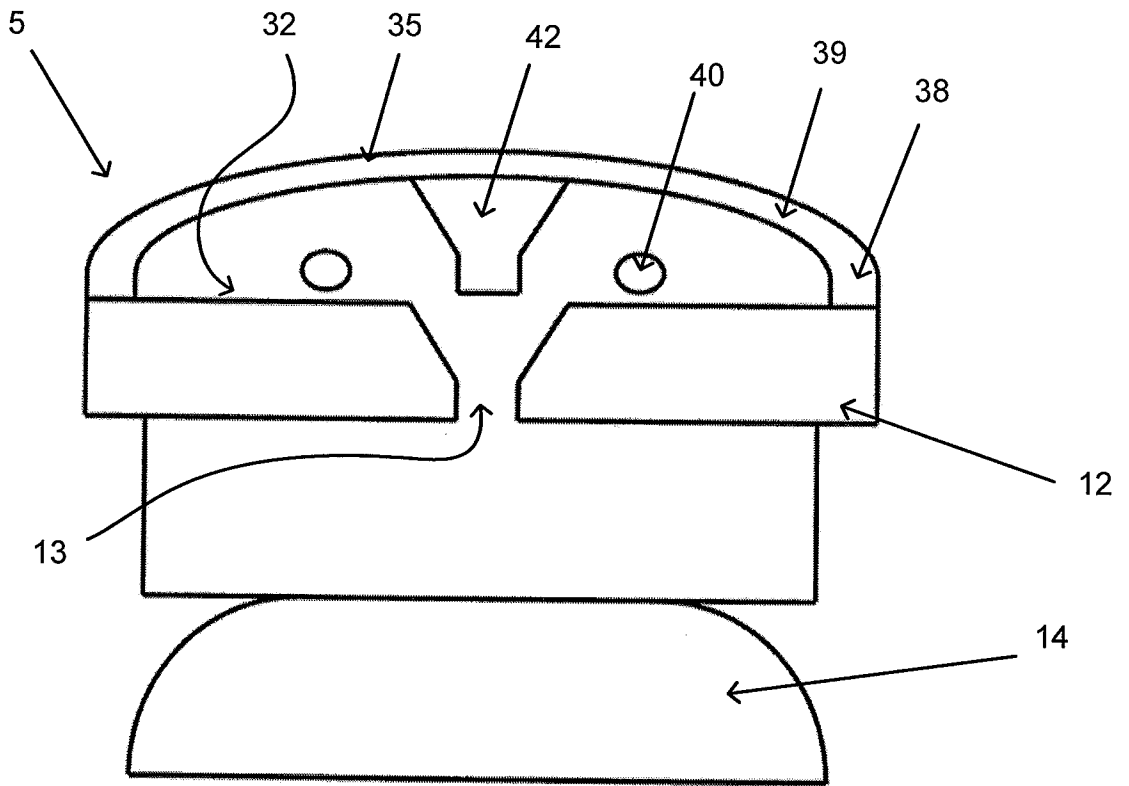


Fig. 12

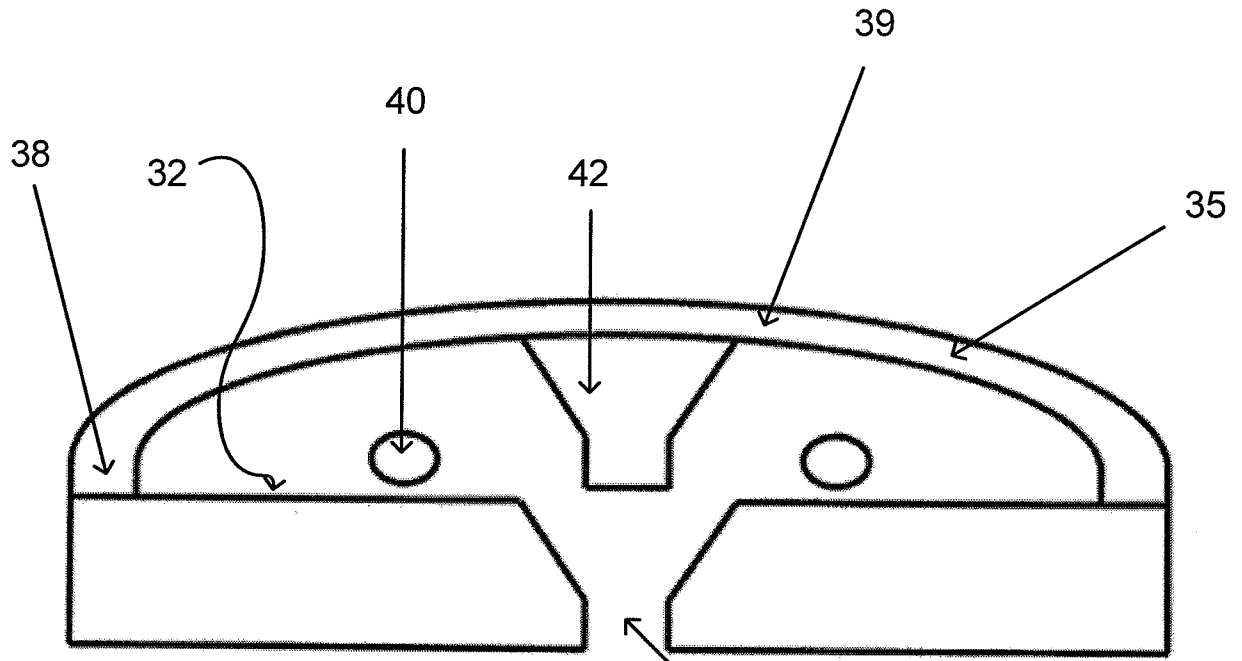


Fig. 13a

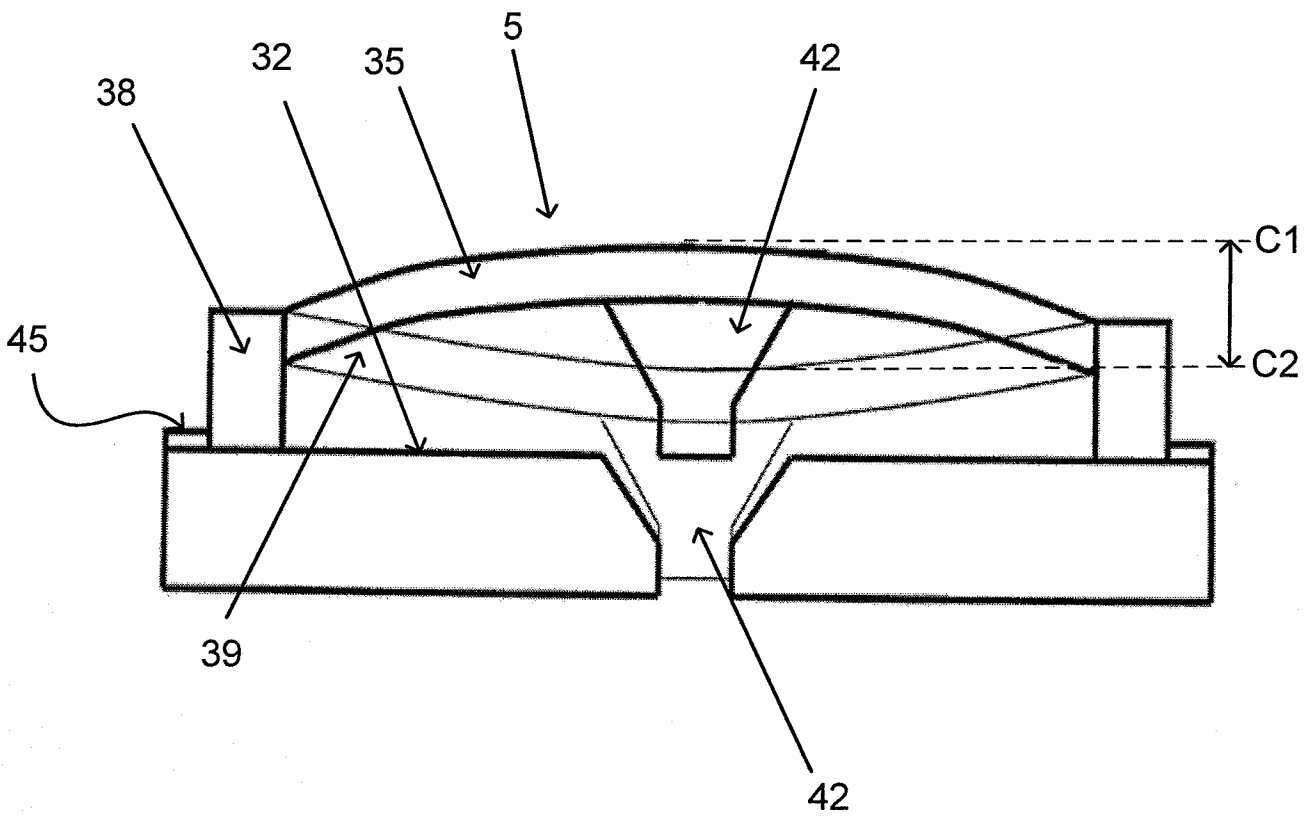


Fig. 13b

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE2010/051435

A. CLASSIFICATION OF SUBJECT MATTER		
IPC: see extra sheet		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
IPC: B01L		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
SE, DK, FI, NO classes as above		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
EPO-Internal, PAJ, WPI data, BIOSIS, COMPENDEX, EMBASE		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JP 5184949 A (FUJI PHOTO FILM CO LTD), 27 July 1993 (1993-07-27); (abstract) Retrieved from: WPI database; Original document: Paragraphs [0001], [0008]-[0010], [0030]-[0036], [0044]-[0046], [0049]-[0054], [0059]-[0062]; figures 1-10 --	1-13, 17-23, 25-26
A	US 4784834 A (HIRSCHMANN ADOLF M), 15 November 1988 (1988-11-15); column 2, line 1 - line 5; column 2, line 46 - line 54; column 4, line 50 - line 58; column 5, line 53 - line 61; column 5, line 67 - column 6, line 2; figures 1-4 --	1-26
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C. <input checked="" type="checkbox"/> See patent family annex.		
* Special categories of cited documents:		
"A"	document defining the general state of the art which is not considered to be of particular relevance	"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
"E"	earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"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)	"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
"O"	document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P"	document published prior to the international filing date but later than the priority date claimed	
Date of the actual completion of the international search 28-02-2011		Date of mailing of the international search report 28-02-2011
Name and mailing address of the ISA/SE Patent- och registreringsverket Box 5055 S-102 42 STOCKHOLM Facsimile No. + 46 8 666 02 86		Authorized officer Andreas Gustafsson Telephone No. + 46 8 782 25 00

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/SE2010/051435

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 5460782 A (COLEMAN CHARLES M ET AL), 24 October 1995 (1995-10-24); column 2, line 40 - line 61; figures 1-6; claim 11 --	1-26
A	DE 10039195 A1 (HIRSCHMANN LABORGERAETE GMBH), 21 February 2002 (2002-02-21); abstract; paragraphs [0002], [0006]-[0008], [0011]-[0013] --	1-26
A	EP 0209705 A2 (DRUMMOND SCIENT CO), 28 January 1987 (1987-01-28); abstract; page 1, line 21 - page 2, line 29; page 3, line 14 - page 4, line 3; page 4, line 14 - line 20; page 5, line 32 - page 6, line 9 --	1-26
A	US 4589421 A (ULLMAN EDWIN F), 20 May 1986 (1986-05-20); abstract; figures 1-13 --	1-26
A	DE 3701250 A1 (CARSTENSEN CARSTEN A), 28 July 1988 (1988-07-28); whole document -- -----	1-26

**Continuation of:** second sheet

**International Patent Classification (IPC)**

**B01L 3/02** (2006.01)

**Download your patent documents at [www.prv.se](http://www.prv.se)**

The cited patent documents can be downloaded:

- From "Cited documents" found under our online services at [www.prv.se](http://www.prv.se)  
(English version)
- From "Anförda dokument" found under "e-tjänster" at [www.prv.se](http://www.prv.se)  
(Swedish version)

Use the application number as username. The password is **QBREICZSQB**.

Paper copies can be ordered at a cost of 50 SEK per copy from PRV InterPat (telephone number 08-782 28 85).

Cited literature, if any, will be enclosed in paper form.

## INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/SE2010/051435

JP	5184949 A	27/07/1993	NONE		
US	4784834 A	15/11/1988	DE	3614085 C2	07/09/1989
			EP	0232517 B1	28/02/1990
US	5460782 A	24/10/1995	NONE		
DE	10039195 A1	21/02/2002	NONE		
EP	0209705 A2	28/01/1987	DE	3688156 D1	06/05/1993
			DK	167999 B1	17/01/1994
			DK	345486 A	23/01/1987
			JP	62027046 A	05/02/1987
			JP	7041171 B	10/05/1995
			JP	2027626 C	26/02/1996
			US	5059398 A	22/10/1991
US	4589421 A	20/05/1986	NONE		
DE	3701250 A1	28/07/1988	NONE		