BME 402 (Biomedical Engineering Design)
Spring 2010

Project #33: Liquid Medication Delivery System (Engineering World Health)

FINAL REPORT

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Table of Contents

Abstract

In the developing world, AIDS has become a rampant problem. One way to combat the problem is by reducing the rate of AIDS transmission from mothers to newborn children. This can be accomplished by delivering single doses of Viramune®, an anti-HIV drug, to newborns within 72 hours of birth. Unfortunately, due to limited healthcare resources, many women in the developing world must give birth at home, and thus must deliver the dose to their newborn themselves. Engineering World Health has developed a foil packet in which Viramune® can be dispensed to expectant mothers. The purpose of this project is to design an inexpensive bottle-top dispenser to dispense Viramune® into the foil packets. A design involving two check valves in series was selected, and tested using a chilled suspension of milk and Campbell's tomato soup. The average mass dispensed corresponded to a volume of 0.5995 mL, with a standard deviation corresponding to 0.0235 mL, and an average percent error of 0.082%. Future work will focus on improving the device's reliability.

Introduction

Acquired immune deficiency syndrome, or AIDS, kills 3.1 million people every year, over 80% of whom live in developing nations[1]. In addition to the pathological consequences associated with the disease, AIDS also has many other secondary effects. Those who have acquired the disease have also acquired both the economic burden of treating their ailment as well as the social stigmatization which often accompanies it.

It is not only the patients of AIDS who suffer. In the developing world, children may have to care for parents with AIDS or may even become orphaned due to AIDS, leaving them to care for siblings. In particularly afflicted areas, there are sharp declines in participation in the educational system and labor force which has wider societal impacts. In extreme cases, a community's entire healthcare system suffers from an increased workload for an already depleted staff.

Background

In developed nations, medications are used to effectively treat AIDS by holding it in a relatively harmless state. However, these medications are quite expensive and thus not a practical solution for many parts of the world. Fortunately, Boehringer Ingelheim donates bottles of their anti-HIV medication, Viramune®, to 59 developing countries on four continents[10]. A single 0.6 mL dose of Viramune® administered within 72 hours of birth has been shown to effectively reduce HIV transmission rates from mother to child by nearly 50%[2,4].

Unfortunately, societies in many parts of the world are not set up with adequate access to healthcare. In many parts of Africa, for example, an expectant mother may only seek prenatal care once and give birth many months later at a location relatively remote from any medical facility or pharmacy[5,6]. Therefore, to prevent the transmission of HIV, HIV positive, expectant mothers must be given an appropriate dose of medication that lasts from her visit to the doctor to the time she gives birth.

Currently, the medication is dosed and delivered in oral dosing syringes, plastic bags, or recycled plastic bottles (Figure 1). The process for filling the containers is slow and tedious. Additionally, the liquid medication is often exposed to the environment, and as a consequence, is frequently spoiled or lost[3].

The dosing process requires opening the bottle, inserting the syringe, inverting the entire construct, measuring the appropriate dosage, and returning bottle to its capped and upright state. Engineering World Health (EWH) is developing a foil packet to protect the dose during this period (Figure 2), but an inexpensive way to measure the dose and dispense it into the packet is still needed[3]. The cost, efficiency, and ease of the entire process would be improved in a novel device.

Figure 1: Liquid nevirapine (Viramune®) medicine bottle with oral syringe and cap currently used to deliver doses. Photo

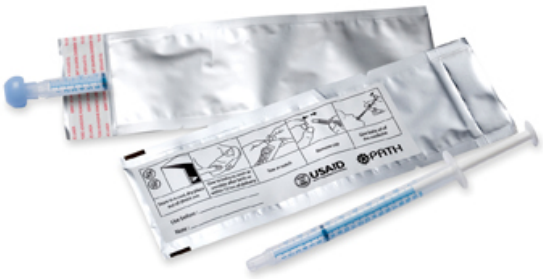


Figure 2: Foil packets used to contain doses of liquid nevirapine. Photo obtained from http://healthcare-

Client's Requirements & Design Constraints

In order to measure out and deliver the dose of medicine more accurately and efficiently, a bottle-top dispenser for the current liquid 240mL nevirapine medicine bottle is necessary. The device has to be able to sterilely deliver fixed doses of liquid nevirapine into the foil packets that have been developed for Engineering World Health. More specifically, it must be able to accurately measure out and dispense 0.6 mL of the medicine with a margin of error of ±0.05 mL, (8%). Along with being accurate, the device must also be reliable. It must remain accurate and reliably dispense the fixed dose for up to 400 doses, which is the maximum number of doses that are contained in the bottle of nevirapine that is currently used in the developing world (240 mL). In addition, the device must be durable enough to remain in operation for at least 6 months, because that corresponds to the maximum shelf life of an open liquid nevirapine medicine bottle. The device should also be able to seal the medicine bottle tightly, so as to prevent contamination from the external environment. Perhaps most importantly, the device must be cheap, so that it can be mass-produced for developing countries. Ideally, the device should cost no more than $2.00 (USD) to manufacture in order for it to be cost effective.

Design Alternatives (Fall 2009)

In light of the above specifications, three design options were considered. These consisted of the Horizontal Syringe Design, the Straw design, and the Two Check Valves Design.

THE HORIZONTAL SYRINGE DESIGN

The Horizontal Syringe Design is illustrated in Figure 3. In this design, a syringe is permanently fastened to a cap which fits the nevirapine bottle. At the interface where the syringe meets the cap, a hole connects the syringe chamber with the medicine bottle. To operate the device, the bottle is flipped upside down, and the liquid medication flows through the hole, filling the syringe. The fluid is then discharged through the tip of the syringe into a foil packet.

This design has both advantages and disadvantages. One advantage is that this design can be kept sterile quite easily. All that is required is

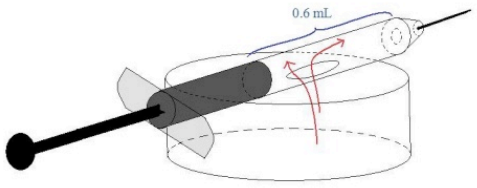


Figure 3: The Horizontal Syringe design. Liquid medication fills the syringe chamber due to the effect of gravity

that a syringe cap be placed on the syringe after each use. Some disadvantages of this design include its poor user interface, problems that a highly viscous fluid could pose, and the fact that it must be manufactured. This device has a poor user interface because it must be flipped over with each use—an awkward and time-consuming maneuver. A viscous fluid like nevirapine also may not fully fill the syringe chamber, resulting in an inaccurate dosage. Furthermore, because the syringe must be fastened into place and a hole must be borne through both cap and syringe, costs would accrue due to these manufacturing processes.

THE STRAW DESIGN

The Straw Design is illustrated in Figure 4. In this design, a straw is permanently fixed to a medicine bottle cap, extending down into the bottle. In the center of the cap, a port through the bottle cap connects this straw to the tip of a syringe. The syringe can lock into place at this port. The straw spans the length of the medicine bottle, from the port located on the cap to just above the base of the container. To use the device, the operator locks the syringe into place at the port, and draws the dose of the liquid medication up through the straw into the syringe. The syringe is then detached, and its contents ejected into the foil packet.

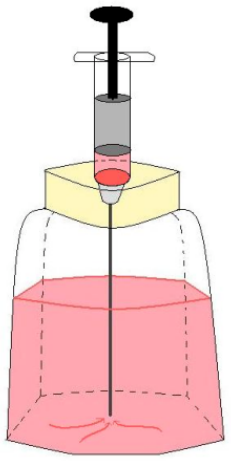


Figure 4: The Straw design. Liquid medication is forced into the chamber of the syringe because the vacuum created

Some advantages of this design are that an accurate dosage can be virtually guaranteed with each use, and it is compatible with viscous fluids. Some disadvantages of this design are that it requires a multistep process (as opposed to one single action) and it too requires manufacturing to assemble.

THE TWO CHECK VALVES DESIGN

This design was proposed by Feest, Maharaj, Cira, and Mogen (2008), and is illustrated in Figure 5. It consists of two check valves in series, with a syringe inserted between them[7]. It functions like a piston pump. When the syringe plunger is pulled, it draws liquid medication through a tube inserted in a hole in the bottle cap. The medication goes through the first check valve, while the second check valve blocks reverse airflow. When the syringe plunger is pushed, the first check valve prevents medication backflow into the bottle, and the medication exits through the second check valve and travels through another tube into the foil packet.

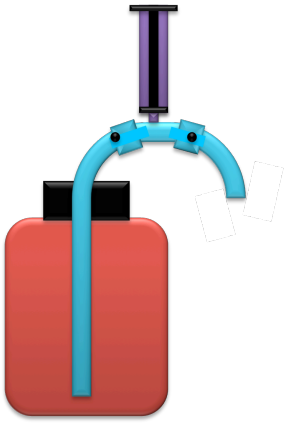


Figure 5: The Two Check Valves design. Liquid medication is drawn into the syringe chamber then expelled into a foil packet in

Some advantages of this design are that it consists of prefabricated pieces, which may reduce production costs. Also, in the event that check valves are unavailable or unaffordable, they can be replaced with clamps. One disadvantage of this design is that check valves are expensive, and two are required for easy use of this design.

Design Matrix

In order to evaluate the three design alternatives, a design matrix was created with several weighted criteria and the designs were ranked in each category (see Table 1).

The cost was determined to be the most critical factor when evaluating the design alternatives because the device cannot be implemented in the developing world unless it is very inexpensive. Most of the cost of the devices would probably be due to manufacturing, so the complexity of the manufacturing process for each of the designs was evaluated. It was decided that the Horizontal Syringe Design would be relatively difficult to manufacture as the curved surface of the syringe would need to be interfaced with the flat surface of the bottle cap. It would probably require a custom-made plastic connection piece, which would probably make it the most expensive of the design options. The Straw Design could also potentially be

difficult to make, because the cap would have to be modified with female threads to match the syringe, and would have to contain a check valve to prevent the medication from falling back into the bottle when the syringe is removed. The Two Check Valves Design, while still somewhat complicated, could be significantly reduced in cost by replacing the valves with simple components, such as clamps, or by using very cheap pre-manufactured valves.

The accuracy and reliability were equally weighted as the next most important evaluation criteria. In order for the device to serve effectively, it needs to consistently and accurately dispense the appropriate dosage. It was decided that the Horizontal Syringe Design might dispense inaccurate dosages due to bubbles becoming trapped in it when the bottle is flipped, and due to variability in ejection speed. The Straw and Two Check Valves designs both use a dosing syringe to accurately measure the expelled volume, but the straw design might be less reliable, due to medication left behind in the port.

The ease of use of the designs was also evaluated. The Horizontal Syringe Design has the same usage problems as the current method: it requires a lengthy and tedious inverting, measuring, and inverting maneuver. The Straw Design is also slow to use, as it requires the syringe to be screwed onto and off of the cap for every dose. The Two Check Valves Design is very simple to use, as its syringe piston need only be pulled back and depressed to accurately deliver the indicated dosage. In the end, it was decided that the Two Check Valves Design be pursued over the other options for reasons of cost and ease of use.

Table 1: Design Matrix

CRITERIA	WEIGHT	HORIZONTAL SYRINGE	STRAW	TWO CHECK VALVES
Monetary Cost	35	17	25	25
Accuracy	25	20	25	25
Reliability	25	20	23	25
Ease of Use	15	5	10	15
TOTAL	**100**	**62**	**83**	**90**

Valve Options

Several check valve designs were considered for the device: the double flapper valve, the ball check valve, and the diaphragm check valve.

The double flapper valve consists of two flaps of rubber which close against each other to prevent reverse fluid flow, as shown in Figure 6. They are held together by their own elastic recoil, and by reverse fluid pressure. This valve design is most often used in larger applications; the team did not find a version of it at our size scale, below 1.3 cm diameter.

The ball check valve consists of a ball which rests against a hole of a smaller diameter. In applications involving viscous liquids, or in which the ball must close against gravity, a spring is commonly used to hold the ball in place, as shown in Figure 7. Springs are also used when a high cracking pressure, at which the valve lets fluid flow through in the correct direction, is desired. The spring also increases

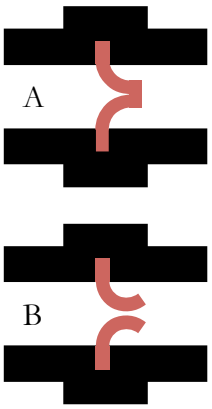


Figure 6: Double flapper valve, closed in

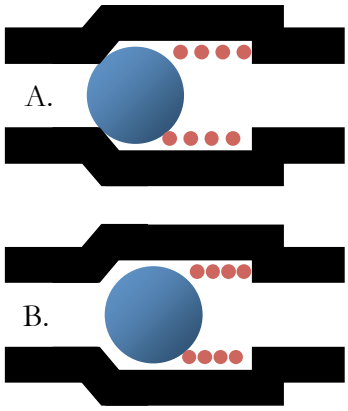


Figure 7: Ball check valve, closed in A, open in B. Image redrawn from Dr. Frank

the speed at which the ball moves back into place, reducing fluid backflow when the fluid pressure is reversed. Because of these benefits, the ball check valve would have been the ideal valve for our application. Unfortunately, a ball check valve could not be found for less than $1.67, making it impractical for this application.

The diaphragm valve consists of a rubber diaphragm covering a hole, which deforms to let fluid through, and then closes via its own elastic recoil and reverse fluid pressure, as shown in Figure 8. Because it lacks a spring to hold it closed, it is more prone to fluid backflow than the ball valve. Also, because it involves deformable components, it is anticipated to be less durable than the ball valve design. However, it is significantly cheaper, costing as little as $0.66. Thus, it was selected for the final design.

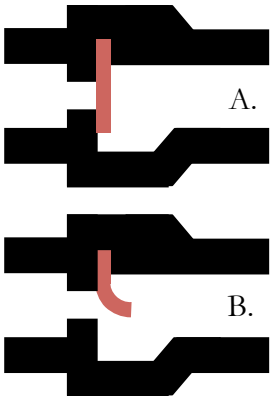


Figure 8: Diaphragm valve, closed in A, open

Final Design (Fall 2009)

As described in the previous sections, the final design consists of two diaphragm check valves in series, with a syringe inserted between them (Figures 9 and 10). The tubing which connects the valves and the medicine bottle is rigid polypropylene. Its rigidity allows it to firmly support the valves and syringe, and allows it to be more easily glued to them. Polypropylene is also chemically inert, making it safe for use with the medication. The upper tubing is flexible PVC, making its tip easy to reposition. A modified Airsoft BB narrows its exit spout. This reduces the spout opening's cross-sectional area, thus reducing the area of liquid available for drips to cling to, and thus reducing the variability in drip volume.

One problem observed during testing is that if the syringe overfills, it can only be emptied through the exit spout, and thus results in an inaccurate dose. A string connecting the syringe piston and chamber prevents this problem.

The materials required to construct the device are tabulated in Appendix II. The steps required for assembly are shown below:

- If the interior diameter of the polypropylene tubing is too small for the valve connections, then it must be widened. This can be done by drilling along the axis of the tubing with a 7.49 mm drill bit. The bit should be inserted approximately 5 cm into the tubing.
- Next, two polypropylene tube segments are cut: a 3 cm segment of the widened tubing, and an additional 20 cm segment with at least one widened end.
- A 6.35 mm hole is drilled through the center of the medicine bottle cap.
- A 4.32 mm hole is drilled transversely through one wall of the 3 cm segment of polypropylene tubing, midway down its length. It is important that the hole only goes through one wall of the tube.
- A check valve is then forced into each end of the 3 cm tube segment. The valves must be aligned so that fluid can flow unidirectionally through the segment.
- The 20 cm segment of polypropylene tubing is then forced onto the intake check valve. A 13.75 cm length of clear vinyl tubing is pressed onto outlet valve's the barbed connector.
- The tip of the 1 mL syringe is inserted into the hole in the side of the 3 cm tube segment, and is glued into place.
- Using a heated needle, a hole is punched through the piston near the top.
- String is then threaded through this hole and tied. The other side of the string is tied to the base of the syringe cylinder so that the piston can only be pulled out to 0.7 mL.

- The 6 mm plastic BB should be of the translucent variety which contains an air bubble in its center. The tip of a thumbtack is heated and lanced into this bubble from two opposite sides, transforming the bubble into a channel which runs through the BB.
- The modified BB is then inserted into the free end of the vinyl tubing, so that the hole in the BB is parallel with the tubing. This forms the dispenser's spout.
- Finally, with the modified cap screwed on to the bottle, the polypropylene tubing is fed through the hole until the tubing reaches the bottom of the bottle.
- The spout can be held in a vertical direction by using thread to tie the spout to the portion of polypropylene tubing just above the cap. The device is then ready for use.

Figure 9: Prototype of final design (without BB) attached to a sample bottle with the same

Figure 10: Prototype of final design (with BB) filled with testing fluid

To operate the device, it is first necessary to unscrew the cap just enough to allow air to enter the bottle, to prevent the formation of a vacuum as liquid is removed from the bottle. With a smooth, continuous motion, the plunger of the syringe should be pulled 0.7 mL of the liquid medication into the chamber of the syringe. This volume is greater than the dose, to compensate for fluid backflow through the valves. The liquid medication can then be delivered to the foil packet by pressing down on the plunger of the syringe. The process can be repeated until the bottle is empty. Before the bottle is stored, the cap should be tightened to prevent contamination.

Testing (Fall 2009)

Due to the high cost of Viramune®, another liquid of comparable viscosity had to be used for testing. At the recommendation of Dr. Vivian Rexroad, PharmD., cold (14.5 °C) Campbell's tomato soup made with milk was used as this substitute.

To measure the accuracy and reliability of the device, it was necessary to measure the amount of fluid dispensed by the device over multiple trials. Volumetric measurements could have been used by dispensing the liquid into a graduated cylinder, and reading the volume. This method, however, was deemed inappropriate because the small size of the volumes dispensed by the device would have made it very easy to overestimate or underestimate the volume in the cylinder. Thus, to make the measurements more objective and precise, mass was measured instead of volume.

First, the mass of the desired dose of testing liquid was measured. The liquid was measured using a syringe. The mass of 0.6 mL of Campbell's tomato soup made with milk was found to be 0.6432 g with a standard deviation of ± 0.0148 mL (n = 5).

For the first testing session, the prototype without a plastic BB attached to the end of the tubing was used. It was determined that, due to backflow through the valves, the syringe in the medication dispenser had to be filled to 0.7 mL to eject 0.6 mL of soup.

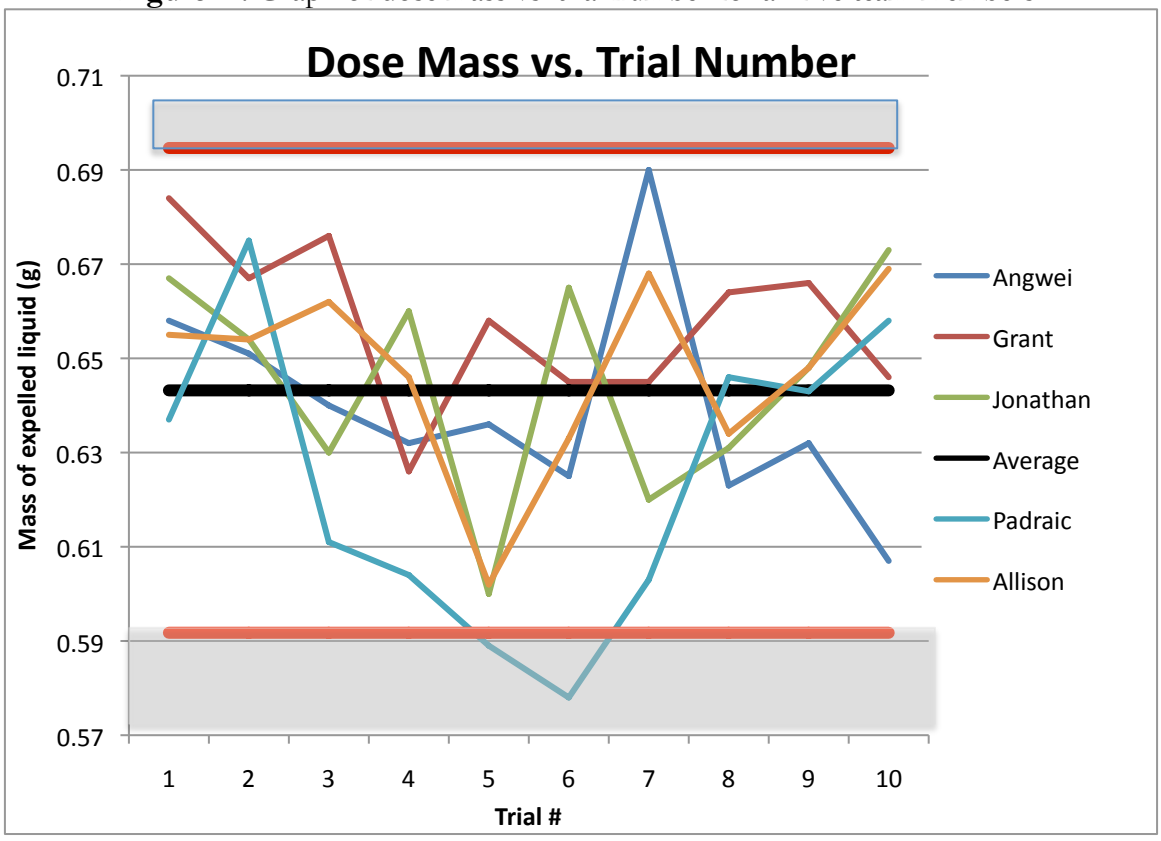
A set of instructions for operating the device was developed, and each member of the design team (n = 5) conducted ten trials. The motivation behind this approach was that, in the developing world, different pharmacists would interpret the directions differently. This testing approach simulated some of this variation. The procedure is as follows:

Instructions:

1. Replace the cap of the medication bottle with device. Slightly loosen the cap before use to allow air intake.
2. Gently pull back and push on the device's syringe piston until medication fills all of the tubing. If necessary, plug the device's spout when pulling on the syringe, to help pull the medication up into the device.
3. Place a foil packet underneath the spout
4. Pull the syringe piston back slowly to 0.7mL (marked) line, and then push it in to dispense the medication
5. Seal the foil packet.
6. If desired, repeat steps 3 and 4 until the bottle is empty.
7. When finished, tighten the cap, and insert a thumbtack into the spout to seal it.
8. Unscrew the device off of the empty bottle, clean it, and place it on a new bottle

Each team member completed ten trials, following step 4. The results are plotted in Figure 11. The black line indicates the mass of 0.6 mL of soup and the horizontal red lines correspond to ± 8% (± 0.05 mL) error, the range in which the product specifications state the device must operate. Two data points out of 50 lies outside of this range.

Figure 11: Graph of dose mass vs. trial number for all five team members.



The summary of the results is shown in Table 2.

Table 2: Summary of trials completed by each team member.

Team Member	Speed (qualitative)	Tapped off drip?	Average (g)	Standard deviation (g)	% Error
Angwei	Slow and constant	Yes	0.6394	0.0228	-0.591
Grant	Fast and constant	Yes	0.6577	0.0173	2.254
Jonathan	Slow and constant	Yes	0.6448	0.0237	0.248
Padraic	Fast and constant	No	0.6244	0.0318	-2.922
Allison	Slow and constant	Yes	0.6471	0.0206	0.606

All team members' average percent errors fell within the ± 8% allotted error range, with the highest average error at 2.922%. This is most likely due to the fact that this member (Padraic) was the only one that did not tap off the last drop. As seen on the graph, Padraic's values were lower on average in comparison to those who did include the drop. The combined trial average (n = 50) was 0.6427 g (0.5995 mL), which is 0.078% lower than the mass of 0.6 mL (0.6432 g). The overall standard deviation was 0.0252 g (0.0235 mL) and the average percent error from the trials was 0.082%, well within the required ± 8% error range (see Appendix III).

Through observation of all trials, it was qualitatively observed that the most accurate volumes are dispensed when the syringe is pulled and pushed with continuous motions and constant speeds. Pulling the syringe at high speeds increased the likelihood of overfilling the syringe. This is a problem because if the syringe is overfilled, the only way to remove the liquid from the syringe is to dispense it out of the spout. An overdrawing prevention mechanism, described in the final design section, was developed after this set of tests and will be evaluated in future tests. Slower speeds seemed to have smaller average percent errors. Future tests will be conducted to measure speed in relation to accuracy.

Another problem observed during testing was that drips of soup hung from the end of the spout, increasing the variability of the dispensed mass. During testing, it was qualitatively observed that this could be remedied by tapping the flexible tubing to knock off the drip. This method, however was not acceptable as a long-term solution, because it allows for variability between users. People who tap the tubing very hard might dispense different volumes than people who tap it only lightly. To provide a more robust remedy to the drip problem, the spout was narrowed by inserting a plastic BB with a small hole poked through it into the end of the flexible tubing. Initial tests qualitatively indicated that the plastic BB did not interfere with the accuracy of the device. It was observed that when the syringe was pulled, a small amount of air was pulled through the BB into the tubing as a result of fluid backflow through the valves as they were closing. This resulting in air bubbles forming in the flexible tubing. This problem is addressed in the section on future work.

Future Work (Fall 2009)

As mentioned in the testing section, other tests will be conducted in the future to calibrate the device and improve the instruction manual. These additional tests will explore how accuracy is affected by speed, how well the proposed overdraw prevention mechanism works, and further quantitative testing with the dripping prevention mechanism.

As described in the section on testing, the plastic BB greatly reduces dripping; however, it increases the frequency of air bubbles in the flexible tubing. These air bubbles could add variability in the dispensed doses. Thus, mechanisms for

preventing air bubbles will be researched and incorporated into future prototypes. One promising option involves nesting a smaller diameter tube inside of the tip of the flexible tubing, so that backflow does not pull air all of the way through the smaller tube into the flexible tubing.

A simple backflow prevention mechanism was developed very late into the design process. It involves connecting the syringe piston and cylinder using thread. As there is no way to return from pulling the plunger too far without wasting some of the expensive medication, future designs should incorporate this mechanism. It will, however, need to be improved. Our initial testing was done with sewing thread, but after several uses, the string became stretched, and started wearing out. A stronger and more reliable material for the string should be used for this purpose, and will be investigated.

One week before the final design was due, the team learned that manufacturing costs should be included in the total device cost of $2.00. As the prototype currently uses all of these funds for material costs, future developments will need to focus on reducing material costs to allow for manufacturing costs. More research will be conducted to determine the manufacturing costs. EWH suggested an approximation of 90% manufacturing cost[9], but due to the ease of assembly of this design, it is likely that the actual percentage will be lower.

The check valves are by far the largest portion of the design cost. As such, it would be very beneficial to find a way to manually recreate the valves out of cheaper materials with little additional manufacturing time. This might be accomplished by nesting sections of tubing inside of the larger tubing with a ball and spring between. One of the nested sections of tubing can be notched such that fluid flows around the ball when it is near that end of the chamber.

The current glue used in the prototype, Loctite plastic-bonder, is not safe for use in contact with medicine. Thus, a more biocompatible glue will be utilized in future designs to ensure complete patient safety. Epoxies will be investigated as a potential solution.

When medication is dispensed from the foil packets and given to the patients, medication residue will inevitably be left in the packet, and thus, if exactly 0.6 mL is dispensed into the packets, the patients will not receive the correct dose[8]. Research will be conducted to find the appropriate volume of medication that should be dispensed into the packets so that patients receive the correct dosage. This will probably be conducted in collaboration with the EWH team which is developing the foil packets.

Finally, more reliability testing will have to be conducted with both the medication and the foil packets. In addition to the previously mentioned tests, the prototype will be tested for reliability after delivering 400 doses (equivalent to one full bottle of medicine). The effects of long-term usage and storage will also be investigated.

Conclusion (Fall 2009)

The goal of this project was to design and test a device that replaces the existing cap of the liquid nevirapine medicine bottle and accurately measures out individual 0.6 mL doses of Viramune® into foil packets. After considering several designs including the Horizontal Syringe and Straw designs, the Two Check Valves design was selected as the final design for both its accuracy and ease of use. A prototype was built and tested using a cold mixture of milk and Campbell's tomato soup as a substitute for the medicine. The average mass dispensed corresponded to a volume of 0.5995 mL, with a standard deviation corresponding to 0.0235 mL, and an average percent error of 0.082%. In the future, the prototype will be refined, and further testing will be carried out to determine its reliability.

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APPENDIX I: PRODUCT DESIGN SPECIFICATIONS

PROJECT TITLE:

Liquid Medication Delivery System (Engineering World Health)
(Project Number: 33 / Project Code: medication_delivery)

PROJECT DESCRIPTION:

The purpose of this device is to seal bottles of nevirapine, and to allow pharmacy technicians to sterilely dispense 0.6 mL doses of nevirapine into foil packets developed by Engineering World Health (EWH).

DESIGN REQUIREMENTS:

1. Physical & Operational Characteristics

a. **Accuracy & Reliability:** The device must dispense within ± 0.05 mL of 0.6 mL of nevirapine (Feest, Maharaj, Mogen, Cira, 2008).

b. **Life in Service:**

   i. The device must accurately deliver up to 400 doses, thus dispensing the maximum number of doses contained in a nevirapine bottle (240 mL).

   ii. The device must remain in operation for a minimum of 6 months, which is the maximum shelf life of an open nevirapine bottle (Feest et al., 2008).

   iii. The device must have a shelf life of at least 5 years (Feest et al., 2008).

c. **Operating Environment:**

   i. The device must be able to be dropped from a minimum of 2 meters (Feest et al., 2008).

   ii. The device must be able to withstand temperatures ranging from -10 °C to 50 °C (Feest et al., 2008).

   iii. The device must withstand 0 to 100% humidity.

   iv. The operating environment may be contaminated with dirt, dust, insects, and aerosolized contaminants. The device must maintain the sterility and purity of the medication before, during, and immediately following use.

d. **Ergonomics:** The forces required to operate the device should be low enough that a minimum of 98% of people over 13 years old can use the device.

e. **Size:** The device must seal the nevirapine bottle that is currently used. "Nevirapine is patented by Boehringer Ingelheim (BI), and they have one type of bottle that all nevirapine is distributed in" (Cooper, 2009).

f. **Weight:** The device must weigh less than an empty nevirapine bottle.

g. **Materials:** Though not an essential requirement, the device's component materials ought to be available in developing nations; specifically, in rural regions of Peru, The Congo, and India.

2. Production Characteristics

a. **Production:** The device will be mass-produced, and preferably be assembled from parts available in developing nations.

b. **Cost:** The device must cost less than $2.00 USD (Feest et al., 2008).

3. Miscellaneous

a. **Quantity:** The device will be mass-produced.

b. **Customer:** The device will be used by pharmacy technicians in developing nations.

c. **Patient-related Concerns:** If the device is accepted by EWH, then EWH will own all of the intellectual property rights pertaining to the device, and the device will be placed in the public domain (Feest et al., 2008).

d. **Competition:** A variety of liquid medication delivery devices are available, including one produced by BI, but are too expensive for widespread use in developing nations (Feest et al., 2008; Cira, 2009).

REFERENCES:

1. Cira, N. Sept. 4, 2009. Personal Communication.
2. Cooper, J. 2009. "RE: Senior Design Project Update." Email to the authors.
3. Feest, A., Maharaj, V., Mogen, B., Cira, N. 2008. "Product Design Specifications." Accessed Oct. 1, 2009, at <http://homepages.cae.wisc.edu/~bme300/ewh_f08/secure/reports/Product_Design_Specifications.pdf>

APPENDIX II: COST ANALYSIS

QUANTITY	ITEM	PRICE PER UNIT (¢)	SUB-TOTAL (USD)
2	1/4" Polypropylene Liquid/Gas Check Valves[1]	66.300	1.33
1	Polypropylene Cap with Foamed Polyethylene Liner[2]	5.000	0.05
1	Precision-Glide, Tuberculin Syringe – 1 mL[3]	22.110	0.22
1 serving	Loctite Plastic Bonder[4]	5.440	0.05
23 cm	5/16″ Outer Diameter x 3/16″ Inner Diameter Polypropylene Tubing[5]	0.984	0.23
1	6 mm, 0.12 g Translucent Green Airsoft BB[6]	0.240	0.00
15 cm	Bonded Nylon #46 Thread[7]	0.003	0.00
1	Thumb Tack[8]	0.935	0.01
13.4 cm	1/4″ Inner Diameter Clear Vinyl Tubing[9]	0.82	0.11
TOTAL:			**2.00**

References

1. U.S. Plastic Corp. (2009). "1/4" PP Liquid/Gas Check Valves." Accessed December 10, 2009, at <http://www.usplastic.com/catalog/item.aspx?itemid=32233&catid=489&clickid=searchresults%20>.

2. U.S. Plastic Corp. (2009). "Polypropylene Cap with Foamed PE Liner." Accessed December 10, 2009, at <http://www.usplastic.com/catalog/item.aspx?itemid=22820&catid=683>.

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5. McMaster-Carr. "Tubing: Part Number: 5392K35." Accessed December 10, 2009, at <http://www.mcmaster.com/#57115t22/=4vhd2h>.

6. HobbyTron.com. (2007). "6mm BBs 10,000 .12g Translucent Green Airsoft Gun Accessory." Accessed December 10, 2009, at < http://www.hobbytron.com/6mm-BBs-10000-12g-Translucen-Green.html>.

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8. Hiolo. (2009). "Wholesale - BAZIC Assorted Color Decorative Thumb Tack." Accessed December 10, 2009, at <http://www.hiolo.com/products/BAZIC_Assorted_Color_Decorative_Thumb_Tack-64980-974.html>.

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APPENDIX III: RAW TEST DATA FROM FALL 2009

MEASUREMENTS FOR COMPUTING MASS OF 0.6 mL OF SOUP:

Trial	Measurements (g)
1	0.654
2	0.638
3	0.661
4	0.623
5	0.640
Average	0.6432

INDIVIDUAL MEASUREMENTS:

Trial	Angwei (g)	Grant (g)	Jonathan (g)	Padraic (g)	Allison (g)
1	0.658	0.684	0.667	0.637	0.655
2	0.651	0.667	0.654	0.675	0.654
3	0.64	0.676	0.63	0.611	0.662
4	0.632	0.626	0.66	0.604	0.646
5	0.636	0.658	0.6	0.589	0.602
6	0.625	0.645	0.665	0.578	0.633
7	0.69	0.645	0.62	0.603	0.668
8	0.623	0.664	0.631	0.646	0.634
9	0.632	0.666	0.648	0.643	0.648
10	0.607	0.646	0.673	0.658	0.669
Average (g)	0.6394	0.6577	0.6448	0.6244	0.6471
Standard Deviation (g)	0.022823964	0.017275866	0.023696226	0.031833595	0.020151923
Percent Error	-0.59079602	2.254353234	0.248756219	-2.92288557	0.606343284
Overall Average		0.64268 g			
Overall Standard Deviation		0.025212922 g			
Overall Percent Error*		-0.080845771			

*The overall percent error is the average of the percent errors for each individual.

All team measurements were taken when soup temperature was 14.5 °C.

APPENDIX IV: ADDITIONAL REPORTING FROM SPRING 2010 SEMESTER

Please refer to the poster from the final semester for additional information regarding the final cost breakdown and final device description. Additional questions and comments can be received by contacting team members:

Jonathan Meyer
(608) 322-8550

Allison McArton
(414) 940-9293

Padraic Casserly
(507) 269-9901

Angwei Law
(310) 804-7028

Grant Smith
(414) 418-4569

Additional thoughts from…

Grant Smith:

On whether the project is actually useful, we discussed this frequently and our reasoning was that EWH knows better than us, and that they seem to think individual, sealed packets will have higher compliance rates and lower spoilage rates than the currently used dosing syringes. Also, perhaps a reusable bottle-topping device will be more cost-effective than handing out dosing syringes filled with medication to pregnant mothers.

On device manufacture, EWH said that industrial manufacture typically represents a 90% cost increase over raw materials. We never looked into contracting the device manufacture for our final design. The most feasible options are looking for donations from companies to support the project (US Plastics Corporation – a distributor of all the materials, or the manufacturers directly) or working through the EWH Kits program. EWH director Professor Malkin suggested injection molding; this may be a feasible option for a new or similar design if a large number of units are to be produced. I looked into it briefly and the cost of manufacturing the initial mold is quite high, but this might be the cheapest option for cost per unit if a large volume of units are desired (at least one thousand, probably ten thousand would be necessary to make this a feasible alternative economically). If sponsors can be found, it would be the ideal alternative assuming fewer than ten thousand units are requested by EWH. Were the project to blossom into an actual business venture, the device would need to be redesigned and manufactured in a different way (injection molding, factory labor, automated assembly, etc.) Local manufacture would require using companies in or recyclable parts from the developing world; this is probably the most difficult option to use and would require a number of redundant designs using different parts due to local availability concerns for specific parts.

On making this a realistically marketable solution, a few major concerns would need to be addressed. The device is not idiot proof; it can be misused easily which would result in the need to clean it and the loss of medication; plastics glues are expensive; alternative manufacture may solve this problem. The plastics used may leech the medicine and/or degrade over time and contaminate the medicine especially under extreme conditions (most notably direct sunlight but there might be others); again, injection molding facilities can probably help you find an appropriate plastic for medical applications. I would suggest talking to a plastics expert and researching plastics currently used in medicine. (The ether-based version of the polyurethane and the polypropylene we used are probably both acceptable; I included this concern because I'm not

certain.) Shipping would increase the cost of the devices significantly if only a few units were desired and if sponsorship were not provided.

On the whole, I would start the next semester by CALLING, not emailing Dr. Malkin of EWH to discuss many of these issues such as understanding the scope of their program/programs (in particular the Kits program as well as the scope of EWH on the whole and the extent of the Viramune® project) and especially, how many bottle-topper units are required and over what time frame(s). For example, 'What would a successful business plan for this project entail? Over what time frame should it be implemented? How many design iterations would be appropriate as the project scales up in scope? Etc.?' By the last question I am again referring to the problems detailed earlier regarding the cost relationships of various design alternatives and the feasibility/necessity of implementing these alternatives over various volume-frames and timeframes.

APPENDIX V: RAW TEST DATA FROM SPRING 2010

MEASUREMENTS FOR COMPUTING MASS VIRAMUNE ANALOG:

Trial	Measurements (g)
1	0.796
2	0.796
3	0.799
4	0.791
5	0.791
6	0.804
7	0.803
8	0.802
9	0.817
10	0.798
Average	0.7997

INDIVIDUAL MEASUREMENTS:

Trial	Angwei (g)	Allison (g)	Grant (g)	Padraic (g)
1	0.801	0.808	0.803	0.806
2	0.797	0.801	0.795	0.808
3	0.814	0.814	0.803	0.815
4	0.807	0.807	0.792	0.819
5	0.802	0.812	0.803	0.793
6	0.803	0.819	0.788	0.812
7	0.807	0.8	0.81	0.792
8	0.811	0.806	0.812	0.804
9	0.793	0.798	0.798	0.793
10	0.807	0.807	0.804	0.803
Average (g)	0.8042	0.8072	0.8008	0.8045
Standard Deviation (g)	0.006321041	0.006545567	0.007583608	0.009513149
Percent Error	0.562711017	0.937851694	0.137551582	0.600225084
Overall Average		0.804g		
Overall Standard Deviation		0.008g		
Overall Percent error*		0.560		

*The overall percent error is the average of the percent errors for each individual.

All team measurements were taken when soup temperature was 14.5 °C.