

**METHODS AND DEVICES FOR HANDLING A FLUID AND**  
**DELIVERING THE FLUID TO THE EYE**

**FIELD OF THE INVENTION**

5    [0001]       The invention is directed to methods and devices for handling a fluid and for delivering the fluid to the eye.

**BACKGROUND OF THE INVENTION**

10   [0002]       Fluid delivery to the eye presents a number of challenges. The fluid should be provided with a controlled droplet size and delivered at a controlled velocity for comfort while delivered at high enough velocity to deliver the entire dose. Another challenge with fluid delivery to the eye is the need for rapid delivery so that an eye blink does not interfere with delivery.

15   [0003]       Fluid delivery devices for the eye have used a piezoelectric element to vibrate an element, such as a plate, with holes through which the fluid is ejected. A problem with many of these devices is that they are typically “wet” systems in which the fluid is exposed through the holes in the plate when stored which may lead to undesirable evaporation and contamination between uses.

20   **SUMMARY OF THE INVENTION**

25   [0004]       The present invention is directed to methods and devices for handling a fluid and delivering the fluid to the eye. In one aspect, the fluid to be delivered to the eye is contained in an enclosure which holds the fluid to be dispensed in a chamber defined by the enclosure. The enclosure holds the dose of fluid in proximity to the openings so that the fluid may be ejected in a short amount of time and with little residual volume left.

30   [0005]       The enclosure has a lip positioned adjacent a vibrating element having openings through which the fluid is ejected. The lip may be unattached to the vibrating element but still in contact with the vibrating element or may be spaced apart a short distance so that surface tension holds the fluid in the chamber. The vibrating element may have a relatively small maximum amplitude when vibrated which is less than an average separation

distance between the lip and the vibrating element or less than a minimum separation distance between the lip and the vibrating element.

[0006] The enclosure may also be shaped to cooperate with the vibrating element to avoid capillary feed near the openings in the vibrating element. To this end, the enclosure  
5 may be spaced apart from the vibrating element so that at least 75%, at least 95%, or all of the openings are spaced at least 0.014 from the nearest part of the enclosure. Capillary feed may be incorporated in other aspects of the invention without departing from those aspects of the invention. The enclosure is also shaped so that all of the fluid can reach the openings in a short period of time. The enclosure has an internal surface in contact with the fluid shaped so  
10 that at least 75%, at least 95%, or even all, of the internal surface is no more than 0.060 inch, or no more than 0.040 inch, from a nearest of the plurality of openings. Stated another way, the enclosure has an internal surface shaped so that the chamber is formed with at least 75%, at least 95%, or all, of the internal surface has direct line of sight to at least one of the openings. The inner surface of the enclosure may be hydrophobic over at least 70% of the  
15 inner surface in contact with fluid.

[0007] The lip may be biased against the vibrating element with a modest force to prevent the fluid from escaping while not overly dampening vibrations. The lip may exert a force of no more than 3 gram-f on the vibrating element measured in the direction of a central axis of the vibrating element. The lip may also apply a spring load to the vibrating element so  
20 that minor displacements due to temperature, pressure or shock from an impact (dropped) can be accommodated. The spring load may also help to address manufacturing tolerances which affect the load applied by the lip to the vibrating element. The lip may exert a spring load on the vibrating element with an average spring constant of no more than 60 gram-f/mm for displacements up to 0.050 mm. The enclosure itself may be resilient with a wall of the  
25 enclosure having a tapered portion with a relatively thin wall to provide flexibility. The tapered portion of the wall and has a ratio of radial displacement to longitudinal displacement of at least 1 to 3, at least 1 to 2 and may be at least 1 to 1. Stated another way, the tapered portion also extends radially with respect to the open end of the enclosure for at least half of an effective radius of the open end of the enclosure. The lip and/or the vibrating element may  
30 have a PTFE coating adjacent to the other to reduce friction therebetween. The coating(s) may extending around at least 270 degrees when viewed along the central axis.

[0008] The enclosure may allow air into to replace ejected fluid through the openings and/or between the lip and the vibrating element and may include no dedicated vent opening. The maximum amplitude may be somewhat small which permits air to enter the chamber

while still preventing fluid from escaping from the chamber. The enclosure to vibrating element interface defines an enclosed border (which may be defined by either the vibrating element or the enclosure) which is somewhat larger than the extent of the openings with an excess area which extends radially outwardly at least 0.3 times the effective radius of the enclosed feed area.

[0009] The enclosure may include a wall opening through the wall which exposes the chamber through the wall. The wall opening extends through the wall to expose the chamber through the wall without permitting fluid to escape while permitting air to enter when fluid is ejected. The wall opening has a longitudinal dimension measured from the lip in the direction of the central axis and a radial dimension measured in a radial direction relative to the central axis. The enclosure also has an internal wall with a side facing the openings in the vibrating element. The longitudinal dimension of the wall opening is at least 80% of a separation distance between the vibrating element and the side of the enclosure facing the openings. The radial dimension of the wall opening may be no more than 10%, or no more than 5%, of a equivalent circumference of the lip.

[0010] The wall opening tapers as it extends proximally away from the lip. The wall opening extends from the lip proximally and a circumferential dimension of the wall opening tapers down as the wall opening extends proximally from the lip. The wall opening tapers so that a tapered shape is oriented in the direction of the fluid inlet to the chamber when viewed along the central axis. The wall opening may also extend through the frustoconical portion of the wall and may extend proximally from the lip for at least 80% of the length of the frustoconical portion.

[0011] The fluid may be delivered rapidly and at relatively high velocity and pressure to encourage all of the fluid to gather in the chamber. The total downstream volume of the fluid path from a pump or valve which isolates the chamber may be sized somewhat larger than the volume to permit the fluid to move within the enclosure somewhat and coalesce into a single droplet due to surface tension. The volume of the fluid may be 40%-70% of the total downstream volume.

[0012] The enclosure may also split the fluid flow into at least two (and may be three, four or more) inlets to the chamber. Each of the inlets directs the fluid at a sidewall before being directed at the plurality of openings. The enclosure has a main inlet which directs the flow in a direction within 30 degrees of the central axis while the inlets to the chamber are oriented 60-90 degrees from the central axis and directed at the sidewall. The enclosure may be an integrally formed structure which defines the chamber.

[0013] The pump may have a first part and a second part which reciprocate between a stored position, to a forward stroke position and back to the stored position in a single cycle. A cavity is formed between the two parts in which the fluid is drawn and subsequently expelled into the chamber. An air make-up chamber may also be coupled to the pump to  
5 force air into a fluid container during each cycle to actively vent the fluid container.

[0014] The present invention may be practiced as a device or method. As to the device it is understood that a therapeutic delivery device may be separated into reusable and disposable portions in innumerable different combinations. As such, the present invention provides inventive concepts that may be logically grouped together in various ways which  
10 define a subset of the device which may be a disposable or reusable portion. For example, the fluid container may be replaced with the enclosure or may be independent and, therefore, may be claimed in either manner. The enclosure may form part of a reusable device together with the vibrating element or may be part of a disposable (with or without the fluid container) without departing from the scope of the invention. The claimed invention lies in the  
15 methodology and structure rather than in specific delineation of the disposable and reusable parts. Thus, it is understood that the disposable parts may be defined in virtually any suitable manner and the claims may define any such limited aspect or combination. As further examples, the claims may define the pump and the fluid container, the enclosure and the vibrating element, or even a single structure such as the enclosure by itself. Each of these  
20 could be part of reusable device, a single-use device, or as a disposable and may be claimed as such.

[0015] These and other features will become apparent from the following description of the preferred embodiments, claims and drawings.

## 25 BRIEF DESCRIPTION OF THE DRAWINGS

[0016] Fig. 1 shows a device for handling a fluid and delivering the fluid to the eye with a cap removed for introducing a fluid container.

[0017] Fig. 2 shows a vibrating element with openings through which the fluid is ejected.

30 [0018] Fig. 3 shows the locking mechanism for the fluid container.

[0019] Fig. 4 shows a first housing part with an outer cover removed to show a shutter with an aperture through which the fluid is dispensed.

- [0020] Fig. 5 shows a cross-section of a second housing part which houses the control system and battery.
- [0021] Fig. 6 shows a front view of the device with the outer cover removed.
- [0022] Fig. 7 shows the fluid delivery path from the fluid container to an enclosure.
- 5 [0023] Fig. 8 shows a cross-section of the enclosure.
- [0024] Fig. 9 shows another cross-section of the enclosure.
- [0025] Fig. 10 shows a perspective view of the enclosure.
- [0026] Fig. 11 shows a bottom view of the enclosure including the flow splitting chamber.
- 10 [0027] Fig. 12 shows an enlarged cross-sectional view of the enclosure.
- [0028] Fig. 13 shows a cross-sectional view with the device in a stored position.
- [0029] Fig. 14 shows the pump advanced during the forward stroke with fluid contained in pump.
- [0030] Fig. 15 shows the pump at full forward stroke.
- 15 [0031] Fig. 16 shows the pump at the end of fluid delivery through the tube and into the enclosure.
- [0032] Fig. 17 shows the pump during the return stroke.
- [0033] Fig. 18 shows a front view with the shutter in a stored position.
- [0034] Fig. 19 shows a front view with the shutter in a ready position.
- 20 [0035] Fig. 20 shows a rear view of the device with the pump in a stored position.
- [0036] Fig. 21 shows a rear view of the device with the pump in the full forward stroke position.
- [0037] Fig. 22 shows a perspective view of the device with the pump return springs removed.
- 25 [0038] Fig. 23 shows a perspective view with the cap and outer cover removed.
- [0039] Fig. 24 shows a perspective cross-sectional view of the fluid delivery path and shutter.
- [0040] Fig. 25 shows the shutter mechanism and a firing button in a stored position.
- [0041] Fig. 26 shows the shutter in a ready state with the shutter spring loaded.
- 30 [0042] Fig. 27 shows actuation of the firing button which releases the shutter.
- [0043] Fig. 28 shows the shutter displaced upwardly by the pump spring at the end of the fluid delivery.
- [0044] Fig. 29 shows a partial cross-section of the device showing the shutter mechanism.

[0045] Fig. 30 shows a perspective view of Fig. 29.

[0046] Fig. 31 shows the shutter in the ready state and a sensor which prevents delivery of fluid when the shutter is blocking fluid delivery.

[0047] Fig. 32 shows a plan view of another enclosure having a wedge-shaped wall opening.

[0048] Fig. 33 is a perspective view of the enclosure of Fig. 32.

[0049] Fig. 34 is a side view of the enclosure of Figs. 32-33.

[0050] Fig. 35 is a cross-sectional view of the enclosure of Fig. 34.

## 10 DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0051] The present invention is directed to methods and devices for handling a fluid and delivering the fluid to the eye. Referring to Figs. 1, 2 and 7, a device 1 is shown which includes a fluid ejector 2 (Fig. 2) and a fluid handler 14 (Fig. 7). The fluid ejector 2 includes a vibrating element 4 having a plurality of openings 6 which is vibrated with a piezoelectric element 15 coupled to the vibrating element 4. The term fluid as used herein refers to any flowable substance and does not refer only to the liquid state of a material.

[0052] The device 1 has a housing 5 which may include a first housing part 7 and a second housing part 9 which lock together with any suitable engagement such as a twist or snap-fit. Referring to Fig. 5, a control system 11 which includes a printed circuit board 13 is mounted to the first housing part 7. The control system 11 is coupled to and controls the piezoelectric element 15 as is known in the art. A battery 19 powers the control system 13 and the driving electronics for the piezoelectric element 15 as is known in the art. The fluid handling system 14 is coupled to the second housing part 9. The control system 11 may be reusable while the fluid handler 14 may be disposable. Furthermore, the fluid may be held in a fluid container 17 which may be locked to the first housing 7 to prevent removal so that the fluid handler 14 is disposable after (with) the first fluid container 17. Of course, the fluid handling system 14 may also be used with more than one container 17 or the container 17 may have a reservoir that is filled without departing from numerous aspects of the invention. Furthermore, the entire system 1 may be disposable or reusable or separated into disposable and reusable portions in any manner without departing from most aspects of the present invention.

[0053] The piezoelectric element 15 may be an annular disc 23 coupled to either a delivery side 8 or a fluid side 10 of the vibrating element 4 with the openings 6 positioned in

an open central region 26 of the annular disc 23. The piezoelectric element 15 may be made of any suitable material (such as Lead zirconate titanate; an intermetallic inorganic compound with the chemical formula  $\text{Pb}[\text{Zr}_x\text{Ti}_{1-x}]\text{O}_3$ ). The piezoelectric element 15 may be bonded, adhered, molded or otherwise coupled to the vibrating element in any suitable manner as is known in the art. A flexible circuit 21 is in electrical communication with the piezoelectric element 15 to control the piezoelectric element 15. The flexible circuit 21 is coupled to the control system 1 (see Fig. 5) which controls the piezoelectric element 15 to induce vibrations in the piezoelectric element to vibrate the element 4 and eject fluid from the openings 6. The vibrating element 4 is vibrated at a frequency of 100 to 160 khz which may be a resonant frequency. The resonant frequency may be predetermined, measured, determined or tuned as is known in the art. The driving frequency of the piezoelectric element 15 is described further below. Of course, the frequency of operation may be at a frequency other than a resonant frequency.

**[0054]** The fluid side 10 of the vibrating element 4 at the openings 6 is in contact with the fluid to be delivered and ejects the fluid to the delivery side 8. Fluid is ejected through the openings 6 toward the eye when the vibrating element 4 is vibrated. The openings 6 may taper from the fluid side 10 to the delivery side 8. For example, the opening 6 at the fluid side may have a diameter of 160-240 microns (and may be 200 microns) while the diameter at the delivery side may be 20-60 microns (and may be 40 microns). A column of consistent diameter (20-60 microns) extends to the delivery side 8 and has a length of 10-40 microns and may be about 25 microns in length. The openings 6 may have a curved wall between the fluid and delivery sides with a radius of curvature of 100 microns. The openings 6 at the fluid side 10 and the delivery side 8 may have a circular cross-sectional shape. As used herein, the cross-sectional area (or other dimension) may be defined by an effective diameter (or effective radius) for a circle having the same area.

**[0055]** The vibrating element 4 may have a thickness of 100 to 180 microns, or 120-160 microns, and may be about 140 microns, and may be made of any suitable material such as PEEK or Polyimide, with additional layers consisting of copper, polyimide, nickel, and/or gold. The vibrating element 4 may have a thickness of 125 microns and the coating/plating having a total thickness of about 15 microns so that the vibrating element 4 has thickness of about 140 microns. Of course, numerous other configurations may be practiced within the scope of the invention with respect to the materials and manufacture of the vibrating element 4 and piezoelectric element 15 and dimensions of the openings 6.

[0056] Fluid may be ejected so that an average ejection velocity is 2.5 m/s to 15 m/s, as it leaves the opening 6 at the delivery side 8 and may be about 5-6 m/s. The vibrating element 4 defines a central axis CA which is a central orientation of the plurality of openings 6 defined by a geometric center of the ejection orientation of the plurality of openings 6. For a circular pattern of openings 6 of even density distribution with a flat vibrating element 4 the central axis CA extends perpendicular to plane of vibrating element 4 at the center of the circular pattern of openings 6. Stated another way, the central axis CA is perpendicular to a plane defined by the vibrating element 4 and is aligned with the geometric center of the ejection direction that the openings 6 are aligned or with a geometric center of a spray pattern created by the plurality of openings 6. The central axis CA may be defined by an average or geometric center without departing from scope of the invention when, for example, the openings 6 are clustered or an irregular or asymmetrical shape or varying density of openings 6 (number of openings)/mm<sup>2</sup> as used herein.

[0057] Referring to Figs. 1, 3 and 7, multiple doses of the fluid are stored in the fluid container 17 which is locked to the housing 5 (specifically the second part 9) when a recess 22 engages locking tabs 24 on a container lock 26. A snap-fit connector 28 (Fig. 3) locks to a manifold 30 (Fig. 7) of a pump 32 described below. When the container 17 is pushed downward and locked to the housing 5, a fluid delivery needle 34 passes through a pierceable element 36 such as a septum 38 in the container 17. A vent needle 40, which may be independent or concentrically arranged with the fluid delivery needle 34, also passes through the pierceable element 36. Fluid is drawn from the container 17 through a fluid conduit 42 with the pump 32 as explained further below. Air is drawn into an air intake lumen 27 (covered by a filter 29) which is used to vent the container 17 as explained below.

[0058] Referring to Figs. 7-12, individual doses of the fluid are delivered to a chamber 16 formed by an enclosure 18 and the vibrating element 4. The chamber 16 may be substantially dry after delivery of the fluid and dry when stored which may provide advantages over “wet” systems which may suffer from undesirable contamination or evaporation. The enclosure 18 has a wall 44 with a lip 46 positioned adjacent the fluid side of the vibrating element 4. The lip 46 extends around the plurality of openings 6. The enclosure 18 and the vibrating element 4 together define the chamber 16 or the chamber 16 may be defined by the enclosure 18 bounded by an open end 33 of the enclosure 18 while the open end 33 is bounded and defined by the lip 46. The wall 44 extends from the open end 33 to a hub 35 which has a main inlet 52. The main inlet 52 is coupled to a lumen 54 formed in a tube 56 through which fluid is delivered by the pump 32. The enclosure 18 may be formed

together with the tube 56 or as separate parts as shown. The tube 56 may be formed with the manifold 30 which may be defined as part of the pump 32 so that the pump 32 delivers the fluid directly to the enclosure 18. The manifold 30 has a mounting rib 31 (Fig. 22) which engages the housing. The tube 56 may also be defined separate from the pump 32 as used  
5 herein, for example, the tube 56 may be part of the enclosure 18 (either as a disposable or a reusable part).

**[0059]** The lip 46 of the enclosure 18 is positioned adjacent to the fluid side 10 of the vibrating element 4 to prevent the fluid from escaping or leaking between the lip 46 and the vibrating element 4. The lip 46 and the vibrating element 4 are adjacent one another along a  
10 closed loop which encircles the openings 6 and has a diameter of 0.190-0.240 inch and may be 0.210 inch. The enclosure 18 also defines a central axis CA which is a geometric center of an area bounded by the lip 46 at the open end of the enclosure 18 and oriented perpendicular to the area bounded by the lip 46. As used herein, the term central axis CA may mean any one of the definitions herein applicable and may be interchanged when applicable and such  
15 substitutions are expressly incorporated wherever the term central axis CA is used such as when the two are co-linear. Of course, the central axis CA of the enclosure 18 and the central axis CA of the vibrating element 4 may be offset and/or skewed without departing from the scope of the invention as described below and the independent definitions are specifically applied.

**[0060]** The lip 46 of the enclosure 18 may be spaced apart from the vibrating element 4 so that the lip 46 does not impede vibrations of the vibrating element 4. Of course, the lip 46 must be close to the vibrating element 4 so that surface tension prevents escape of the liquid. For example, the lip 46 may be spaced apart from the vibrating element 4 by less than 250 microns or less than 125 microns. The vibrating element 4 may not touch the enclosure  
25 18 during vibration when the maximum amplitude is small enough to prevent contact. Stated another way, the lip 46 has a surface spaced apart from the vibrating element 4 less than 250 microns average, or less than 125 microns average, and is spaced apart from the vibrating element 4 for at least 270 degrees of total angular extent which does not contact the vibrating element 4. Stated yet another way, the surface is spaced apart by a separation distance of at  
30 least 125 microns around at least 270 degrees of the plurality of openings 6 when viewed along the central axis CA. The lip 46 may extend completely around the openings 6 without contacting the vibrating element 4 even during vibration for fluid delivery. The interface on either side may be interrupted rather than continuous without departing from the scope of the invention. For example, the surface of the lip 46 may contact the vibrating element 4 along

four small sections which span 20 degrees each so that the lip 46 does not contact the vibrating element 4 along at least 270 degrees even though not continuous. As used herein, the chamber 16 is defined by the enclosure 18 and the vibrating element 4 so long as the fluid is prevented from escaping between the enclosure 18 and the vibrating element 4 and the chamber 16 shall be defined as the fluid retaining space even though the chamber 16 is not entirely enclosed. The term “lip” as used herein simply refers to the surface adjacent the vibrating element 4 and does not require any particular structure or shape and may simply be an end of the wall 44 or coating at the end of the wall 44. For example, the lip 46 may be wider like a flange, a rim of a rigid cup, or a rippled surface, undulating or sawtooth shaped surface without departing from the meaning of “lip” as used herein. Although the fluid may be held in the chamber 16 by surface tension along the lip 46 when the lip 46 is spaced from the vibrating element 4, the majority of the fluid may be free of capillary feed features as is sometimes used in the prior art. Such prior art systems that incorporate capillary feed typically do so along the fluid feed area immediately adjacent to the openings 6 in the vibrating element 4. As described below, the present invention may provide sufficient space adjacent to the openings 6 so that capillary action is not required or incorporated to deliver fluid to the openings 6.

**[0061]** The lip 46 may also be in contact with the vibrating element 4, rather than spaced apart, while not overly restraining the vibrating element 4 and still retaining the fluid. To this end, the lip 46 may be biased against the vibrating element 4 with a relatively low force. For example, the force exerted on the vibrating element 4 by the lip 46 may be less than 3 gram-force, and may be less than 2 gram-force, measured in a direction of the central axis CA of the enclosure 18 (and the vibrating element 4 as well). The lip 46 may also exert a controlled spring load on the vibrating element 4 with an average spring constant of no more than 60 gram-f/mm or even no more than 40 gram-f/mm for displacements up to 0.050 mm in the direction of the central axis CA. The controlled spring constant may aid in operation in extreme conditions which may affect interaction of the lip 46 and vibrating element 4 for extreme temperatures, pressures, and impact loads (dropped). The controlled spring constant may also aid in manufacturability in that manufacturing tolerances can affect the load ultimately exerted by the lip 46 on the vibrating element 4.

**[0062]** The lip 46 and/or the wall 44 may also be made of a resilient material for compliant contact between the lip 46 and the vibrating element 4 and the resilient material and geometry of the enclosure 18 may contribute to develop the spring force response. For example, the lip 46 may be made of a material having a durometer of less than 60A. The wall

44 may have a thickness of 0.003 to 0.007 inch surrounding the chamber 16. The resilient nature of the enclosure 18 may be provided by the material of the lip 46 itself and/or mechanically with a tab, leaf spring, coil spring, cantilever, a resilient mounting for the container 17, or any other suitable mechanism or combination. For example, the enclosure 18  
5 may be a rigid cup with an elastomer coating along the rim with an appropriate spring exerting a force on the cup in accordance with this aspect of the invention.

[0063] The wall 44 of the enclosure 18 includes a sidewall 56 which may also contribute, and in some cases the largest amount, to the resilient nature of the engagement with the vibrating element 4. The sidewall 56 extends from the lip 46 to the hub 35 and  
10 extends completely and around the central axis CA. The resilient nature of the enclosure 18 may be provided for in whole or part by the shape of the sidewall 56. The sidewall 56 may have a tapered portion 60 extending from a large end (diameter of 0.210 to 0.220 inch) to a small end (diameter of 0.180 to 0.190 inch) with the large end positioned nearer to the vibrating element 4 (and may be adjacent the lip 46 at the distal end) and surrounds and  
15 encompasses a larger area than the small end. The tapered portion 60 of the sidewall 56 may also include a first frustoconical portion 62 extending from the lip 46 and a radial extension 64 extending primarily radially inward from the small end of the first frustoconical portion 62 to the hub 35. The radial extension 64 extends radially inward with respect to a central axis CA of the enclosure 18. The orientation and relative dimensions of the parts of the wall 44  
20 and sidewall 56 are described herein with reference to a cross-sectional shape at a plane on which the central axis CA (of the vibrating element 4 and/or the enclosure 18) lies for a total angular extent of at least 270 degrees when viewed along the central axis CA (or completely around the central axis CA as shown). The radial extension 64 extends radially inward at least 20% of an equivalent radius of the open end. The radial extension 64 may have a ratio of  
25 radial to longitudinal displacement of at least 3 to 1 relative to the central axis CA with the central axis CA representing the longitudinal direction and may be positioned 0.014 to 0.030 inch or 0.014 to 0.040 inch from the vibrating element 4 measured along a central axis CA. As used herein, “equivalent radius” or “equivalent diameter” refers to the radius or diameter of a circle having the same area. The tapered portion 60 of the sidewall 56 has a second  
30 frustoconical portion 63 extending from the radial extension 64 to the hub 35.

[0064] The tapered portion 60 of the sidewall 56 extends from the lip 46 to the hub 35. In total, the tapered portion 60 may have a radial to longitudinal displacement ratio of at least 1 to 3, at least 2 to 3 or at least 1 to 1 relative to the central axis CA. As used herein, “tapered” does not require a gradual or continuous change and only refers to a reduction in

size perpendicular to the central axis CA which represents a feed area. The reduction may be stepped or may extend substantially only radially inward like the radial extension 64 without departing from the definition of “tapered” as used herein. The tapered portion 60 of the sidewall 56 may extend radially (relative to the central axis CA of the enclosure 18) at least 20% of an effective radius of the enclosed boundary of the lip 46 around at least 270 degrees (and may extending completely and fully around the central axis CA) of the enclosure 18 when viewed along the central axis CA. The tapered portion 60 of the sidewall 56 may have a thickness of 0.003 to 0.007 inch and may be about 0.005 inch to enhance the flexibility of the sidewall 56. The sidewall 56 extends to the hub 35 and a connector 66 is formed which engages an end of the tube 56 (Fig. 7) having a mating connector (not shown). The main inlet 52 is formed by the hub 35 which receives the fluid from the lumen 54 in the tube 56. The other end of the lumen 54 in the tube 56 receives fluid from the pump 32.

**[0065]** The lip 46 may be unattached to the vibrating element 4 while still being in contact with the vibrating element 4. The terms “no attachments”, “not attached” or “unattached” as used herein means no connection other than frictional contact. Stated another way, the lip 46 may be free to move away from the vibrating element 4 along the central axis CA. Stated still another way, the enclosure 18 (specifically the lip 46) is unattached to have a degree of freedom in the direction of the central axis CA relative to the vibrating element 4. Thus, the lip 46 and the vibrating element 4 may have channels and/or raised baffles or walls which may restrain lateral movement do not constitute an “attachment” as defined herein. The lip 46 may have a curved surface with a radius of curvature of about 0.005 inch to provide a rounded edge to the lip 46.

**[0066]** The vibrating element 4 and lip 46 define an enclosed border 41 at the interface of the two (while each one may define the enclosed border 41 by itself in that they define the same boundary with one another). The enclosed border 41 defines an enclosed feed area 51 (Fig. 11) at the fluid side of the vibrating element 4 which may be 5.3-5.7 mm or about 5.5 mm in diameter. The openings 6 in the vibrating element 4 encompass and define a delivery area 39 of the vibrating element 4 which is circular and has a diameter of 2.6 to 3.0 mm or stated another way of less than 3.0 mm or about 2.8 mm. Of course, other patterns and shapes other than circular may be used with the effective diameter or radius for comparison. The enclosed border 41 may be appreciably larger than the delivery area 39 in that the delivery area 39 may be no more than 75%, or no more than 50%, of the enclosed feed area 51. Stated another way, the enclosed feed area 51 may be at least 30% larger, and may be at least 100% larger, than the delivery area 39. Stated yet another way, the enclosed feed area

51 may be larger than the delivery area 39 so that an excess feed area 58 (defined by the enclosed feed area 51 not coextensive with the delivery area 39 when viewed along the central axis CA) is at least 30% of the delivery area 39 and may even be larger than the delivery area 39 or even up to 50% larger. The excess feed area 58 may be an annular ring for a concentric arrangement or crescent shaped for offset circular areas (which may be non-circular but represented and compared as circles when using equivalent radius or diameter). The delivery area 39 of the vibrating element 4 defines a geometric center and an effective radius for a circle of equivalent area. The enclosed feed area 51 also defines a geometric center and an effective radius for a circle of equivalent area. The geometric center of the enclosed feed area 51 may be above the geometric center of the delivery area 39 and offset by at least 0.3 times the effective radius of the delivery area 39. The fluid held in the chamber 16 also defines a geometric center positioned less than 0.015 inch from the vibrating element 4 when measured in the direction of the central axis CA. The geometric center of the fluid may similarly be positioned at least 0.3 times the effective radius of the delivery area 39 above the geometric center of the delivery area 39 for an offset design. For a concentric embodiment, the geometric center of the fluid (or the volume of the chamber 16) is less than 0.1 times the effective radius of the delivery area 39 from the central axis CA of the vibrating element 4.

**[0067]** Although the enclosure 18 provides a relatively small chamber 16 with a small volume, the chamber 16 may provide fluid to the openings 6 without requiring capillary feed as some prior art teaches. The enclosure 18 has an internal surface 49 which defines the boundary of the chamber 16 as defined by the enclosure 18. The fluid is held in the chamber 16 in contact with the internal surface 49. An internal wall 45 of the enclosure 18 has a side 47 facing the openings 6 which is spaced apart from the openings 6 by a separation which may be about 0.017 inch. The spacing between the internal surface 49 of the enclosure 18 and the vibrating element 4 may be larger than a capillary spacing so that capillary action is not present. Capillary feed may impede fluid flow when it is desired to deliver the fluid quickly and also makes it difficult to completely deliver from the feed system which presents residual fluid problems. To avoid possible capillary action and/or minimize obstruction to flow it may be desirable to have a minimum spacing between the openings 6 and the nearest part of the enclosure 18 so that at least 75%, or at least 95%, or even all, of the openings 6 have a minimum spacing of at least 0.010 inch, or at least 0.014 inch to the nearest part of the internal surface 49 of the enclosure 18.

**[0068]** While it may be desirable at times to avoid capillary action, it is still desirable to provide for quick delivery of substantially all of the fluid and, thus, the enclosure 18 may

still be shaped so that the fluid in the chamber 16 doesn't need to travel far to reach the openings 6 for ejection. To this end, the internal surface 49 of the enclosure 18 may be shaped so that at least 75%, or at least 95% or even all, of the fluid in direct fluid communication with the fluid in the chamber 16 is no more than 0.060 inch, or no more than 0.040 inch, from the nearest opening 6 in the vibrating element 4. Stated another way, the chamber 16 may be shaped and formed by the internal surface 49 of the enclosure 18 so that at least 75%, 95% or even all of the fluid in the chamber 16, and optionally all fluid in fluid communication with the fluid in the chamber 16, has direct line of sight to the nearest opening 6. Many prior art systems have wet feed tubes or conduits which are filled with liquid and are spaced much further than 0.060 inch from the openings 6 and must overcome surface tension and other forces which may tend to hold the fluid in the conduits which may contribute to residual volume. Thus, in some instances it may be desirable to have most, if not all, of the openings 6 separated a minimum distance from the enclosure 18 to avoid capillary action while at the same time still having all of the fluid relatively close to the openings 6 and without impediment for rapid, substantially complete delivery in a short period of time and with low residual volume. When addressing both concerns, the enclosure 18 forming the chamber 16 may be spaced apart by 0.014-0.040 inch from all of the openings 6 when viewed and measured in the direction of the central axis CA of the vibrating element 4. "Fluid in communication" with another fluid refers to fluid that is continuous which includes feed tubes, pipes, wicks and channels which feed fluid to the openings.

**[0069]** The enclosure 18 may be an integrally formed structure which defines the chamber 16. The integrally formed structure may be made of a thermoplastic elastomer and formed by a suitable method such as injection molding. One example is sold under the name Thermolast ® supplied by Kraiburg as TF5CGN which is a thermoplastic elastomer.

**[0070]** The volume of fluid delivered may fill the chamber 16 only 75-90% full which may provide room during delivery to encourage all of the fluid to gather in the chamber 16 due to surface tension forces. Delivering the fluid at a velocity of at least 0.5 m/s (or at least 1.0 m/s) to the enclosure 18 may also encourage substantially all of the fluid ejected from the tube 56 to collect in the chamber 16 rather than being left behind as residual. Stated another way, the pump delivers the fluid at a pressure of at least 200 psi (and may be about 300 psi) which may be sufficient to achieve the velocities desired for many fluids delivered to the eye. In this manner, the small fluid amount remains a single fluid "droplet" which is fired into the enclosure 18.

[0071] The enclosure 18 may split the flow from the main inlet 52 into a first inlet 55 and a second inlet 57 each leading to the chamber 16. The enclosure 18 may also have a third inlet 59 and a fourth inlet 61 and all aspects of the first and/or second inlets 55, 57 are expressly incorporated for the third and/or fourth inlets 59, 61 and the other of the first and second inlets 55, 57 when discussed independently and all such features and limitations are expressly incorporated for all of the other inlets. The first inlet 55 directs the fluid at the internal surface 49 of the enclosure 18, such as the tapered portion 60 of the sidewall 56, before being directed at the openings 6 in the vibrating element 4. The first inlet 55 and the second inlet 57 may lead directly to the chamber 16 with the inlets both being oriented to direct all of the fluid entering the chamber 16 (or at least 90% of the fluid) at the internal surface 49 of the enclosure 18 (such as the internal surface 49 along the sidewall 56) before being directed to the openings 6 in the vibrating element 4. In this manner, the possibility that the fluid is forced through the openings 6 during filling of the chamber 16 may be reduced. In particular, when the fluid is forced into the chamber 16 at a velocity or pressure as suggested herein it may be advantageous to direct the fluid into the enclosure 18 in this manner.

[0072] The main inlet 52 initially directs the fluid at the internal wall 45 opposing the openings 6 which forms part of a flow splitting chamber 66. The internal wall 45 extends from one side of the sidewall 56 to the other relative to the central axis CA to form the inlets. The flow splitting chamber 66 splits the flow into four streams that pass through the four inlets each spaced apart from and directed at the tapered portion 60 of the sidewall 56. The flow splitting chamber 66 may lead directly to the chamber 16 as shown or may have additional baffles or flow altering features. The main inlet 52 directs the flow in a direction within 30 degrees of the central axis CA of the enclosure 18 and may be along and aligned with the central axis CA as shown. The first inlet 55 and the second inlet 57 may be oriented to direct the fluid within 30 degrees of perpendicular to the central axis CA to avoid fluid being directed at the openings 6. The enclosure 18 may have a third inlet and a fourth inlet which are also oriented at the sidewall 56 of the enclosure 18. When viewed along the central axis CA of the enclosure 18, the adjacent inlets are oriented 60-120 degrees from one another and may be about 90 degrees from the adjacent inlets 55, 57, 59, 61 as shown.

[0073] The flow splitting chamber 66 has a cup-shaped wall 68 (which includes the internal wall 45) with a concave side 70 facing toward from the vibrating element 4. The cup-shaped wall 68 has all four inlets formed therein. The cup-shaped wall 68 extends radially outward from a central axis CA of the enclosure 18 for at least 25% of an effective radius defined by the lip 46 for an angular extent of at least 240 degrees relative to the central axis

CA of the lip 46. The first inlet 55 has a radial dimension and a longitudinal dimension relative to the central axis CA with a ratio of the radial dimension to the longitudinal dimension being 0.5 to 1.5. The first inlet 55 and the second inlet 57 extend radially inward toward the central axis to expose some of the main inlet 52 when viewed in the direction of the central axis CA, however, direct longitudinal flow from the main inlet 52 to the vibrating element 4 is prevented by the radial component to the flow which is created by the bulk of the fluid directed radially outward by the internal wall forming the bottom of the cup 68.

**[0074]** The chamber 16 is also formed so that at least two, three or four inlets 55, 57, 59, 61 are provided which, together with the dimensions of the chamber 16, provide a lower energy state to encourage the fluid to collect in the chamber 16 rather than any residual part of the fluid remaining in the splitting chamber 66 or extending between the chamber 16 and the flow splitting chamber 66. Although many aspects of the present invention are directed to minimizing residual fluid, the present invention may be practiced with some residual volume left and, in fact, some aspects the invention may be used with a wet system without departing from those aspects of the invention.

**[0075]** As fluid is evacuated (ejected through the openings 6) from the chamber 16 make-up air must be introduced to vent the chamber 16 during operation. The enclosure 18 may vent air into the enclosure 18 between the lip 46 and the vibrating element 4 with the lip 46 separating sufficiently from the vibrating element 4 during vibration to vent air into the enclosure 18 without releasing fluid. Air vented between the lip 46 and the vibrating element may aid in fluid delivery by moving or displacing fluid at radially outer regions radially inward toward the openings 6 and by simply occupying these radially outer spaces (excess feed space) rather than residual fluid which might occupy this space.

**[0076]** Air may also be drawn into some openings 6 of the vibrating element 4 to vent the enclosure 18 as fluid is ejected through the openings 6. The air is introduced as small bubbles in the chamber 16 which may distribute the fluid among in some sense to find “active” ejection openings 6. The enclosure 18 may include no other vent openings, or no dedicated vent, which simplifies the system and eliminates one possible contamination path or source. Of course, a dedicated vent may be provided for the chamber 16 without departing from the invention as now described.

**[0077]** Referring to Figs. 32-35, another chamber 16A and enclosure 18A are shown which are substantially the same as the chamber 16 and the enclosure 18 and all uses and combinations and all other disclosure related to the chamber 16 and the enclosure 18 (and all other enclosures and chambers described herein) are incorporated here. Likewise, all

discussion for chamber 16A and enclosure 18A are also incorporated for the chamber 16 and the enclosure 18 (and all others). The enclosure 18A has a wall 44A with a lip 46A adjacent the vibrating element 4 (see Fig. 2). A wall opening 124 is formed in the wall 44A to vent the chamber 16A during operation. The wall opening 124 may also have dimensions which enhance the flexibility of the enclosure 18 as described below. The lip 46A may have a PTFE coating 120 adjacent to the vibrating element 4 to reduce friction therebetween. The vibrating element 4 may similarly have a PTFE coating 122 adjacent to the lip 46 to reduce friction therebetween. The coatings 120, 122 may extend around at least 270 degrees when viewed along the central axis CA. Of course, the coating 122 may extend entirely around the central axis CA. An inner surface 123 of the enclosure 16, 16A may be hydrophobic (coated or by virtue of the material property) over at least 70% of the inner surface 123 of the enclosure 18A in contact with the fluid loaded prior to delivery.

[0078] The wall opening 124 may take any suitable shape such as a wedge-shaped opening. The wall opening 124 extends through the wall 44A, specifically a sidewall 56A portion of the wall 44A, to expose the chamber 16A. The wall opening 124 may also form a small gap 131 in the lip 46A, which together with the geometry of the opening 124, is small enough to prevent fluid leakage but may still be large enough to vent the enclosure 18A by permitting air to enter when fluid is ejected. All discussion and applications concerning venting of the enclosure 18 are incorporated here such as discussion of venting between the lip 14 and the vibrating element 4, spacing between the lip and vibrating element and the force-displacement characteristics. Thus, the lip 14A may be in contact with the vibrating element 4 or spaced apart in any manner described herein.

[0079] The wall opening 124 has a longitudinal dimension 126 measured from the lip 46 in the direction of the central axis CA and a radial dimension 128 measured in a radial direction relative to the central axis CA. The longitudinal dimension 126 of the wall opening 124 is at least 80% of a separation 125 between the vibrating element 4 and a side 47A of the enclosure 18A facing the openings 6 and may extend substantially the entire length as shown. The radial dimension 128 of the wall opening 124 is not more than 10%, or no more than 5%, of an equivalent circumference of the lip 46A. The radial dimension 128 may be about 0.025 inch while the longitudinal dimension 126 may be about 0.022 inch. The dimensions of the enclosure 18A, the wall 124A and the chamber 16A may be any suitable dimensions including those associated with the enclosure 18 and all geometric relationships all of which are incorporated here.

[0080] The wall opening 124 extends from the lip 46A proximally and may increase the flexibility of the enclosure 18A due to its position and shape. The wall opening 124 has a circumferential dimension 130 measured in a circumferential manner relative to the central axis CA. The circumferential dimension 130 may be about 0.012 inch at the lip 46A (same as the gap 131) and tapers so that the two sides converge at a proximal end 132 of the wall opening 124. The circumferential dimension 130 is defined herein as a measurement for a line segment that is perpendicular to a radial orientation of the central axis CA. The wall opening 124 tapers down as the wall opening 124 extends proximally from the lip 46A. The wall opening 124 tapers so that a tapered shape 132 of the wall opening 124 is oriented in the direction of (“points at”) at least one of the inlets 55, 57, 59, 61 to the chamber and may be oriented to align with two inlets when viewed along the central axis CA. Orienting the tapered shape 132 of the wall opening 124 with the inlet(s) 55, 57 in this manner increases flexibility since the inlet(s) and wall opening 124 cooperate to increase flexibility given their geometric alignment. The “orientation” of the tapered opening shall be defined as the bisection of the tapered angle extending away from the wall opening 124. The tapered shape 132 is also within 10 degrees of a radial orientation relative to the central axis CA and may be substantially radially oriented as shown. The wall opening 124 is also positioned along a frustoconical portion 62A with the wall opening extending proximally from the lip for at least 80% of the length of the frustoconical portion 62A.

[0081] The pump 32 is now described in more detail. The pump 32 draws discrete volumes from the fluid container 17 and delivers these volumes to the chamber 16. The fluid container 17 may be any other suitable mechanism such as a piston/plunger associated with the fluid container 17 in some applications. The fluid container 17 may have a fluid carrying capacity which is at least 150 times the volume of the chamber 16 (or the volume of the fluid delivered) for a multi-dose device. The pump 32 may be configured to deliver the same (and optionally the only) volume each time. Of course, a variable volume pump 32 may also be used without departing from virtually all aspects of the invention.

[0082] The present invention may be used to provide single dose delivery with substantially the whole dose delivered thereby leaving little residual fluid in the chamber 16. The vibrating element 4 may deliver the fluid from the enclosure 18 so that no more than 5%, or no more than 2%, of a total volume of the chamber 16 is occupied by residual fluid (from a previous fluid delivery) or less than 1 microliter remains. Stated another way, the vibrating element is operated to dispense substantially the entire volume of fluid in communication with the openings 6 so that no more than 5%, or no more than 2%, of the fluid volume (or

less than 1 microliter) remains in the chamber 16 after the fluid is ejected and a single actuation for fluid ejection. In this manner, the chamber 16 is substantially empty after a single application of the fluid (a single firing actuation). An advantage of some aspects of the present invention over other fluid delivery systems is that the chamber 16 receives a single  
5 dose that is nearly completely delivered to leave the chamber 16 substantially dry and free of residual fluid between activations. Contamination and degradation of the fluid may be reduced compared to “wet” systems that maintain the fluid in contact with the vibrating element 4 between uses or which have incomplete delivery.

**[0083]** The enclosure 18 may be sized so that the enclosure 18 may be at least 70-  
10 95% full with the fluid volume as mentioned above which may help the fluid to gather in the chamber 16 as a single droplet. The chamber 16 may define a relatively small volume such as less than 14 microliters or 10-14 microliters. The fluid volume may be 7-12 microliters or 10-12 microliters. The lumen 54 in the tube 56 delivers the fluid through the main inlet 52 to the enclosure 18 with the main inlet 52 having a diameter of 0.040 to 0.060 inch and may be  
15 about 0.054 inch, The flow splitting chamber 66 may have a diameter which essentially matches the main inlet 52 of about 0.054 inch. The tube 56 extends from the main inlet 52 and may have a volume of less than 2 microliters to further minimize residual fluid. The tube 56 may be part of the enclosure 18 and may be formed with the enclosure 18 rather than as separate parts.

**[0084]** In use, fluid delivery to the eye may also be relatively rapid to reduce the likelihood of interference from a blink during delivery. The fluid delivery may take less than 200 ms and may even be less than 150 ms or even 100 ms. The vibrating element 4 may also be operated with a pause between periods of vibration during a single actuation. For example,  
20 the vibrating element may be driven by the piezoelectric element 15 for a first period of operation of about 26 ms with a pause of about 3.65 ms followed by a second period of operation of about 26 ms. The vibrating element 4 may be driven by the piezoelectric element 15 with two pauses with the piezoelectric element 15 being energized or activated for a first period of time, a second period of time and a third period of time with the first and second  
25 periods separated by the first pause and the second and third separated by a second pause in driving vibration of the vibrating element 4. The first and second pauses in driving vibration may be 0.5 ms to 4.0 ms. Each of the first, second and third time periods may be 20-40 ms and the overall time of delivery may be less than 150 and even less than 100 ms and may be about 85.3 ms. Each of the first, second and third periods of vibration may be further  
30 subdivided into periods of activation for about 816us and deactivated for about 586us for the

piezoelectric element 15. During the deactivated time, the vibrating element 4 may continue to vibrate and eject fluid although not being actively driven by the piezoelectric element 15. Similarly, during each pause in activation of the piezoelectric element 15 the vibrating element 4 may continue to eject the fluid. The “pause” may be defined as a continuous  
5 deactivation of at least 2% of the total time and the total pause time for a plurality of pauses being at least 6% and may be about 8.5% of the total delivery time. The deactivated times are defined distinct from the pause in that the pause is at least 2% of the time continuous while the deactivated time is shorter and may be defined as a continuous time of 0.5-1.0% of the total delivery time and a total of the deactivated times being at least 30% of the total delivery  
10 time. Stated another way, the deactivated time is a continuous time of 2.0 to 2.5% of the first period of time (and second and third as well) and a total deactivated time of at least 30% of the first period of time. Of course, the delivery times are defined to illustrate the invention and the activation times and patterns may change depending on the surface tension of the ejected fluids.

15 **[0085]** As mentioned above, the frequency of the alternating signal used to activate the piezoelectric element 15 and subsequently activate and vibrate the vibrating element 4 is induced at a drive frequency of 100kHz to 160kHz. Furthermore, the frequency is selected by the control system 11 as a randomized frequency centered about the drive frequency (ranging from 100kHz to 160kHz) for each of the plurality of activations during a single delivery and  
20 may be randomized at least 20 and may be at least 40 times. Stated another way, the vibration frequency is changed (randomly in a manner centered on the drive frequency) on average at least 33 times for a single firing actuation so that the piezoelectric element 15 is driven at a frequency for no more than 3% of the delivery time (average) before being changed. It is believed that the chaotic nature of the randomization of the drive signal may aid in ejecting  
25 fluid. The randomized nature may be provided by a predetermined randomized set of values which are applied to the centered operating frequency or the randomized values uniquely generated by the control system 11.

**[0086]** The vibrating element 4 may also be designed to vibrate with a relatively low maximum amplitude. For example, the vibrating element 4 may vibrate with a maximum  
30 amplitude of less than 2 microns, less than 1.5 microns or within a range of 0.5-1.5 microns, 0.8-1.2 microns or may be about 0.8 microns. The maximum amplitude of the vibrating element 4 may also be relatively small compared to the size of the openings 6 in the vibrating element 4. For example, the maximum amplitude may be no more than 5%, or no more than 3%, of an effective diameter of the cross-sectional shape of the openings 6 at the delivery

side. For example, when the maximum amplitude is 1.0 microns and the average diameter of the openings 6 at the delivery side is 40 microns the maximum amplitude is only 2.5% of the average diameter or about 2.5% of the average diameter of the fluid droplets ejected. The maximum amplitude also represents a relatively small amount compared to the thickness such as no more than 5.0% or even no more than 3.0% of the thickness of the vibrating element 4 (measured from the fluid side to the delivery side). As used herein, the thickness may be an average thickness for the area bounded by the openings 6. Operation at low amplitude may also contribute to venting through the openings 6 in that air may be admitted through some of the openings 6 having even low displacements. Operation at low amplitude may also help maintain fluid containment between the lip 46 and the vibrating element 4. When the lip 46 is spaced apart from the vibrating element 4, the lip 46 may be spaced apart an average distance greater than the maximum amplitude of the vibrating element 4 during vibration. Stated another way, the maximum amplitude is less than an average separation distance between the surface of the lip 46 and the vibrating element 4.

**[0087]** Referring to Figs. 13-17, the housing is partially removed to expose the pump 32. The pump 32 delivers fluid from the fluid container 17 to the chamber 16 through the lumen 54 in the tube 56 and through the main inlet 52 (see Fig. 12). The fluid container 17 may be any suitable container such as a vial, ampoule, bag, bladder or a fixed container that is filled without departing from the scope of the present invention. Similarly, the pump 32 may be any suitable mechanism for delivering the fluid to the enclosure 18 without departing from various aspects of the invention. The fluid container 17 has a pierceable cap 70 which is pierced by a delivery needle 34 and the vent needle 40. The delivery needle 34 defines part of a delivery flow path and the vent needle 40 defines part of a vent path. The delivery flow path extends to the pump 32 and from the pump 32 through the tube 56 and the main inlet 52 into the chamber 16. Referring to Fig. 3 and 13, the delivery needle 34 and the vent needle 40 are mounted to a container support 70 on which the container 17 is mounted. The container support 70 has a coupling 72 which engages the manifold 30. A vent lumen 73 includes a one-way valve 76, such as an umbrella valve 78, which permits air into the fluid container 17 to make up for the volume of fluid lost as explained below.

**[0088]** The pump 32 has a first part 80 and a second part 82. The first part 80 reciprocates between a stored position (Fig.13) to a partial stroke position (Fig. 14) and to a forward stroke position (Fig. 15) at the greatest displacement. The first part 80 returns to the stored position to complete a cycle which delivers a volume of fluid to the chamber. The second part 82 also reciprocates between a stored position to a forward stroke position at a

greatest displacement and back to the stored position each cycle. The first part 80 has an extension 84 extending from a main body 86. The main body 86 has an end 88 facing an end 90 of a main body 89 of the second part 82. The extension 84 on the first part 80 extends toward and interlocks with an extension 85 extending from the main body 89 of the second part 82. The first part 80 is driven and in turn drives the second part 82 through each cycle by engagement of the extensions 84, 85 and/or the ends 88, 90 of main bodies 86, 89 with one another. A cavity 92 is formed between the first part 80 and the second part 82 with the size of the cavity 92 changing as the first and second parts 80, 82 move toward and away from one another. The cavity 92 increases in size when the first and second parts 80, 82 move away from one another which draws fluid into the cavity 92 during the forward stroke. The cavity 92 decreases in size when the first and second parts 80, 82 move toward one another which delivers the fluid from the cavity 92 to the chamber 16 during the return stroke. The cavity 92 has a volume commensurate with volume of the fluid being delivered which may be 7-12 microliters.

**[0089]** The fluid is drawn into the cavity 92 during the forward stroke of the first part 80. The first part 80 and the second part 82 are movable from a stored position of Fig. 13, to the partial forward stroke position of Fig. 14 and finally to the full forward stroke position of Fig. 15. The first and second parts 80, 82 move to the full stroke position with the first part 80 pulling the second part 82 upward due to the interlocking extensions 84, 85 engaging one another. In the full forward stroke position the pump 32 is ready to deliver the fluid through the tube 56 and into the enclosure 18.

**[0090]** When the first and second parts 80, 82 reach the partial stroke position of Fig. 16 during the return stroke the fluid has been delivered from the cavity 92 to the chamber 16. The first and second parts 80, 82 complete the cycle by moving to the partial reset position of Fig. 17 and to the fully reset position of Fig. 13 again. An additional optional step may be to purge any fluid left downstream of the chamber 16 with a separate displacing medium. The tube 56, the chamber 16 and the flow splitting chamber 66 represent a total downstream volume which is substantially free of fluid prior to delivery of the fluid. The volume of fluid delivered by the pump 32 may be 40-70% of the total downstream volume so that the tube 56 and flow splitting chamber 66 can be substantially empty when the fluid has been delivered to the chamber 16. As mentioned above, the fluid may be ejected at a relatively high velocity of at least 0.5 m/s (or with the pump delivering the fluid at a pressure of at least 200 psi) to “fire” the droplet into the chamber 16 and which may permit surface tension forces to gather and hold the small volume of fluid together.

[0091] The pump 32 may also deliver make up air into the container 17 to make up for the volume of fluid lost. The pump 32 draws air into a make-up chamber 94 during the forward stroke and forces the air from the make-up chamber 94 toward the fluid container 17 so that air enters and vents the fluid container 17 during the return stroke. The first and second parts 80, 82 each have an opposing end 97 positioned opposite the ends 88, 89 which face each other to form the cavity 92. At least one of the opposing ends 97 of the first and second parts 80, 82 may form part of the make-up chamber 94 (such as the opposing end 97 of the second part 82) so that movement through a full cycle also draws air into the make-up chamber 94 during the forward stroke and expels air during the return stroke. Air is forced through the one-way valve 76, through the vent needle 40 and into the container 17 to make up for the volume of fluid lost (delivered). When the first and second parts 80, 82 reach the fully reset position the make-up air has been delivered and the pump 32 is in the stored position again with the first part 80 of the pump 32 blocking the main inlet 52 to the enclosure 18. O-rings are used to seal junctions and spaces between the first and second parts and the manifold and along the vent and fluid delivery paths.

[0092] Referring to Figs. 4, 6 and 18-23 together, a drive mechanism for the pump 32 is shown. The drive mechanism includes the first actuator 94 (which may be a button 95) coupled to a first side 96 of a lever 98. The lever 98 rotates about pivot P in the direction of arrow A as the button moves downward. A second side 100 of the lever 98 is coupled to a support plate 102 of the first part 80 of the pump 32 so that the first part 80 moves upward with the first side 96 of the lever 98 from the stored position of Figs. 18 and 21 to the forward stroke position of Figs. 19, 20 and 22 in which fluid has been drawn into the cavity 92. The lever 98 may provide a mechanical advantage of about 11/6 due to the difference in lever arm length. Of course, a powered system using the battery 19 may also be used to move the fluid without departing from other aspects. A ratchet 104 prevents back-travel as the button 95 is depressed until reaching the necessary downward displacement (full forward stroke) at which point the ratchet 104 is released to permit the return stroke.

[0093] The first actuator 94 (such as the button) also loads the pump return spring 95 (and may load two pump springs 95) during the forward stroke. The loaded pump return spring(s) 95 drives the pump 32 back to the default or stored position during the return stroke. The pump return spring 95 may act on the first actuator 94, the lever or directly on part of the pump 32 itself such as on the first part 80 as shown. The first actuator 94 (button 95) is also returned to the stored position. In the stored position the main body of the first part 80 blocks flow through the lumen 54 in the tube 56 and the main body of the second part 82 blocks the

vent path and the fluid delivery path. In this sense, the pump 32 acts a valve 104 and the present invention may be practiced with a dedicated valve closing the lumen 54 to the tube 56 and fluid being moved in another manner without departing from various aspects of the present invention.

5 [0094] Referring to Figs. 25-31, the device 1 also includes a shutter 105 having an aperture 107 through which the fluid is delivered. The shutter 105 blocks and covers the vibrating element 4 in the stored position and may serve as an “off” switch (or defines the “off” condition) when using a position sensor 110 to detect the position of the shutter 105 (specifically the circled area of the shutter 105). A shutter spring 109 is also loaded as the  
10 first actuator 94 is moved through the forward stroke. Unlike the pump return spring 95, the shutter spring 109 is locked in the loaded position of Fig. 26. The position sensor 110 (which may be an optical, electromagnetic, electrical or mechanical sensor) determines when the shutter 105 is in the firing position in which the aperture 107 is aligned with the fluid openings 6. For example, the sensor 110 may be an optical sensor coupled to the control unit  
15 11 (and the reusable second housing) which senses a marker on the shutter. Fluid ejection is prevented when the position sensor determines that the shutter 105 is blocking (or will block very soon) delivery of fluid. The fluid is delivered upon actuation of a second actuator 106 (which may be a firing or dose button 108) which is unlocked when the shutter 105 is in the position of Fig. 26 and the device is ready for delivery of the fluid. In use as described below,  
20 the firing button 108 mechanically releases the shutter 105 and the fluid ejector is activated by the control system 11 while the aperture in the shutter 105 is aligned with openings 6 in the vibrating element 4 as determined by the position sensor 110.

[0095] The shutter 105 motion is now described in more detail. Referring to Figs. 4, 18 and 23, the shutter 105 is in the stored position. The shutter 105 is moved downward by  
25 the first actuator 94 so that a tab 109 slides downwardly in a slot 111 and is locked in a ready state of Figs. 19 and 26. The device is now in an “on” state by activation of a switch (not shown) when the dose is loaded. During the shutter locked state, another sensor (not shown) may determine the device has loaded fluid and is ready to dispense a dose. Activation of the dose button 108 and the subsequent activation and deactivation in accordance with the  
30 position sensor’s 110 determination of the shutter 105 position is the mechanism by which the dose/ejection is triggered and terminated. Of course, numerous other methods of timing delivery may be used and, furthermore, the fluid may be delivered in a manner independent of the shutter 105 operation.

[0096] A shutter lock 115 is displaced by the firing button 108 to the position of Fig. 27 so that the tab 109 on the shutter 105 moves upward in a release slot 117 having a ramp 119. The firing button 108 is mounted to a resilient arm 121 having a pair of hooks 123 which engage the shutter lock 115 and pulls the shutter lock 115 back to the stored position in part due to the resilient nature of the arm 121. A button return spring 125 (see Fig. 17) is compressed upon actuation and returns the button 108 to the ready state and may also serve to return the shutter lock 115 to the stored position.

[0097] Use of the device to handle and deliver a dose of the fluid is now described. The fluid container 17 may be mounted prior to use or may be pre-loaded or loaded from a prior use. When loading the fluid container 17 for the first (and optionally only) time, the fluid container 17 is mounted in a cavity 92 and the button is placed over the fluid container 17. The user then depresses the first actuator 94 to force the container 17 downward so that the vent needle 40 and the delivery needle 34 pierce the fluid container as shown in Fig. 7. The fluid container 17 may be locked to prevent removal and replacement of the fluid container 17. The device may be stored in this condition.

[0098] Immediately before deciding to deliver the dose, the fluid is delivered to the chamber 16 by actuating (depressing) the first actuator 94 (cap) which moves the pump 32 through a full cycle to load the fluid in the chamber 16. Once the actuator 94 has returned to the default position, the fluid is contained in the chamber 16 and ready for delivery. The first actuator 94 may be any suitable actuator such as the button 95, a lever, a slider, a twist knob or any other suitable mechanical or electro-mechanical actuator without departing from numerous aspects of the present invention. Of course, the fluid may be delivered to the chamber 16 during delivery of the fluid to the eye or immediately before and in a continuous process without departing from virtually all aspects of the present invention. After delivery of the fluid to the chamber 16, the device may also clear the tube 56 of fluid. For example, the pump 32 may draw a volume of displacing medium and deliver the displacing medium into the tube 56 to displace any fluid in the tube 56 into the enclosure 18 prior to delivery.

[0099] When the user is ready, the user then actuates the firing button 108 to deliver the fluid to the eye. To aim and align the device, the user positions the device adjacent the eye and looks into the device through the aperture 107 in the shutter 105 and views the vibrating element 4. A light emitting element 114, such as a light tube 116, illuminates part of the device, such as the vibrating element 4, to visually aim and align the device. Of course, any other suitable aiming/aligning method may be used. Once the device is properly aimed, the firing button 108 is actuated to deliver the fluid to the eye. The second actuation may be

with the same actuator or a different actuator such as the firing button 108. Although the present invention has been described with a two-step actuation process the two steps may be combined in a single actuation which delivers the fluid to the chamber 16 then determines an appropriate time to deliver the fluid such as by optically differentiating the eyeball from the eyelid. The device delivers substantially all of the fluid and the device is ready for storage after a single actuation and delivery of a single dose or quantity to the eye.

**[00100]** All aspects of the methods and devices as claimed may be applied to the other methods and devices and such claim combinations are expressly incorporated. Furthermore, combinations of size range, ratio, angular or linear coverage, percentage or any other quantity are expressly incorporated into the claims even if the specific combination has not been previously expressly claimed. For example, the alternative ranges 75%, 95% and “all” are used to describe various values which may be used or substituted for one in combination with the other quantities. The terms “first” and “second” shall be interchangeable in the claims since they are not used as terms of natural order but merely to distinguish one from the other. In addition, the claim terms “have” “having” “includes” “including” “comprises” and “comprising” (and all other forms of these terms such as “has”) are all open ended as used herein in that “A has B” or “A includes B” means A includes B but may also include other elements or method limitations. Finally, the present invention has been described with reference to some aspects, advantages or operating conditions which are difficult to quantify and directly due to the small volume and fast delivery time. Thus, direct observation and measurement are at times not feasible, however, qualitative information supports some of the assertions. For example, it has been observed that water at the interface of the lip 46 and vibrating element 4 outside the enclosure 18 is drawn into the enclosure 18 when fluid is ejected indicating that air may likely be admitted as well. Furthermore, the fluid is smoothly ejected even with no dedicated vent opening.

**[00101]** The present invention has been described with reference to preferred embodiments, however, various modifications may be made without departing from the features and aspects of the invention. For example, the pump 32 may be a syringe, the enclosure 18 may be a rigid dome or the enclosure 18 may be attached to the vibrating element 4 without departing from aspects of the invention.

## Claims

1. A device for delivering a microdose volume of fluid to an eye, comprising:
  - a housing;
  - a fluid ejector located within the housing, the fluid ejector having a vibrating element with a plurality of openings, the vibrating element having a fluid side and a delivery side with the plurality of openings extending from the fluid side to the delivery side, the fluid ejector ejecting fluid from the fluid side through the plurality of openings to the delivery side when the vibrating element is vibrated;
  - a microdose volume enclosure positioned adjacent the fluid side the vibrating element, the enclosure and the vibrating element forming a microdose volume chamber; and
  - a pump having an outlet fluidly coupled to the microdose volume chamber, wherein the pump is configured to draw a discrete dose of liquid from a fluid container into a variable volume cavity and eject the discrete dose from the cavity into the chamber at a pressure of at least 200 psi,
  - wherein the microdose volume enclosure includes a wall having a lip positioned adjacent the fluid side of the vibrating element, the lip extending around the plurality of openings, the microdose volume enclosure and the vibrating element together defining the microdose volume chamber which holds the discrete dose to be dispensed.
2. The device of claim 1, further comprising:
  - a first actuator operably coupled to the pump, wherein actuation of the first actuator activates the pump to deliver the discrete dose to the microdose volume chamber.
3. The device of claim 1, further comprising a second actuator operably coupled to the vibrating element, wherein actuation of the second actuator causes the vibrating element to vibrate and eject the microdose volume fluid through the plurality of openings.
4. The device of claim 1, wherein the microdose volume chamber defined by the microdose volume enclosure is configured to hold a maximum microdose liquid volume of 10-14 microliters.
5. The device of claim 1, wherein the lip is spaced apart from the fluid side of the vibrating element by less than 150 microns.

6. The device of claim 1, wherein the lip is spaced apart from the fluid side of the vibrating element by less than 250 microns about an angle of at least 270 degrees when viewed along a central axis.
7. The device of claim 1, wherein the microdose volume enclosure has an internal surface in contact with the fluid which forms the chamber, the internal surface being shaped so that at least 75% of the internal surface in contact with the volume of fluid is no more than 0.040 inch from a nearest of the plurality of openings.
8. The device of claim 1, further comprising a piezoelectric element coupled to the vibrating element.
9. The device of claim 1, wherein the vibrating element has a maximum amplitude which is less than an average separation distance between the lip and the vibrating element.
10. The device of claim 1, wherein the vibrating element has a thickness measured from the fluid side to the delivery side of 100-180 microns.
11. The device of claim 1, wherein the lip is in contact with the vibrating element around at least 270 degrees of the plurality of openings when viewed along a central axis, to hold the fluid in the microdose volume enclosure.
12. The device of claim 1, wherein the lip has no direct attachments to the vibrating element.
13. The device of claim 1, wherein the lip is made of a resilient material having a durometer of less than Shore 60a.
14. The device of claim 1, wherein the lip is biased against the vibrating element in the direction of a central axis of the vibrating element.
15. The device of claim 1, wherein the lip exerts a force of no more than 3 gram-f on the vibrating element measured in the direction of a central axis of the vibrating element.

16. The device of claim 1, further comprising a mechanism for biasing the lip against the vibrating element.

17. The device of claim 1, wherein the lip and the vibrating element are adjacent one another to prevent fluid from passing therebetween along a closed loop which encircles the plurality of openings.

18. The device of claim 1, wherein the lip is spaced apart from the vibrating element by a separation distance of at least 125 microns around at least 270 degrees of the plurality of openings when viewed along a central axis of the vibrating element.

19. The device of claim 1, wherein the microdose volume enclosure does not include a vent opening to vent air into the enclosure when the fluid is ejected through the openings other than between the lip and the vibrating element and through at least some of the plurality of openings.

20. The device of claim 1, wherein  
the fluid container fluidly coupled to the microdose volume chamber of the microdose volume enclosure, the fluid container having a fluid carrying capacity is at least 150 times the volume of the enclosure; and  
wherein the pump delivers one dose size only.

21. The device of claim 1, wherein the vibrating element defines an enclosed border positioned adjacent to the surface of the lip, the enclosed border defining an enclosed feed area bounded by the enclosed border, the openings in the vibrating element encompassing and defining a delivery area of the vibrating element.

22. The device of claim 1, wherein the microdose volume enclosure has a sidewall and a main inlet which receives fluid, wherein fluid flow from the main inlet is split between a first inlet and second inlet to direct fluid at a sidewall of the microdose volume enclosure before being directed at the plurality of openings.

23. The device of claim 22, wherein the first inlet and the second inlet direct at least 90% of fluid at the enclosure and less than 10% of fluid is directed at the vibrating element before being directed at the microdose volume enclosure.

24. The device of claim 1, further comprising:

a tube having a lumen; and

the microdose volume enclosure having a main inlet fluidly coupled to the lumen in the tube, the main inlet being oriented to direct the fluid at an inner wall of the microdose volume enclosure which forms a flow splitting chamber, the flow splitting chamber having at least two separate inlets leading to the microdose volume chamber and each inlet to the microdose volume chamber directing the fluid at a sidewall of the microdose volume enclosure.

25. The device of claim 24, wherein the flow splitting chamber has a third inlet and a fourth inlet corresponding to a third flow path and a fourth flow path, respectively.

26. The device of claim 1, wherein

the vibrating element has a central axis defined by a central orientation of the spray pattern emitted by the plurality of openings; and

the microdose volume enclosure has a main inlet which directs the flow in a direction within 30 degrees of the central axis, the microdose volume enclosure having a sidewall and a flow splitting chamber fluidly coupled to the main inlet to receive the fluid, the flow splitting chamber having a shape which redirects and splits the fluid flow from the main inlet to at least a first inlet and a second inlet oriented 60-90 degrees from the central axis, the first inlet and the second inlet being directed at the sidewall of the microdose volume enclosure before the fluid is directed to the plurality of openings.

27. The device of claim 1, further comprising:

a tube having a lumen with a volume of less than 2 microliters;

a valve having an open position which permits fluid flow through the lumen and a closed position which prevents fluid flow through the lumen; and

the microdose volume enclosure having a main inlet fluidly coupled to the lumen in the tube.

28. The device of claim 1, wherein the pump has a first part and a second part movably coupled to one another to change a size of the variable volume cavity, wherein the first part and the second part are configured to reciprocate between a stored position, a partial stroke position, and a full forward stroke position, wherein, when the first part and the second part are moved from the stored position toward the partial stroke position, the first part moves away from the second part and the cavity increases in size to draw the discrete dose,

wherein, when the first part and the second part are in the full forward stroke position, the first part and the second part are at a greatest displacement from one another, the cavity is at maximum size and aligned with a lumen into the chamber, and

wherein, when the first part and second part are moved from the full forward stroke position toward the stored position, the first part and the second part move toward one another and the cavity decreases in size to eject the discrete dose.

29. The device of claim 28, wherein the first part of the pump has a first extension and the second part of the pump has a second extension, wherein the first extension extends toward the second extension and interlocks with the first extension, the first part driving the second part through the cycle.

30. The device of claim 28, further comprising a first actuator operably coupled to the first part, the actuator driving the first part through the forward stroke and also loading a pump return spring during the forward stroke, the loaded pump spring moving the first pump part and the second pump part back to the stored position from the forward stroke position.

31. The device of claim 28, wherein fluid is drawn into the variable volume cavity formed between the first and second parts during the forward stroke of the first part.

32. The device of claim 28, wherein fluid is drawn into the variable volume cavity during the forward stroke, the variable volume cavity being formed between the first part and the second part, a size of the variable volume cavity changing as the first and second parts move toward and away from one another.

33. The device of claim 28, wherein the variable volume cavity of the pump holds a volume of 7-12 microliters which is delivered to the microdose volume enclosure during use.

34. The device of claim 1, further comprising:

a tube having a lumen fluidly coupled to the chamber; and

a valve which is opened to permit fluid flow through the lumen and closed to block fluid flow through the lumen, a total downstream volume is defined by a total volume including at least the lumen and the microdose volume chamber tube which is downstream of the valve, the volume of fluid delivered to the microdose volume chamber may be 40%-70% of the total downstream volume.

35. The device of claim 1, further comprising an air make-up chamber coupled to the pump, the pump forcing air from the make-up chamber into the fluid container during each cycle.

36. The device of claim 28, further comprising an air make-up chamber coupled to the pump, wherein the pump draws air into the air make-up chamber during the forward stroke of the first part and forces air into the fluid container during a return stroke of the first part returning to the stored position.

37. The device of claim 1, further comprising:

a shutter having an aperture, the shutter being movable from a stored position, which covers the plurality of openings when viewed along a central axis, to a delivery position in which the plurality of openings are exposed when viewed along the central axis through the aperture of the shutter; and

a shutter spring coupled to the shutter, the shutter spring being loaded when the first actuator moves the first part of the pump during the forward stroke, the shutter spring being coupled to the shutter which is moved from the delivery position back to the stored position by the shutter spring.

38. The device of claim 1, further comprising a control system mounted to the housing, the control system being coupled to a first actuator and being operably coupled to the vibrating element to control the vibrating element.

39. The device of claim 1, wherein the housing includes a first housing part and a second housing part, the first housing part being removably coupled to the second housing part; the control system being mounted to the first housing part.
40. The device of claim 1, wherein the lip has a PTFE coating adjacent to the vibrating element to reduce friction therebetween, the coating extending around at least 270 degrees when viewed along a central axis of the vibrating element.
41. The device of claim 1, wherein the vibrating element has a PTFE coating adjacent to the lip to reduce friction therebetween, the coating extending around at least 270 degrees when viewed along a central axis of the vibrating element.
42. The device of claim 1, wherein an inner surface of the enclosure is hydrophobic over at least 70% of the inner surface in contact with fluid.
43. The device of claim 1, further comprising a wall opening extending through the wall to expose the microdose volume chamber.
44. The device of claim 43, wherein the wall opening forms a gap in the lip.
45. The device of claim 43, wherein the wall opening has a longitudinal dimension measured from the lip in the direction of a central axis and a radial dimension measured in a radial direction relative to the central axis, the microdose volume enclosure having an internal wall with a side facing the openings in the vibrating element which is spaced apart from the openings by a separation.
46. The device of claim 43, wherein the wall includes a frustoconical portion, the wall opening extending proximally from the lip for at least 80% of the length of the frustoconical portion.
47. The device of claim 45, wherein the longitudinal dimension of the wall opening is at least 80% of the separation between the vibrating element and the side of the enclosure facing the openings.

48. The device of claim 43, wherein the wall opening vents the enclosure by permitting air to enter the microdose volume chamber when fluid is ejected, the wall opening being small enough to prevent the fluid from passing therethrough.