# Calibrated Eye Dropper

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## Abstract

Glaucoma is a disease of the eye that can cause loss of vision and may lead to blindness. Researchers at the University of Wisconsin-Madison use animal test subjects for glaucoma medication testing. Eye drops are delivered to the eyes of the animals via a micropipette. This method endangers the animal. The researchers need a new eye dropping mechanism which minimizes time between drop deliveries, is accurate and precise, and does not pose danger to the animals in case of contact with the eye. A miniaturized pipette has been fabricated which incorporates the commercially available MiniFIX into an ergonomic grip with a tip ejector. An Eppendorf holder accompanies this device. Testing has shown that the fabricated grips appeal to the users and the design delivers $4.6 \pm 0.2 \mu L$.

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## Problem Statement

A lab in the Department of Ophthalmology and Visual Sciences needs a device to accurately and efficiently deliver 5μL drops of experimental drugs into the cornea of the eye for glaucoma therapy testing in animals. Currently, the client uses standard micropipettes which deliver exactly 5μL drops. However, this method is time consuming, poses a danger to the safety of the animal, and makes drop placement difficult. The objective is to optimize accuracy, efficiency, and animal safety in optical drug delivery.

## Motivation

Glaucoma is a disease of the eye that occurs when the fluid pressure inside the eye slowly rises [1]. This causes damage to the optic nerve and can eventually lead to vision loss and blindness (Figure 1). Glaucoma can be diagnosed by an ophthalmologist. Upon diagnosis, medication is available and is typically administered in the form of eye drops or pills. Current research in the area uses animal test subjects. Dr. Paul Kaufman from the Department of Ophthalmology and Visual Sciences at the University of Wisconsin-Madison focuses his studies on the optic nerve and drugs that lower intraocular pressure [2]. Research specialists in Dr. Kaufman's lab administer eye drops to the central cornea of the animal's eye. Instead of using a typical dropper bottle which delivers larger volumes than desired (30μL), the researchers utilize micropipettes. Problems are associated with the drug delivery when using pipettes. Although the pipettes accurately deliver the desired volume, their length is a safety hazard to the animal. With the animal's safety in mind, the researchers are looking for a new eye dropper apparatus that maintains the accuracy of the pipette but increases the speed and safety of drug delivery [4].

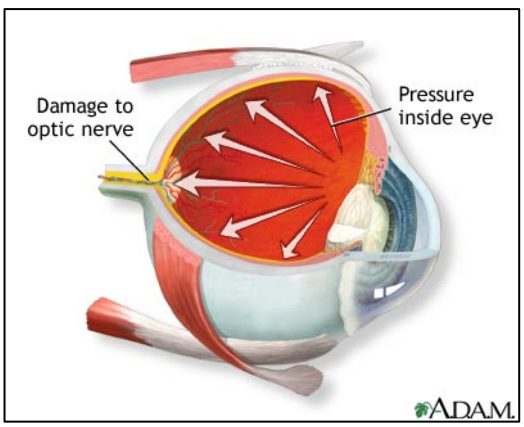



**Figure 1**. Glaucoma creates fluid pressure inside the eye that can cause damage to the optic nerve [3].

## Current Devices

Many devices exist that fulfill some of the client's needs, but none are exactly what the client would prefer to use in the lab. The MiniFIX Micropipette from Dynalab Corporation is a 13cm long pipette which can deliver a fixed 5μL volume (Figure 2). However, these pipettes are slender, making them uncomfortable to hold. The MiniFIX also does not have a tip ejector. Rainin creates pipettes scaled to 10μL and can be adjusted to 5μL, but the length of these pipettes exceeds the specifications of the client. The MicroZippette Handheld Dispenser from VWR-Jencons is scaled to 1mL and can be used for repeated liquid deliveries. However, the device cannot be scaled to micro liters (Figure 3) [5]. Several US patents (6610036, 7073733, and 5881956) exist that utilize mini ophthalmic pumps, but these are not exactly what the client would like to use in her studies and they are not commercially available [6][7][8]. The Eppendorf Repeater Plus Pipettor from Eppendorf (Figure 4) is a pipette/syringe combination that delivers specified volumes in a continuous fashion [9]. This method saves time between deliveries, but its added length with the specialized tips increases safety hazards.


**Figure 2.** MiniFIX micropipettes from DynaLab Corporation [10].


**Figure 3.** MicroZipette Handheld Dispenser from VWR-Jencons [5].

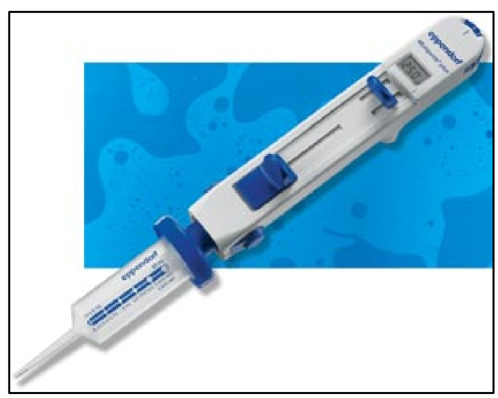


**Figure 4.** Eppendorf Repeater Plus Pipettor from Eppendorf with syringe tip [9].

## Design Specifications

Per the client's request the device must have the functionality of a typical eye dropper and the accuracy of a calibrated 5µL micropipette [4]. The device must be small, but large enough to fit in the average human's hand comfortably, meaning the grip should be approximately 3.5 inches tall [11]. This will allow the user to maintain a steady hand while delivering the drugs and make it easier to control the device if the animal moves. The device should be relatively light, weighing less than 100 grams; this also adds to the user's level of comfort. The device must accurately deliver 5µL with only 1% error, which is the standard for micropipettes on the market at this time. Not only should the device be able to deliver this specific volume, but it should also be able to deliver liquids with a wide range of viscosities. To improve speed when using the device and to allow for multiple deliveries in a short time span, an attached reservoir, mechanical parts, or tubing may be incorporated. The device should allow the user to maintain to keep one hand on the animal during use. Depending on how the device is constructed and if there are disposable parts or not, the device should be capable of performing 2000 times each month [12]. If the tips are disposable, the device should function accurately without calibration for at least a year before recalibration is needed. The target cost for this prototype is $200 or less; this cost should include extra features which make the device ergonomically favorable.

## Design Alternatives

### Miniaturized Pipette

The current device used by the client to deliver 5µL drops is a calibrated micropipette. The major issue with this method of drug delivery is that the pipette is too long. This makes it hard for the user to stabilize his or her hand and increases the probability of misplacing an eye drop or poking the animal in the eye. In order to improve the current device, the team has incorporated the idea of a shortened micropipette

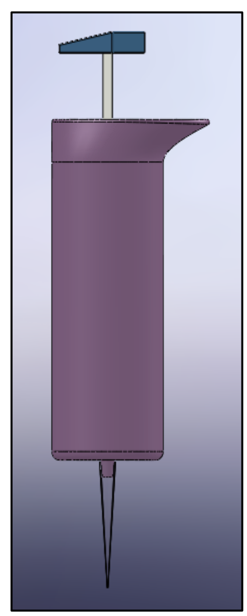


**Figure 5.** Preliminary external design of the miniaturized pipette.

(Figure 5) into each of their design alternatives. This pipette will retain the accuracy needed to deliver a 5μL drop as well as be more efficient and easier to use.

The concept of the shortened pipette will be achieved by condensing spaces between elements inside the current standard micropipette. The shortened micropipette will use a pre-fabricated spring and piston already calibrated to 5μL because these elements require very tight tolerances and would be difficult for the team to fabricate with accuracy. The shaft through which the piston travels will be shortened to allow just enough space for 5μL of air displacement and an attachment site for the pipette tip. The shaft tip needs to fit with commercially available micropipette tips because fabricating custom tips will not be accurate or cost effective. The gripping area on the shortened pipette will be reduced to 3.5 inches in length to accommodate the average hand size. The pipette will be operated by moving a plunger at the top with the thumb.

The internal elements of the shortened pipette will be the same as those in current micropipettes. With the exception of the positive displacement design, air is displaced by a piston which is connected to a plunger button and is operated by the user's thumb. A calibrated spring ensures the correct piston displacement. The pipette will use 10μL tips that are commercially available to ensure accuracy, and the pipette tips will be ejected in a similar way to standard micropipettes.

Because this design is calibrated to deliver 5μL drops and is easier for the operator to stabilize, it is incorporated into each of the team's design alternatives. However, each alternative has a different added mechanism to minimize time between dispenses and, overall, make drug delivery more efficient.

**Flexible Straw**

The flexible straw design incorporates a 5-15mL plastic holding tank attached to the body of the miniaturized pipette (Figure 6). The holding tank is attached on the grip next to the base of the user's palm so it will not interfere with tip visibility and will still be comfortable to hold. At the base of the 5-15mL holding tank, there is a piece of flexible tubing that reaches to the end of the pipette tip. The tubing can be moved into any position and retain its shape, so it can move to the pipette tip when aspirating the drug and then can move away from the tip so it does not interfere with drop dispensing.

At the opening end of the tube, there is a one-way valve which can only be opened when the pipette tip pushes through the valve to draw up 5μL of the drug. This valve prevents the drug from being spilled during drop delivery or if the pipette is set down. To aspirate the drug, the user moves the straw to the end of the pipette tip, where the tip pushes through the valve to access the drug inside the tubing. The plunger, operated by the user's thumb, moves the internal piston so that 5μL of air is displaced inside the tip to draw up the drug. The straw is then removed from the pipette tip and moved to the side so the drop can be administered. This process is repeated between each drop. The pipette tips for the flexible straw design would be common 10μL tips that are commercially available.

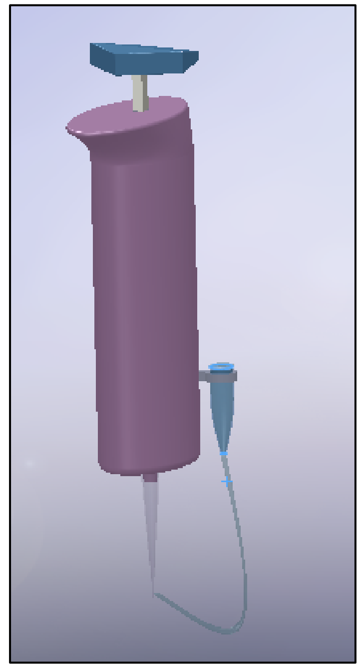


**Figure 6.** Flexible straw design with reservoir attached to body of shortened pipette and straw reaching to end of pipette tip.

One advantage of the flexible straw design is that it would be accurate because it uses standard tips. However, there is a chance air bubbles could be aspirated into the tip, making it less accurate. A disadvantage of this design is that the straw would have to be cleaned before using a different drug.

**Positive Displacement**

The positive displacement design also incorporates a 5-15mL holding tank that attaches to the body of the pipette. However, the tubing from the base of the holding tank does not attach at the end of the micropipette tip. In the positive displacement design, the tubing connects to the end of the micropipette directly above the site where the disposable tip attaches to the shaft.

The main feature of this design is the use of a disposable piston inside the tip, which is used to displace the 5μL volume. As opposed to an air displacement pipette, the disposable piston in this design comes in direct contact with the drug and forces the drop out of the tip when dispensing (Figure 7) [13]. For this reason, this type of pipette is ideal for viscous liquids. When the plunger pulls up the piston, the drug flows due to gravity from the reservoir, through the flexible tubing, and into the positive displacement tip. When the plunger pushes the piston down, the drug is expelled through the tip. When the disposable piston is drawn back up, it displaces a 5μL volume inside the tip. The drug is able to flow into the displaced volume due to gravity to prepare for another drop delivery.

The advantage of this design is that it is the most efficient in minimizing the time between drop deliveries because the tip refills itself. One disadvantage is that the team would need to fabricate custom tips that are calibrated to hold exactly 5μL, which would be time consuming and not cost effective.

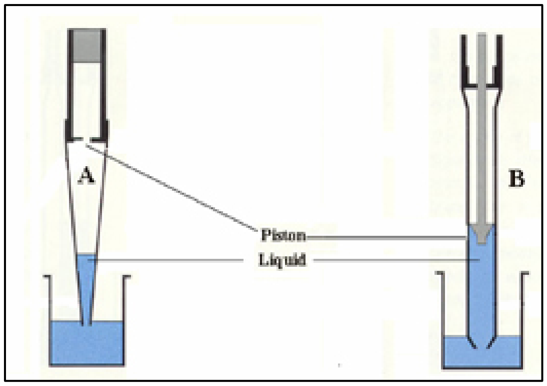



**Figure 7.** Principle of positive displacement vs. air displacement in micropipette tips. Tip A shows air displacement while Tip B shows positive displacement where the piston comes in direct contact with the liquid [13].

## Eppendorf Track

The sliding reservoir micropipette (Figure 8) includes a reservoir attached to the micropipette by a sliding, vertically oriented track. This track would lock into place when not in use. To refill the pipette, the user would manually slide the reservoir down the track to the level of the pipette tip. Part of the track would also extend in order to allow the reservoir to reach the level of the pipette tip. The extendable portion of the track would be free to rotate so that the reservoir could move from the side of the micropipette into the correct position for liquid intake, directly below the tip. After aspirating the liquid, the user would rotate the reservoir back to the side of the micropipette and raise it to the locked position on the track. The lock mechanism for the track would be a small button that protrudes outward

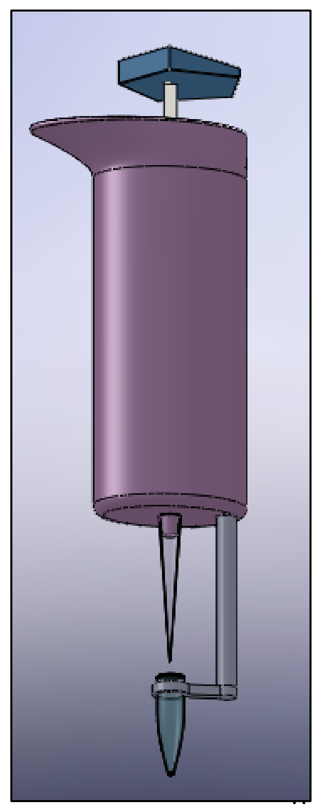


**Figure 8.** Sliding reservoir design. The track is fully extended, and the Eppendorf is positioned directly under the micropipette tip.

from the body of the pipette when locked. To unlock the track, the user would push the button inward and slide the reservoir down. This design requires the user to hold the micropipette in one hand and to use his or her other hand to move the reservoir between drug deliveries.

The internal elements of the micropipette would be the same as those in current micropipettes. The pipette would be operated by air displacement, and a calibrated spring would ensure the correct piston position. Furthermore, the pipette tips for the sliding reservoir micropipette would be common 10μL pipette tips that are available commercially.

One advantage of the Eppendorf track design is that it will be accurate because it uses standard parts and tips. One disadvantage of this design is that it will take a long time to refill the tip because the user has to move the Eppendorf down the track.

**Eppendorf Clip**

The main feature of the eppendorf clip design (Figure 9) is the ablility to store a removeable Eppendorf on the side of the pipette. A clip with a shape similar to an Eppendorf cap will be attached to the side of the piptette body. This part will be positioned on the body so that it will not interfere with visibility of the tip and can accommodate both left and right-handed users. A normal Eppendorf with the cap removed will be used to hold the drug. The Eppendorf will fit securely on the clip so that no liquid can escape if the pipette is laid on its side, and a reasonable amount of force will be required to detach the clip.

To refill the pipette tip, the user would detach the Eppendorf with one hand and move the pipette tip into the Eppendorf to aspirate the drug. Once the tip is refilled, the user would return the Eppendorf to the clip and dispense the liquid.

The internal elements of the micropipette would be the same as those in current micropipettes. The pipette would be operated by air displacement, and a calibrated spring would ensure the correct piston displacement. Furthermore, the pipette tips for the Eppendorf clip micropipette would be common 10μL pipette tips, and the design will incorporate standard 1.5mL Eppendorfs, both of which are available

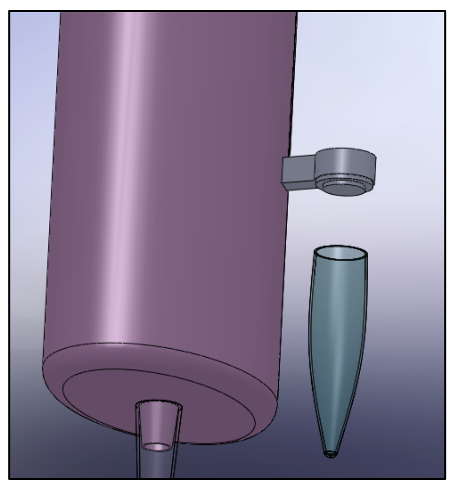


**Figure 9.** Eppendorf clip design. The Eppendorf is removed from the clip on the pipette body.

commercially.

One advantage of the Eppendorf clip design is that it will be accurate and cost efficient because it will use standard parts and tips. A disadvantage of this design is that the amount of time between dispenses will be longer than a repeat dispense pipette such as the positive displacement design.

## Design Matrix

In order to choose our final design, the team created a matrix (Table 1) that rated each design alternative on six different criteria. Higher possible points were given to the more important criteria. The points for all criteria were added to give each design a total score out of 100 possible points. The Eppendorf clip design had the highest total score, so it was chosen as our final design.

**Table 1. Design Matrix**

| Criteria | Flexible Straw | Eppendorf Track | Positive Displacement | Eppendorf Clip |
|---|---|---|---|---|
| **Accuracy (30)** | 27 | 30 | 24 | **30** |
| **Speed (25)** | 20 | 18 | 25 | **22** |
| **Size/Safety (20)** | 17 | 17 | 17 | **17** |
| **Cost (10)** | 5 | 8 | 3 | **10** |
| **Feasibility (10)** | 6 | 8 | 1 | **9** |
| **Ease of Use (5)** | 3 | 4 | 3 | **5** |
| **TOTAL (100)** | **78** | **85** | **73** | **93** |

Designs were rated out of 100 total points based on the 6 listed criteria. The Eppendorf clip had the highest score.

## Final Design

Since the mid-semester presentation, the final design has acquired some changes. New information came to light about the accuracy of the commercially available MiniFIX pipettes. The MiniFIX Micropipette from Dynalab Corporation is a 13cm long pipette which delivers only 5µL volumes which is the same volume that the client works with (Figure XX). Although initially these pipettes seemed unsuitable for this project, the accuracy of the MiniFIX was found to be lower than previously believed. The 1.5% error stated by the company was acceptable to the client [14]. With this new information the team rethought the design alternatives and decided to incorporate the MiniFIX pipette as the core of the miniaturized pipette. When discussing this new design idea with the client, the team received feedback that an Eppendorf clip attached to the pipette grip was not preferred. The client strongly encouraged a pipette design that could be operated with only one hand [15]. With new information and specifications, the team critiqued the miniaturized pipette design and developed the design for an Eppendorf holder.

The MiniFIX has a grip that is uncomfortably narrow and lacks a tip ejector. Therefore, the team decided to modify an existing standard micropipette grip so that an ergonomic grip would be available to the user as well as the convenience of a tip ejector. The grip of an existing micropipette was modified so that the MiniFIX pipette could be positioned inside of the grip (Figure 10).

**Figure 10.** Modified grips containing MiniFIX pipettes.

The polymer polymethyl methacrylate (PMMA) was used to create a tight sleeve to hold the MiniFIX inside of the existing grip. PMMA powder and liquid monomer are mixed and harden creating a strong solid that can be drilled if necessary [16]. The team applied this knowledge to create a mold of the MiniFIX inside of the existing grip. The mold secures the MiniFIX inside of the grip during use while still allowing the MiniFIX to be removed. It is necessary that the MiniFIX be removable since it cannot be calibrated and, therefore, must be replaced occasionally. Although the MiniFIX will need to be replaced about twice a year by the client, the grip is fully reusable.

The team created two prototypes of same design. See Appendix D for more pictures. The only difference between these prototypes is the style of the grip. The weight of the purple grip prototype with the MiniFIX and pipette tip is 46.93g. The prototype with the blue grip weighs 49.80g including the MiniFIX and the pipette tip. Both prototypes are 12.3cm in length without the pipette tip and 14.9cm in length including the pipette tip. This is about half of the length of the standard micropipette which is currently used by the client.

In addition to the miniaturized pipette, the team designed an Eppendorf holder which reduces the risk of the drugs being knocked over by the animal. The Eppendorf holder is a small dish 3cm in diameter and 1.2cm deep which can be worn on the user’s finger (Figure 11). Three Eppendorf tubes can be placed securely in this holder since there are three holes in the base of the dish precisely drilled to accommodate 0.5mL Eppendorf tubes. This holder can be adjusted to the size of the user’s finger by gently bending the metal ring portion. By utilizing the Eppendorf holder, the experimental drugs are still readily available to the user but are removed from the table surface and the subsequent danger of spilling.

**Figure 11.** Eppendorf holder with three Eppendorfs.

**Ergonomics**

The two prototypes were designed with human ergonomics in mind. Some important factors that were incorporated in the prototypes to make a universal design are as follows:

- The device fits comfortably in the average human hand which is approximately 3.5 inches in width.
- The diameter of the device makes gripping for extended periods of time more comfortable.
- The device is symmetrical and can be used by both right and left handed users.
- Pressure required to push the plunger down completely is minimal.
- Tips can be added and removed with little effort using the modified tip ejector.
- The length of the device is about half the length of a standard micropipette.
- Assemblage is easy and requires little to no instruction.
- The parts can be ordered and replaced with little knowledge of working mechanisms.
- The materials used are light weight, yet durable.

Originally, the diameter of the MiniFIX pipette was narrow and uncomfortable to hold. To increase comfort, a standard micropipette grip was added to the outside of the MiniFIX. This additional material makes the device easy to hold without stressing the hand in any way. The shorter length of the pipette decreases both eye strain as well as hand and arm muscle strain. With a shorter length, the prototype requires less focus and effort to control than a pipette of standard length.

## Fabrication Process

Refer to Figure 12.

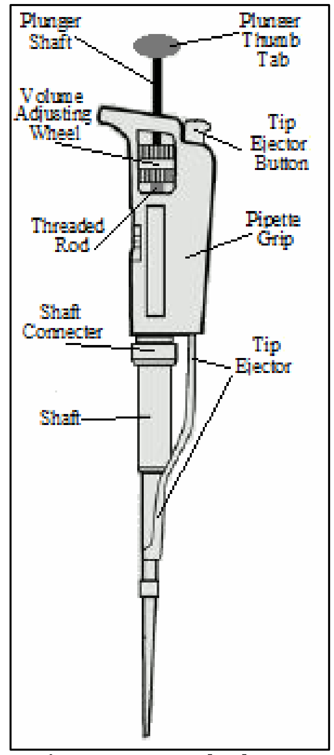



**Figure 12**. Standard micropipette with labeled parts [17].

The first part of the fabrication process was to remove the piston and calibration mechanisms of the micropipettes. To do this, the tip ejector was easily pulled down and off the tip ejector rod that was housed inside the pipette grip. Then the shaft was removed by unscrewing the shaft connecter from the pipette grip. With the shaft came the piston and piston springs.

In the micropipette, a hollow threaded rod was threaded through a brass nut embedded in the middle of the plastic grip. The plunger shaft was inside the hollow threaded rod and flared just above the top of the threaded rod and then protruded through the top of the pipette grip. A thick plastic wheel called the volume adjusting wheel had a hole in the center the diameter of the threaded rod. This plastic wheel was fitted over the plunger piston and then attached to the top portion of the threaded rod and held in place by three hex screws evenly spread out around the diameter of the plastic wheel that tighten on to the threaded rod. This wheel also kept the plunger from coming out of the pipette. The plunger thumb tab was easily pulled off the top of the plunger. Then the three hex screws were loosened and the plastic wheel was pulled off the top of the shaft; the plunger rod came out also. After this was complete, the threaded rod was screwed out the bottom of the pipette and removed.

Surrounding the area where the threaded rod used to be and above the brass nut were all of the volume display wheels. They were held in place from the top by a plastic cover. The plastic cover was held down by a retaining ring that was fitted to the internal sides of the pipette grip. The retaining ring was removed and the plastic cover and volume read out wheels were easily pulled out.

The tip ejector button was easily pulled off the tip ejector rod. Below the tip ejector button was a retaining ring clipped on to the tip ejector rod. This retaining ring held down the spring which pushed the rod back up to the starting position after a tip was ejected. When the retaining ring was removed, the spring came off and the rod fell out the bottom of the pipette grip. After this the pipette grip was striped of all of its components.

**Figure 13.** Standard micropipette grip with internal components removed and notch cut out for MiniFix.

The first altercation to the pipette grip was to cut off the threads that held the shaft connector to the pipette grip using a band saw. Then the area was sanded smooth and flush with the bottom of the pipette grip. Next a notch was cut out of the top of the pipette to fit the handle of the MiniFIX pipette with a Dremel drill. See figure 13.

The brass nut had a hole smaller than the diameter of the MiniFIX pipette. In order for the MiniFIX pipette to fit in the pipette grip the brass nut was bored out with a size X drill bit to fit the diameter of the MiniFIX pipette with a drill press.

The inside of the pipette grip was then roughed using a roughing bit on a Dremel drill to give the PMMA a rough surface to bond with.

A MiniFIX pipette was wrapped tight with aluminum foil and taped together. The aluminum foil was lubricated with Vaseline so it would slide out of the PMMA mold after it hardened. Then the MiniFIX pipette was placed in the pipette grip and held in place by clamping the MiniFIX pipette handle to the pipette grip.

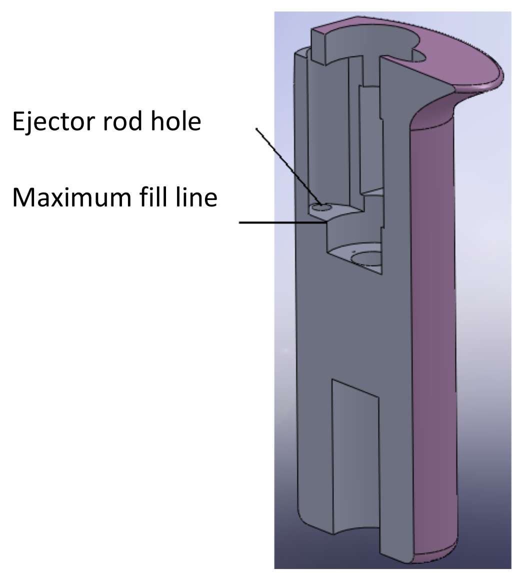



**Figure 14.** Cross-section of grip.

The next step was done in a fume hood to avoid inhaling a pervasive odor from the PMMA. The PMMA was mixed according to the product specifications. Then the PMMA was poured around the MiniFIX pipette from the top being careful not to fill higher than shown in Figure 14 to prevent filling the tip ejector rod hole. Once the PMMA was poured it was allowed to harden for 24 hours. Then, without removing the MiniFIX pipette the pipette grip was turned upside down and the bottom of the pipette was filled with PMMA making sure not to overflow the hole and allowed to harden for 24 hours. Then the MiniFIX pipette was removed and cleaned. The PMMA in pipette grip was cleaned of Vaseline.

The tip ejector rod had a half inch section cut off from the bottom which brought the tip ejector closer to the bottom of the pipette. It was placed back into the pipette grip. The spring and retaining ring were put back in place and the tip ejector button was placed back on the rod.

The tip ejector was cut in half and the half that had the rod connector rod was flattened up to the rod connector. It was then bent at a 90 degree angle right below the rod connector. The altered tip ejector was placed back on the ejector rod that was in the pipette grip. Then a MiniFIX pipette was placed in the grip and a circle was drawn on the tip ejector where the tip of the MiniFIX came in contact with the tip ejector. The tip ejector was taken off and a 19/64 inch hole was drilled. The excess tip ejector on the opposite side of the hole was cut off and the corners of the end were rounded. The tip ejector was then placed back onto the ejector rod. This step completed the fabrication process.

## Cost Analysis

**Table 2. Total Expenses**

| Item | Manufacturer | Quantity | Cost |
|---|---|---|---|
| MiniFIX micropipette | Dynlab Corp. | 5 | $99.00 |
| Ultra precision compression springs | McMasterCarr | 3 | $7.70 |
| | | | **Total: $106.70** |

The total expenses for the team this semester. Total cost was $106.70.

Our team purchased five MiniFIX micropipettes from Dynalab Corporation and three compression springs from McMasterCarr for a total of $106.70 (Table 2). The compression springs were purchased to fit with the team's design alternative of miniaturizing a standard micropipette. However, these springs were not used in the final prototype.

Many of the materials used to construct the final prototype were donated to the team. The standard micropipette grips and tip ejectors were donated by Clint Kisting from VWR

International, and the PMMA was donated by Greg Gion, a polymer specialist from Medical Art Prosthetics, LLC. In addition, the dental hygienist ring used to create the Eppendorf holder was donated by Teresa Gohla, a family contact. The team researched the cost of these donated materials and calculated the total cost of each prototype, which was approximately $104.05 and within the budget specified by the client (Table 3).

**Table 3: Cost Per Prototype**

| Item/Material | Purchased/Donated | Cost |
|---|---|---|
| MiniFIX micropipette | Purchased | $19.80 |
| Standard micropipette grip | Donated | $50.00 |
| Tip ejector | Donated | $28.00 |
| PMMA | Donated | $3.57/oz (1 oz. used) |
| Hygienist ring | Donated | $2.50 |
| | | **Total per prototype: $104.05** |

The total cost for each prototype is $104.05 and is within the team's budget.

## Testing

The two prototypes were tested for their drop volume accuracy and their ergonomics. For complete test results refer to Appendix C.

To determine the accuracy of the prototypes, drops of distilled water were pipetted onto an analytical balance using three different MiniFIX pipettes inside the prototypes. Knowing that 1μL of distilled water weighs 1μg, the average drop volume was calculated to be $4.6 \pm .27$μL. The average error was 8.78%. The results from pressing the plunger to the second stop were disregarded because this is incorrect use of the pipette.

To test the ergonomics of the prototypes, 10 individuals were surveyed. They were asked to hold and envision using the two prototypes, a MiniFIX, and a standard micropipette and then rank them from best to worst. The individuals were told that they were delivering drops to animal eyes and should consider animal safety, comfort of the pipette, and controllability of the pipette. They were also told to consider that they would be using the pipette for at least one hour. The pipettes ranked first, second, third, and fourth received 4, 3, 2, and 1 point respectively. The average score for each pipette is shown in Figure 15.

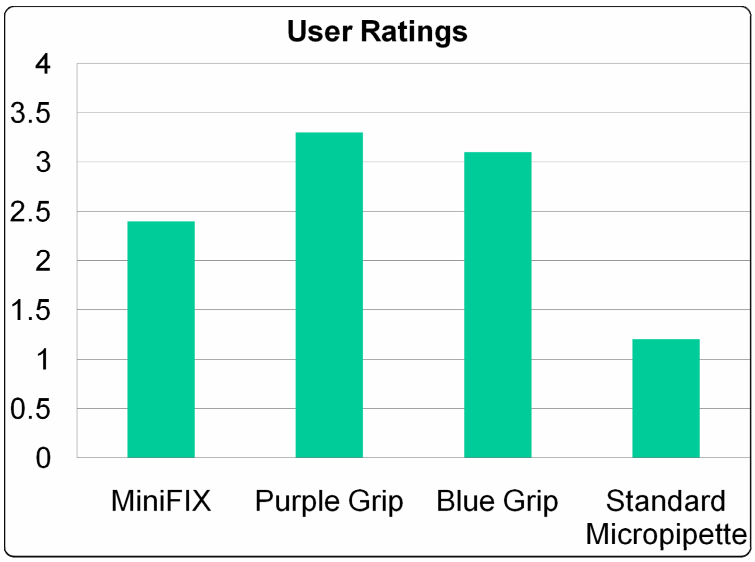



**Figure 15.** Average scores from 10 users with 4 being the highest and 1 being the lowest. The two prototypes were rated the highest.

The two prototypes were rated the highest. Several users commented that the standard pipette was too difficult to control and that they thought they would poke the animal in the eye. Users also commented that the MiniFIX would be uncomfortable to hold for long periods of time.

## Ethical Considerations

This semester the team benefited from an ethical consierdations video and discussion. Although it is often a faint line between what is ethically acceptable and what is unethical, the team did not encounter significant ethical dilemas. The team used parts from a variety of companies, each of which was acknowledged in the presentation as well as the team's poster. The existing pipette grips, since they were donated and not fabricated by the team, had the trade names BioPette and AXYPET marked on the grips. These were not removed so that the original manufacturers can receive proper credit.

## Future Work

Although the final prototype fulfills many of the client's specifications, there are still some aspects that can be improved upon in the future. From the testing results, the team found that the MiniFIX pipettes do not have the percent error rating of 1.5% stated by Dynalab Corporation, which is also the percent error rating desired by the client. In order to improve upon this, the team can search for another existing product or create a miniaturized micropipette with higher accuracy. Also, the team would like to continue ergonomics testing with more test subjects. When performing the ergonomics testing of the prototypes, the test subjects chosen were other biomedical engineering students. However, the team would like to perform testing with subjects who work in the client's lab and analyze feedback from them. Feedback from potential users of the team's prototype will help the team decide whether the prototype is ergonomic and easily controlled or if additional modifications need to be made.

Another aspect to be considered is the possibility of the drugs spilling from the Eppendorfs. The current caps on the Eppendorfs, when open, increase the possibility of the drugs spilling from the Eppendorf holder if the user tips his or her hand too far. To improve upon this, two products can be considered. One is an 8mm polyethylene plug cap with starburst top ($50.78/1000 units) and another is a red silicone Cepure Zero Injection Port Septa cap ($41.15/10 units) (Figure 16) [18][19]. Both products are piercable caps that fit on the Eppendorfs so that the drugs can still be accessed by the pipette through the cap, and spillage will be prevented.

**Figure 16.** Cepure Zero Injection Port Septa, Red Silicone [19].

By reducing the size of the eye dropper device and adding the Eppendorf holder, the team was able to increase the speed of drug delivery, but this can still be improved upon. One solution would be to create a miniaturized repeat dispense pipette, which aspirates a larger volume and delivers repeated incremental drops. This would decrease the amount of time between drop deliveries. Also, even though the prototype is smaller than the standard micropipettes currently used by the client, the client would prefer a device that is even smaller, optimally the size of a 15mL dropper bottle. One way to accomplish this would be to compress the pipette's internal mechanism to the size of a dropper bottle. However, this would require very precise fabrication and calibration tolerances. Another method would be to create a valve to fit a 15mL dropper bottle that is able to deliver 5μL drops. All of these alternatives can be considered to further improve the team's existing prototype.

The team accomplished the goals set out by the client this semester. The team was able to design and fabricate a functional miniaturized micropipette that fulfills the client requirements. The final prototype delivers the correct volume of drugs, and its shortened length enhances ergonomics and animal safety while delivering drops. Although the team has created a prototype that has improved upon the device the client currently uses, it can still be further modified by creating mechanisms to increase speed of drug delivery and prevent drug spillage.

# Appendix A

## References


[1] *Glaucoma*. (2008, November). Retrieved February 26, 2009, from National Eye Institute Website: http://www.nei.nih.gov/health/glaucoma/glaucoma_facts.asp

[2] Rasmussen, C. A., Gabelt, B. T., & Kaufman, P. L. (2007). Aqueous Humor Dynamics in Monkeys in Response to the Kappa Opioid Agonist Bremazocine. *Trans Am Ophthalmol Soc, 105*, 225.

[3] *Glaucoma*. (2008, August). Retrieved April 29, 2009, from MedlinePlus Website: http://www.nlm.nih.gov/MEDLINEPLUS/ency/imagepages/9349.htm

[4] B. Gabelt, personal communication, January 27, 2009.

[5] *The MicroZipette, Handheld Dispenser*. (2009). Retrieved March 4, 2009, from VWR International Website: http://uk.vwr.com/app/Header?tmpl=/jencons/microzip.htm

[6] *US Patent 6610036 - Eye drop dispensing system.* (2003, August). Retrieved May 6, 2009, from Patent Storm Website: http://www.patentstorm.us/patents/6610036/fulltext.html

[7] *US Patent 7073733 - Microdispensing pump*. (2006, July). Retrieved May 6, 2009, from Patent Storm Website: http://www.patentstorm.us/patents/7073733/fulltext.html

[8] *US Patent 5881956 - Microdispensing ophthalmic pump*. (1999, March). Retrieved May 6, 2009, from Patent Storm Website: http://www.patentstorm.us/patents/5881956/fulltext.html

[9] *Eppendorf Repeater Plus*. (n.d.). Retrieved March 4, 2009, from Eppendorf North America Website: http://www.eppendorfna.com/int/index.php?l=131&sitemap=2.3&pb=9ce798080b018b20&action=products&contentid=1&catalognode=9620&productpage=1

[10] *MiniFIX Micropipettes*. (n.d.). Retrieved March 4, 2009, from Dynalab Corp. Website: http://www.dynalabcorp.com/news_micropipette.asp

[11] Agnihotri, A. K., B. Purwar, N. Jeebun, S. Agnihotri (2006). Determination of Sex By Hand Dimensions. *The Internet Journal of Forensic Science, 1*. Retrieved May 6, 2009, from: http://www.ispub.com/ostia/index.php?xmlFilePath=journals/ijfs/vol1n2/hand.xml

[12] B. Gabelt, personal communication, February 4, 2009.

[13] *Technical Info*. (2007). Retrieved March 4, 2009, from Calibration Technology Website: http://www.calibrationtech.ie/page.php?id=pippete%20technical%20info

[14] B. Gabelt, personal communication, March 25, 2009.

[15] B. Gabelt, personal communication, March 31, 2009.

[16] G. Gion, personal communication, March 30, 2009.

[17] *Basic laboratory skills.* (n.d.). Retrieved May 5, 2009, from FAO Website: http://www.fao.org/DOCREP/005/AC802E/ac802e05.htm

[18] *Wheaton Science Products.* (n.d.). Retrieved May 7, 2009 from Issuu Website: http://issuu.com/lsdcorp.com/docs/wheaton_/88

[19] *Cepure Zero Injection Port Septa*, *Red Silicone*. (n.d.). Retrieved May 7, 2009 from Pawling Engineered Products Website: http://www.cepure.com/details.php?prodId=101&category=17

## Appendix B

**Calibrated Eye Dropper Product Design Specifications**

May 7, 2009

Eamon Bernardoni, Jim Mott, Brooke Sampone, Sarah Switalski, Michelle Tutkowski

**Problem Statement:**

A lab in the Department of Ophthalmology and Visual Sciences needs a device to accurately and efficiently deliver 5µL drops of experimental drugs into the cornea of the eye for glaucoma therapy testing in animals. Currently, the client uses standard micropipettes which deliver exactly 5µL drops, but this method is time consuming, poses a danger to the safety of the animal and makes drop placement difficult. The objective is to optimize accuracy, efficiency, and animal safety in optical drug delivery.

**Client Requirements:**

- Eye dropper mechanism to deliver 5µL of fluid to central cornea
- Minimizes chance of eye damage in case of contact
- Device accommodates different viscosities
- Apparatus should hold 5-15mL of liquid
- Minimizes time intervals between dispenses
- Device should be small for stabilization of hand
- Device should allow operation with only one hand
- Parts easily sanitized or disposable
- Ergonomically favorable

**Design Requirements:**

1. Physical and Operational Characteristics
   a. *Performance requirements:* The device should deliver 5µL of liquid to animal eyes with precision and accuracy.
   b. *Safety:* Must not injure the animal eye if contact should occur.
   c. *Accuracy and Reliability:* Must deliver same liquid amount repeatedly during each use and must be calibrated to 5±0.05µL.
   d. *Life in Service:* The device will be used about 2000 times per month.
   e. *Shelf Life:* If it has replaceable tips, then it should be useable for a year without calibration. If solution is put inside the device, then it would be disposed of after each study. Device will be at room temperature. Components must not degrade.
   f. *Operating Environment:* Used in research laboratory. Chemicals may be spilled on the device in which case, the device should be easily sanitized.
   g. *Ergonomics:* The device will be hand held so it must be comfortable and easy to operate with minimal effort.

h. *Size:* The device should fit in the human hand (The average hand is approximately 3.5 inches in width). The gripping area must be at least 3.5 inches tall.
i. *Weight:* The target weight is that of standard pipette which less than 100 grams.
j. *Aesthetics, Appearance, and Finish:* The device should be neutral in color with a smooth, cylindrical shape.

2. Product Characteristics:
   a. *Quantity:* One prototype device is required for this semester.
   b. *Target Product Cost:* $200, which is similar to the cost of a standard pipette.

3. Miscellaneous
   a. *Standards and Specifications:* FDA approval is not required due to the fact that the device will be considered a "custom device" by the FDA. As such, FDA regulations do not require review and approval for the use of the device.
   b. *Customer:* The device will be used by lab technicians.
   c. *Patient (animal)-related concerns:* The device must be sterilized between uses so cross contamination does not occur.
   d. *Competition:*
      i. The MiniFIX Micropipette is similar to the size constraints desired, but does not have repeated deliveries and the accuracy is 30%.
      ii. RAININ products makes micropipettes calibrated to 10µL with respectable accuracy, but when scaled to 5µL the percent accuracy increases past the desirable amount.
      iii. MicroZippette Handheld Dispensers can be used for volumes of 1mL, but it can be used for repeated deliveries. However, the device cannot deliver the desired volumes.
      iv. The eye drop dispensing system, US patent number 6610036, allows delivery of a predetermined quantity to the eye. It includes a replaceable cartridge with a collapsible bag for ophthalmic liquid.
      v. The microdispensing pump, US patent number 7073733, can be used for ophthalmic applications when an accurate dose is necessary.
      vi. US patent number 5881956 is a microdispensing ophthalmic pump which allows repeated delivery of volumes as small as 5µL.

# Appendix C

## Test Results

### Drop Volume Accuracy

| Trial | Water Weight (mg) | Percent Error | Pipette Stop | Pipette Number |
|---|---|---|---|---|
| 1 | 0.0041 | 18 | 1 | 1 (blue) |
| 2 | 0.0045 | 10 | 1 | 1 |
| 3 | 0.0043 | 14 | 1 | 1 |
| 4 | 0.0041 | 18 | 1 | 1 |
| 5 | 0.0039 | 22 | 1 | 1 |
| 6 | 0.0055 | 10 | 2 | 1 |
| 7 | 0.0039 | 22 | 1 | 1 |
| 8 | 0.0039 | 22 | 1 | 1 |
| 9 | 0.0047 | 6 | 1 | 1 |
| 10 | 0.0045 | 10 | 1 | 1 |
| 11 | 0.0045 | 10 | 2 | 1 |
| 12 | 0.0059 | 18 | 2 | 1 |
| 13 | 0.0062 | 24 | 2 | 1 |
| 14 | 0.006 | 20 | 2 | 1 |
| 15 | 0.0054 | 8 | 2 | 1 |
| 16 | 0.0062 | 24 | 2 | 1 |
| 17 | 0.0053 | 6 | 2 | 1 |
| 18 | 0.006 | 20 | 2 | 1 |
| 19 | 0.0053 | 6 | 2 | 1 |
| 20 | 0.0053 | 6 | 2 | 1 |
| | **Pipette 1 average** | 14.7 | | |
| | **Stop 2** | 13.81818182 | | |
| | **Stop 1** | 15.77777778 | | |
| 21 | 0.0048 | 4 | 1 | 2 (purple) |
| 22 | 0.0048 | 4 | 1 | 2 |
| 23 | 0.0047 | 6 | 1 | 2 |
| 24 | 0.0046 | 8 | 1 | 2 |
| 25 | 0.0047 | 6 | 1 | 2 |
| 26 | 0.0048 | 4 | 1 | 2 |
| 27 | 0.0046 | 8 | 1 | 2 |
| 28 | 0.0046 | 8 | 1 | 2 |
| 29 | 0.0043 | 14 | 1 | 2 |
| 30 | 0.0045 | 10 | 1 | 2 |
| 31 | 0.0045 | 10 | 1 | 2 |
| 32 | 0.0047 | 6 | 1 | 2 |

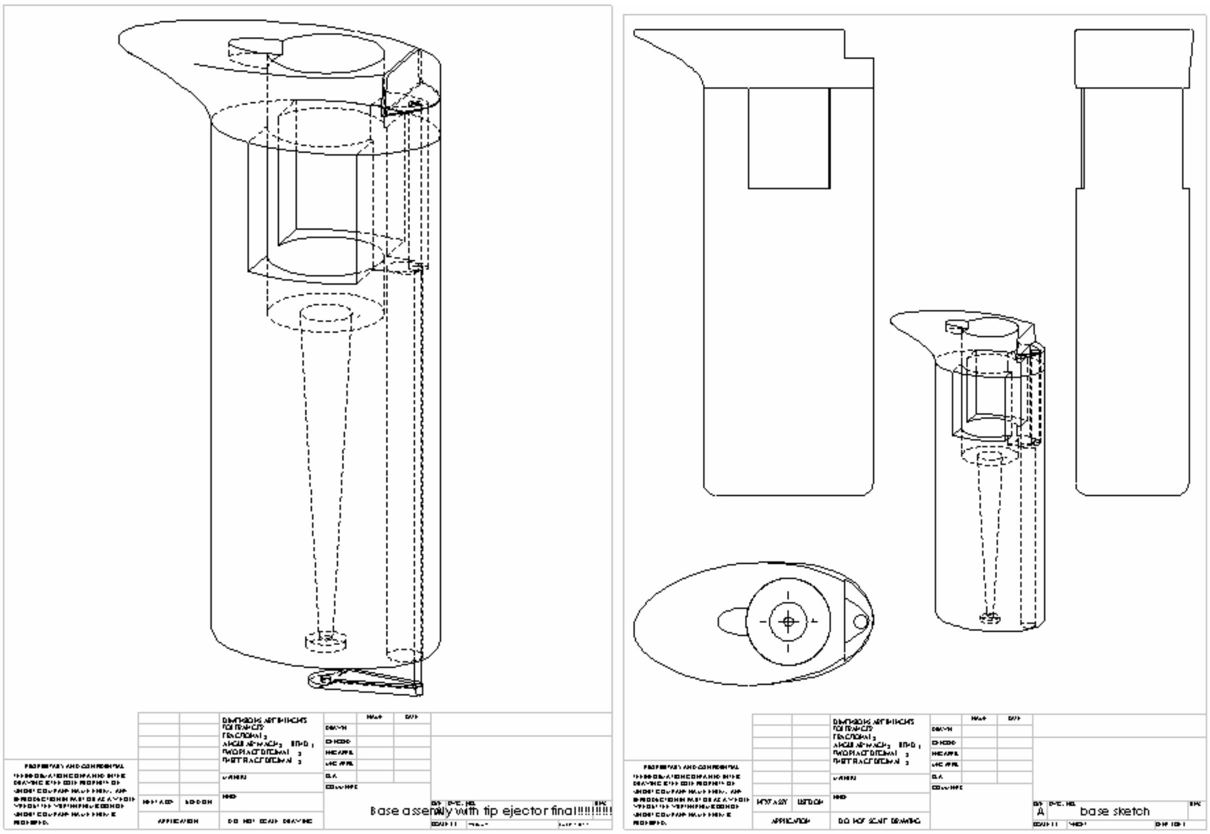
| | | | | |
|---|---|---|---|---|
| 33 | 0.0046 | 8 | 1 | 2 |
| 34 | 0.0047 | 6 | 1 | 2 |
| 35 | 0.0047 | 6 | 1 | 2 |
| 36 | 0.005 | 0 | 1 | 2 |
| 37 | 0.0049 | 2 | 1 | 2 |
| 38 | 0.0045 | 10 | 1 | 2 |
| 39 | 0.0048 | 4 | 1 | 2 |
| 40 | 0.0044 | 12 | 1 | 2 |
| | **Pipette 2 average** | 6.8 | | |
| 41 | 0.0045 | 10 | 1 | 3 (purple) |
| 42 | 0.0047 | 6 | 1 | 3 |
| 43 | 0.0049 | 2 | 1 | 3 |
| 44 | 0.0044 | 12 | 1 | 3 |
| 45 | 0.0043 | 14 | 1 | 3 |
| 46 | 0.0046 | 8 | 1 | 3 |
| 47 | 0.0046 | 8 | 1 | 3 |
| 48 | 0.0048 | 4 | 1 | 3 |
| 49 | 0.0047 | 6 | 1 | 3 |
| 50 | 0.0047 | 6 | 1 | 3 |
| 51 | 0.0045 | 10 | 1 | 3 |
| 52 | 0.0046 | 8 | 1 | 3 |
| 53 | 0.0046 | 8 | 1 | 3 |
| 54 | 0.0044 | 12 | 1 | 3 |
| 55 | 0.0043 | 14 | 1 | 3 |
| 56 | 0.0044 | 12 | 1 | 3 |
| 57 | 0.0048 | 4 | 1 | 3 |
| 58 | 0.005 | 0 | 1 | 3 |
| 59 | 0.0048 | 4 | 1 | 3 |
| 60 | 0.0048 | 4 | 1 | 3 |
| | **Pipette 3 average** | 7.6 | | |

| | |
|---|---|
| **Overall Stop 1 % error average** | **8.7755** |
| **Average volume dispensed (mL)** | **0.0046** |
| **Standard deviation** | **0.000266** |

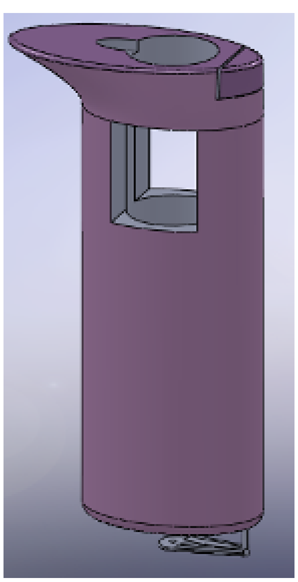
## User Ergonomics Ratings

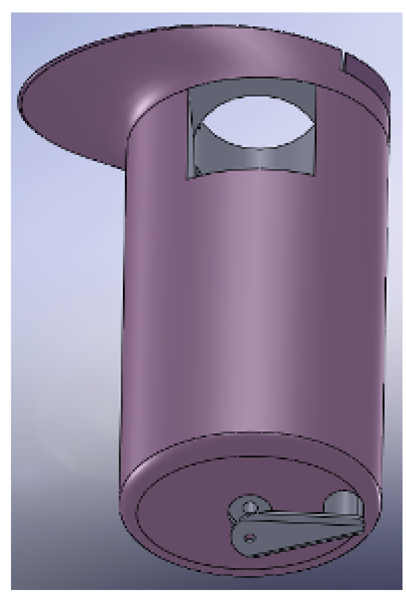
| Person | MiniFIX | Purple | Blue | Standard |
|---|---|---|---|---|
| 1 | 2 | 4 | 3 | 1 |
| 2 | 4 | 2.5 | 2.5 | 1 |
| 3 | 4 | 2.5 | 2.5 | 1 |
| 4 | 4 | 3 | 2 | 1 |
| 5 | 1 | 4 | 3 | 2 |
| 6 | 1 | 3 | 4 | 2 |
| 7 | 2 | 3 | 4 | 1 |
| 8 | 2 | 4 | 3 | 1 |
| 9 | 2 | 4 | 3 | 1 |
| 10 | 2 | 3 | 4 | 1 |
| **Average** | **2.4** | **3.3** | **3.1** | **1.2** |

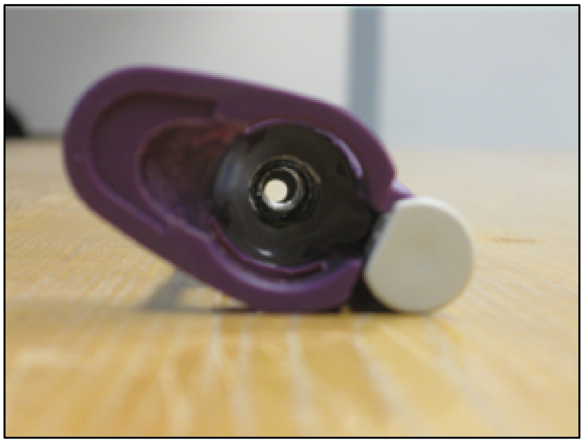
# Appendix D




Sketches of final design







Top view of prototype without MiniFIX

Side view of prototype

Bottom view of prototype without MiniFIX



Partially modified tip ejector

Bottom view of protype with MiniFIX