# Liquid Medication Delivery System (Revised May 2010)

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***Abstract*— In the developing world, AIDS has become a rampant problem, especially its transmission from mothers to newborn children. In order to combat the spread of AIDS, single doses of nevirapine, an anti-HIV drug, are given to infected pregnant mothers. This project seeks to design an inexpensive bottle-top dispenser for Viramune®, a brand of nevirapine. By consistently, easily, and efficiently measuring single doses of medication, the treatment will become more affordable; thus, more patients can be reached and the spread of disease will slow. The team designed a device that incorporates two clamps which act like manually operated one-way valves. A prototype was assembled and tested. Preliminary results suggest the device meets expectations, most notably cost restrictions.**

***Index Terms*— Biomedical Engineering, Engineering World Health, HIV, nevirapine, medication dispenser.**

## I. Introduction

ACQUIRED IMMUNE DEFICIENCY SYDROME, or AIDS, kills 3.1 million people every year, over 80% of whom live in developing nations [1]. 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 are not a practical solution for many parts of the world. Fortunately, Boehringer Ingelheim, a pharmaceutical company, donates bottles of their anti-HIV medication, Viramune®, to 59 developing countries on four different continents [2]. 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% [3].

Unfortunately, societies in the many parts of the world are not set up with adequate access to health care. In rural Africa for example, expecting mothers may only receive prenatal care from a physician once prior to giving birth. Furthermore, this care may be given several months prior to childbirth, which itself may be many miles away from the nearest health facility [4,5]. Therefore, to reduce the rate of transmission of HIV, expecting mothers who are infected must be given an appropriate dose of medication which lasts from their visit to the doctor until the time of delivery.

Currently, the medication is dosed and delivered in oral dosing syringes, plastic bags, or recycled plastic bottles (Fig. 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 [6]. In response to this, Engineering World Health (EWH) is developing a foil packet to protect the dose from spoilage (Fig. 2), but an inexpensive device to measure the dose and dispense it into the packet is still needed [6]. Desirable elements that should be addressed by such a device include: compatibility with the 240 mL Viramune® bottle, the ability to accurately and sterilely deliver fixed doses of liquid medication into foil packets, and a low cost to allow for distribution in developing countries. The objective of this study was to develop a device which would address these elements.

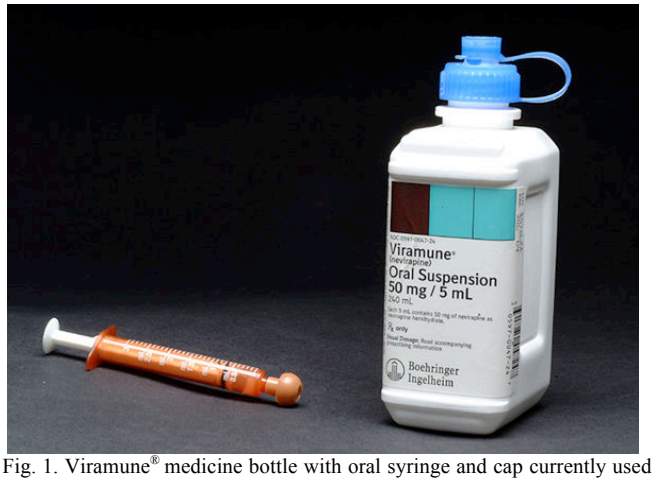


Fig. 1. Viramune® medicine bottle with oral syringe and cap currently used to deliver doses. Photo courtesy of Dr. Vivian Rexroad, PharmD.

## II. Device Design, Fabrication, and Cost

### A. General Design Description

The technical aspects of the device were designed to satisfy the following design criteria:

1. liquid medication bottle-top dispenser that seals the medicine bottle and prevents contamination;
2. delivers 400 fixed doses of liquid nevirapine into foil packages over the course of 6 months;
3. dispenses 0.6 mL (± 0.03 mL, 5% error margin) of medicine;
4. costs less than $2.00 (USD).

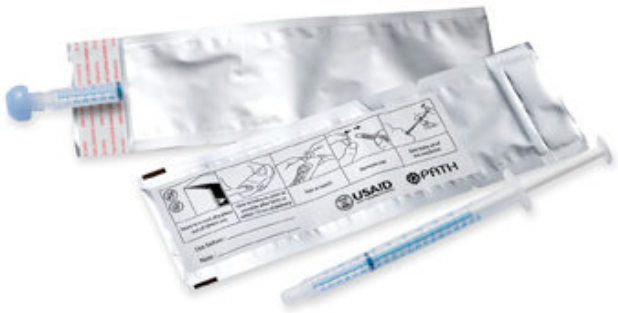


Fig. 2. Foil packets used to store doses of Viramune®. Photo obtained from http://healthcarepackaging.com/images/PATH.jpg.

The final device is assembled from nine individual pieces. All tubing is made of ester-based Superthane® manufactured by NewAge Industries. A 16 cm piece of 1/4" outer diameter (OD), 1/8" inner diameter (ID) tubing extends from the bottom of the medication bottle through a hole in the cap of the Viramune® bottle, protruding 3 cm above the top of the cap. The hole is drilled slightly narrower than the outer diameter of the tubing so that the tubing fits tightly in the hole. The inlet clamp is located at the top of this piece of tubing, opening upwards. The middle outlet of a 1/16" polypropylene T-connector connects to the top of this piece of tubing. To the other two outlets are attached a 5 cm piece of 1/4" OD, 1/8" ID tubing and a 1.5 cm piece of 3/16" OD, 1/8" ID tubing respectively. The syringe is connected to the vacated end of the shorter piece of tubing. The outlet clamp is placed around the 5 cm piece of tubing, opening toward the outlet of the device. The inlet and outlet clamps are identical acetal pinch clamps named differently so as to distinctly identify them for device operation. An 8 cm piece of 1/8" OD, 1/16" ID tubing is forced 1 cm into the remaining end of the 5 cm piece of tubing (Fig. 3).

Operation of the device is carried out as a sequence of six simple actions involving three components of the device: the inlet clamp, the syringe, and the outlet clamp (Fig. 3). First, the inlet clamp is opened. Second, the syringe is withdrawn, filling it with the desired dosage of medication. Third, the inlet clamp is closed. Fourth, the outlet clamp is opened. Fifth, the syringe is depressed, ejecting the desired dosage of medication. Finally, the outlet clamp is closed. Additionally, it is important to avoid three ways to operate the device incorrectly: 1) Never operate the syringe (withdraw or depress) without having exactly one clamp open; 2) Never pull forcefully on any element of the device; and 3) Never open both clamps at the same time. Each mistake can be easily corrected, but medication will be wasted unnecessarily. These rules should all be ignored if one is required to sanitize or otherwise clean the device, in which case complete disassembly is recommended.

### B. Valves

Several types of one-way valves were considered during the construction process of the device, each having its own advantages and disadvantages. The first valve considered was a ball-check valve. 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. The spring increases 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 too expensive for this application.

Next, we considered a diaphragm valve. 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. 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. It is also relatively expensive at 66¢ per valve.

Finally, we considered tubing clamps which can function as one-way valves when manually operated. When closed, these clamps prevent the flow of fluid through the tubing at the clamp site. When opened, fluid is allowed to freely pass through the tubing at the clamp site. A disadvantage of using the clamps is that their use requires extra work for the operator when compared to the passive opening and closing processes of the ball-check and diaphragm valves. However, because the clamps are 14¢ each and fluid is completely prevented from passing through the tubing when the clamp is in the closed position, this became the most suitable valve option for our design.

### C. Cost

The final device cost $0.97, less than half of that stated by the design criterion. The most expensive components of the device were the two clamps, the syringe, and the T-connector, which cost 28¢, 22¢, and 26¢ respectively.

## III. Experimental testing

As the team was unable to obtain the actual medication for testing purposes, we created a liquid with a viscosity that closely mimics nevirapine. Using this mixture, accuracy and reliability testing were performed.

### A. Viscosity Testing

In order to mimic the Viramune® medication passing through the device, an analog fluid with similar viscosity was desired. Corn syrup and water were mixed at varying concentrations in order to determine a ratio which would give 400 cP at room temperature (22ºC). To determine the viscosity of the solutions, a steel ball was dropped into a graduated cylinder filled with the liquid. The amount of time the ball took to pass between two points at a given distance was recorded and velocity was calculated. The following equation (Stokes' Law) was used to determine viscosity for each mixture:

$$\mu = \frac{2}{9}\frac{(\rho_b - \rho_l)}{v_t} g R^2$$

In this equation, $\mu$ is viscosity of liquid, $\rho_b$ is the density of ball, $\rho_l$ is the density of liquid, $v_t$ is the terminal velocity of the ball, $g$ is gravitational acceleration, and $R$ is the radius of ball.

### B. Accuracy Testing

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. First, the mass of the desired dose of testing liquid was measured. The liquid was measured using a syringe.

A set of instructions for operating the device was developed, and each member of the design team ($n$ = 4) 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. Open the inlet clamp.
2. Pull the syringe piston back slowly to 0.6 mL.
3. Close the inlet clamp.
4. Open outlet clamp and place foil packet underneath output tubing.
5. Push syringe piston in.
6. Close outlet clamp.
7. When the device is empty, remove it from the empty bottle, clean it, and place it on a new bottle.

Each subject completed ten trials, following steps 1-6.

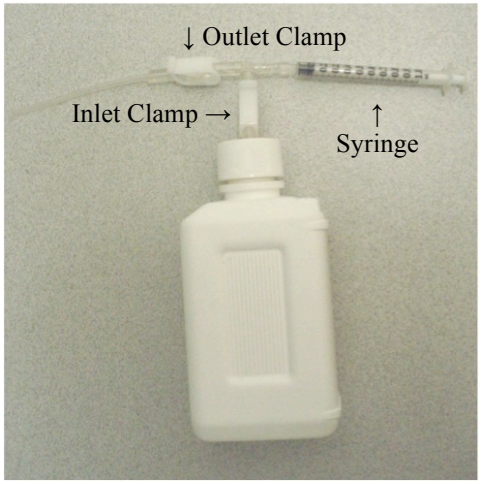


Fig. 3. Photograph of device.

## IV. Results

The final mixture of corn syrup and water contained 15.5% water by volume. The mixture had a viscosity of 419 cP.

Using a syringe, the average mass of 0.6 mL of the corn syrup/water mixture was 0.800 g (SD=0.008 g). This was used as the standard to compare all subsequent trials against. The overall accuracy of the device, summing the trials conducted by all four subjects, was very good. The average mass of 0.6 mL of mixture delivered by the device was 0.804 g (SD=0.008 g), constituting a 0.56% deviation from the standard. This percent error is well within the allowable error margin of 5%, according to the design constraints. To account for variability due to operation by different personnel, descriptive statistics were also obtained for individual subjects. Subject 1 obtained an average mass of 0.804 g (SD=0.006 g), which corresponds to a 0.56% deviation from the standard. Subject 2 yielded an average mass of 0.807 g (SD=0.007 g), which deviated by 0.94% from the standard. For Subject 3, the average mass of 0.6 mL of mixture was 0.801 g (SD=0.008 g), deviating by 0.14% from the standard. Finally, Subject 4 obtained an average mass of 0.804 g (SD=0.010 g), corresponding to a 0.60% deviation from the standard. The individual errors obtained by each subject were all less than 1%, which suggests that the device remains accurate even under variation in operation by different personnel. A summary of the accuracy testing results is shown in Fig. 4, and descriptive statistics are shown in Table I.

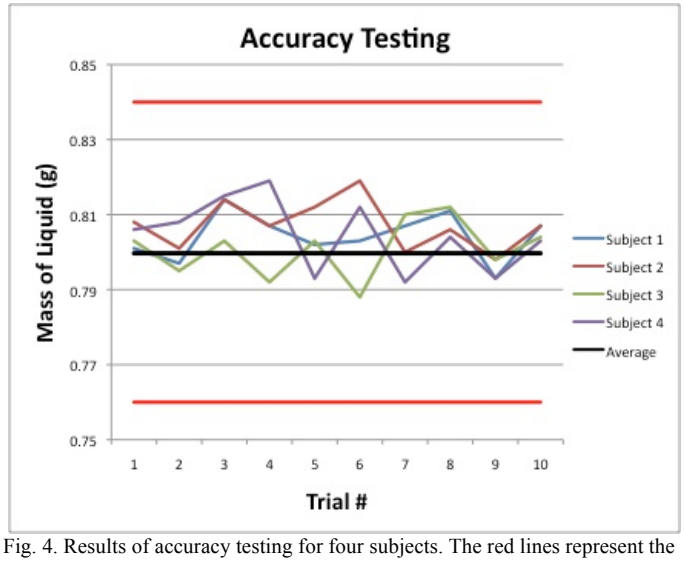


Fig. 4. Results of accuracy testing for four subjects. The red lines represent the 5% limit of accuracy required by EWH.

**TABLE 1**
SUMMARY OF TRIALS FOR EACH SUBJECT

| Subject | Average (g) | Standard deviation (g) | % Error |
|---|---|---|---|
| 1 | 0.804 | 0.006 | 0.56 |
| 2 | 0.807 | 0.007 | 0.94 |
| 3 | 0.801 | 0.008 | 0.14 |
| 4 | 0.804 | 0.010 | 0.60 |

## V. Discussion

The objective of this study was to develop and test a low-cost bottle-top dispenser for the Viramune® medicine, to be used in developing countries. The medicine is currently delivered and stored in oral dosing syringes, plastic bags, or recycled plastic bottles. This method is cumbersome because the medicine bottle has to be uncapped each time, which also exposes the medicine to an increased risk of contamination from the outside environment or unclean syringes. Wastage may also occur due to inaccurate methods of delivering the medicine. As a result, a more accurate, reliable, and sterile method of delivering the Viramune® doses is required.

The current device seeks to address this issue by using off-the-shelf materials that can be assembled to form a dispenser that is incorporated into the medicine bottle's cap. The device includes the use of two clamps which act as manually operated one-way valves to ensure unidirectional flow of medicine through the tubing. A syringe is used to measure out the desired dose and dispense it. Since assembly of the individual components is relatively simple and does not require additional tools (apart from drilling a hole in the bottle cap), the device can be distributed as a kit with detailed instructions to volunteers at Engineering World Health (EWH) for them to assemble at no extra cost. This would negate the manufacturing cost, ensuring that the device remains cheap so that it is affordable for widespread use in developing countries.

We were unable to obtain samples of the actual Viramune® medicine to carry out testing with, so we sought to derive our own analog with a similar viscosity. Viscosity was chosen as the most important parameter because we wanted to closely mimic the liquid's resistance to flow to see how it would affect the operation of our device. Through an experiment using Stokes' Law, we obtained a liquid with a viscosity of about 400 cP, which is similar to that of Viramune® [5]. This liquid was a mixture of corn syrup and water, containing 15.5% water by volume.

The liquid that we obtained was used to test the accuracy of our device. Using a total of forty trials, the device proved to be very accurate, deviating by 0.56% on average from the actual amount of liquid dispensed. Given that the design constraints require the device to be able to deliver (0.6 ± 0.03) mL of medicine, or within a 5% margin of error, our testing results show that the device meets the accuracy requirement.

Even though all the trials fell within the error margin, there was a trend across all four subjects showing that the amount dispensed by the device was slightly higher than the actual amount. Since only a limited number of trials were carried out, it is unclear whether this is due to random error or a systematic error caused by an inherent property of the device. Additional trials should be carried out by different personnel to ascertain whether this trend continues. If it does, the device might have to be calibrated to further improve its accuracy.

During the process of testing the device, we encountered some limitations. First, the reliability of the device over repeated usage was not addressed. The device had to be accurate for 400 doses, which corresponds to the entire volume of the Viramune® medicine bottle. However, we only tested the device over 40 trials, and although all of them produced very accurate results, we are not sure how they would be affected over repeated uses. Second, testing was not carried out with the actual Viramune® medicine. Although we synthesized a liquid with similar viscosity, it might not encompass all the fluid properties of the medicine (e.g., contact angle, surface tension) that might affect the testing procedure. Third, the long-term degradation of the materials used to construct the device has not been investigated. We have not tested the durability of the materials over prolonged use and/or storage, as well as under different climate conditions (since the climates in developing countries tend to be different from the climate in the United States). This could potentially lead to safety concerns if the materials used are unable to chemically withstand long-term, wear and tear.

Future research will seek to address the limitations mentioned and prepare the device components for assembly as a kit. Specifically, detailed instructions will be drawn up to educate volunteers on the proper assembly procedure for constructing the device from its component parts. Additionally, a video or instruction manual will be created to illustrate proper operation of the device.

## VI. Conclusion

We have developed a cost-effective bottle-top dispenser for Viramune®, an anti-HIV transmission medication. The device is simple to assemble and operate, and preliminary testing has shown that it is accurate to within 0.56% of the amount measured to be dispensed. The device can be packaged into a kit with detailed instructions for assembly, but further testing is first required to ascertain its reliability and durability.

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