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New Design for Prefilled Syringe

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Department of Biomedical Engineering

Honors Research Project

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The Honors College

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New Design for Prefilled Syringe

Stringent Syringes

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Final Report

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Abstract

Prefilled syringes are currently available as treatment options for individuals with diabetes, allergies, and other medical conditions mandating delivery of drugs by injection. However current prefilled syringes are often bulky, conspicuous, require specific storage conditions, and may prematurely deploy. Because of these factors, patients may be less compliant to treatment regimens and feel that their lifestyles and independence are inhibited. The newly designed prefilled syringe should be portable, practical, and easy-to-use. This project will be completed for Bionix Corporation located in Toledo, OH. Our contacts at this company are Mr. Ed Markewitz, Product Development Program Manager, and Mr. Cody Harder, Product Development Engineer. Cody Harder has served as our main contact throughout the duration of the project. The purpose of this project is to develop a prefilled syringe for Bionix that competes with currently available syringes. Currently, Bionix has no such product, as they mainly specialize in radiation therapy equipment. Bionix also has a Medical Technologies division that makes disposable medical instruments, and Bionix is looking for a syringe product that it may sell and distribute to drug companies. Through the design of the new prefilled syringe, Stringent Syringes intends to improve the quality of existing products from a patient perspective my enhancing ease of use and making the syringe less conspicuous than existing products. Stringent Syringes has completed this project by designing a compact and user-friendly prefilled syringe using a folding plunger to reduce the overall size of the device. The newly designed syringe is portable, able to withstand considerable mechanical forces, and meets the criteria established in the literature by users of prefilled syringes.

Introduction

Problem Statement

Prefilled syringes are currently available as treatment options for individuals with diabetes, allergies, and other medical conditions mandating delivery of drugs by injection. However, current prefilled syringes are often bulky, conspicuous, require specific storage conditions, and may prematurely deploy. Because of these factors, patients may be less compliant to treatment regimens and feel that their lifestyles and independence are inhibited. The newly designed prefilled syringe should be portable, practical, and easy-to-use.

Customer Information

This project will be completed for Bionix Corporation located in Toledo, OH. Our contacts at this company are Mr. Edward Markewitz, Product Development Program Manager, and Mr. Cody Harder, Product Development Engineer. Cody Harder has served as our main contact throughout the duration of the project.

Purpose of Project

The purpose of this project is to develop a prefilled syringe for Bionix that competes with currently available syringes. Currently, Bionix has no such product, as they mainly specialize in radiation therapy equipment. Bionix also has a Medical Technologies division that makes disposable medical instruments, and Bionix is looking for a syringe product that it may sell and distribute to drug companies. Through the design of the new prefilled syringe, Stringent Syringes intends to improve the quality of existing products from a patient perspective by enhancing ease of use and making the syringe less conspicuous than existing products.

Background Information

Prefilled syringes date back to the 1970s as injectable drug delivery devices in many applications, and the market is expected to grow 12.8% per year (Longworth, 2009; Soikes, 2009). More than 13 million injection devices are used daily for insulin alone (Gold, 2011). As a result, multiple prefilled injection devices exist for every-day use.

Although daily medication administration has become a minute part of everyday life for most patients, there is well-documented evidence suggesting that prefilled syringes have many unstated social implications that are important to patients. In order to maintain high rates of patient adherence to treatment regimens, patients must feel comfortable using their syringes (Anderson & Redondo, 2011). For example, diabetics who are expected to self-administer two doses of insulin daily may be less inclined to pursue this regulated treatment schedule if they feel uncomfortable or embarrassed to use their products. In addition, if syringes are user-friendly, administration of drugs may not require the assistance of caregivers for children or elderly individuals. In turn, self-confidence in patient self-administration will be improved. The physical appearance of syringes also influences use; much psychological research has been devoted to understanding a common fear of needles that affects many patients who require blood tests, infusions, or injections (Anderson & Redondo, 2011). One design aspect that has been largely ignored by many manufacturers of prefilled syringes is size and portability. A small, lightweight, and inconspicuous syringe is more likely to be carried by users (Anderson & Redondo, 2011). It also appears that patients prefer color-coded syringes that make dosing fast and simple (Anderson & Redondo, 2011). For those patients for whom the self-administration of drugs may be difficult, such as elderly individuals or patients with visual complications caused by diabetes, a large display or loud clicking noise may assist with accurate dosing (Antinori-Lent, 2012). These patient considerations must be made when designing a new device.

Objectives and Goals

Throughout the development process, Stringent Syringes achieved multiple goals. Within the team, we have sought to come prepared to weekly meetings, to complete literature searches, and to solve conflicts

in a professional manner while considering our customer's needs. We have considered our customers to be Bionix as the company who originally requested the novel design, primary users of prefilled syringes, healthcare personnel, caregivers, and military personnel. Stringent Syringes also aimed to keep in contact with Bionix throughout the process with regular meetings and updates.

The design process has required Stringent Syringes to determine various requirements for a new prefilled syringe design. The main objective has been to create an inconspicuous prefilled syringe that will be discrete and portable. Our designs have been oriented toward improving user confidence and treatment compliance. Functionally, the syringe should deploy easily, withstand mechanical forces required for injection, dispense the drug reliably, and have a compact design. On the material side, the syringe should be constructed from biocompatible materials that cause no allergic reactions or immune response. The materials should not absorb the drug, should be lightweight for transportation and easy use, and be able to withstand reasonable temperature changes in a typical living environment. FDA regulations have also been considered as a requirement.

Bionix has dictated few constraints and limitations on the design. They have not provided material constraints other than "FDA compliance," nor have they identified a specific injection site, customer, or disease treatment targets for the product. They are primarily interested in pursuing a device that will be appealing to drug companies as a novel, minimally-sized syringe.

Throughout the design process, different objectives and requirements were added to our original goals. Some of these features included manufacturing the syringe to include a minimal number of parts and inclusion of safety features to prevent malfunction or premature deployment.

Methods and Procedures

Stringent Syringes began its fall semester by compiling the prior knowledge of its members in order to gain a working definition of the problem at hand. Each member performed an independent literature search for a different facet of the project, and we merged these results in order to obtain a functional understanding of the project and its prerequisites. Upon our first meeting with our customer, we prepared a

series of preliminary questions to ask Bionix. We met with Mr. Edward Markewitz and Mr. Cody Harder, the Product Development Program Manager and a Product Development Engineer, respectively. This meeting was the first time that Bionix elucidated their expectations concerning our project, our final prototype device, and our team.

During this meeting, we specifically inquired if Bionix had any prefilled syringe products on the market as of present. They did not. This was Bionix's first investigation into developing a prefilled syringe product. Bionix requested that we make an appealing prefilled syringe design in hopes of ultimately adding the prefilled syringe to their product line. They briefly mentioned a foldable plunger design. We acknowledged that we had already considered this idea. Bionix stated that they had no specific medical need for which they were creating the syringe, but would like to design a product that would be popular based on total number of syringe uses. This request, in combination with our subsequent literature review, directed our decision to pursue an insulin delivery device.

A literature and patent search revealed that most user complaints with insulin delivery products are that they are difficult to use for patients with limited dexterity and that syringes are painful to use and oftentimes bulky, conspicuous, and inconvenient. In order to solve some of these patient-identified problems with syringes, we investigated alternative injection technologies, such as jet-stream injection and powder injection syringes. We also created a survey that we distributed to users of prefilled syringes and prefilled pens in order to understand the benefits and drawbacks of current devices. We believed that directly requesting this information from syringe and pen users was the most reliable way to design a desirable product. Table 1 provides a summary of the questions provided on the survey and of the percentage of surveyed individuals that responded "yes" to each question. Figure 1 is a bar chart summarizing the most prominent responses to our survey. These responses formed the basis of our subsequent additions to functional requirements in the spring.

We began the spring semester by meeting with Bionix over Skype to deliver a presentation which expressed our progress to-date. We agreed with Bionix to pursue a prefilled insulin syringe due to its popular and widespread usage. We also presented some basic sketches of designs we discussed the week

prior to this meeting. These designs included: 1. a syringe with telescoping plunger, 2. a syringe with a foldable plunger, 3. a syringe with an air pump, and 4. a syringe with spring pump, 5. a needleless syringe with an air pump, 6. a needleless syringe with a spring pump, and 7. a needleless syringe powered by pyrotechnics. During our meeting, Cody expressed his opinion that Bionix would prefer to keep the prefilled syringe as simple as possible, which ruled out further pursuit of a needleless injection system. Bionix also expressed that the syringe should not be reusable, but disposable; therefore, it was necessary that the device incorporate changeable dosing. We discussed that we would move forward with two of these ideas, the syringes with telescoping and foldable plungers. We then distributed different tasks among members of the group. During product development, we discovered a third low-cost, simple design. Thus, we drafted three basic syringe designs: 1. a syringe with a foldable plunger (Figure 2), 2. a syringe with a telescoping component (Figure 3), and 3. a syringe with a screw-on plunger (Figure 4).

Additional requirements were added to the models. These included criteria such as needle length and needle gauge. From our research, a needle length of 6 mm and a needle gauge of 30 were selected for use in the SolidWorks models (Syringe and Pen Needle Sizes, 2015). Similarly, we discussed that in order to accommodate the comfort of patients, we must consider a pointed or rounded barrel end in our design (Syringe and Pen Needle Sizes, 2015). Another consideration we decided to pursue is that insulin must be monitored to make sure it remains in solution (Storing Insulin and Prefilling Syringes, 2014).

At this point, Stringent Syringes was faced with a difficult design complication. We were trying to find a way to make a disposable syringe with varying insulin dosage volumes. These dosages changed for each customer and multiple times a day per customer. We looked at different options such as a single changeable cartridge to dispense varying amounts, different size cartridges, and multiple cartridges for a single dose. After further research into the specific insulin dosages, we realized that this field is has been thoroughly optimized for insulin dosages in other syringes such as the prefilled pens.

Later in the semester, Bionix suggested that we design the syringe for a “hypothetical drug X” (such as a vaccine) that would dispense a larger, consistent volume and also suggested that we avoid designing an insulin-specific syringe. From this point forward, insulin-specific delivery was not considered

in our device design. Rather, we moved forward by considering our device as a delivery vehicle for "hypothetical drug X." Stringent Syringes, along with Bionix, decided to evaluate our options between the folding and screw-on plunger designs and to choose one. We then decided to explore patents similar to the screw-on syringe to evaluate the similarities between those designs and ours. In doing so, we ruled out the screw-on design, and as a team, we decided to pursue the folding syringe design.

We completed a re-design of the folding syringe to incorporate the changes that would be needed to make this device applicable to "hypothetical drug X" instead of insulin. These changes included making the plunger fold into the finger holds on the syringe and increasing the syringe volume to hold a standard vaccine dosage. We designed the syringe with the intention of delivering a hypothetical vaccine due to Bionix's implication that our device may be good for vaccines that have a volume of about 3mL. We discussed other potential design improvements resulting in an addition of a safety feature: to have a ridge that allows the plunger to snap into the hold for a secure fit. This will decrease any risk of the syringe unfolding or deploying prematurely. With slight design changes, we reduced the overall number of parts for the device by discussing the possibility of molding the pins into another piece. Stringent Syringes presented the improved folding plunger syringe design to Bionix as shown in Figure 5. Bionix approved the design with the suggestion that we add a "step" piece to the syringe finger hold in order to prevent accidental deployment. We agreed to add this piece to the design and finalized the design in Figure 6 before prototyping.

We ordered a prototype of this design from Shapeways. The design was 3D printed from frosted ultra-detail plastic and was quickly delivered (less than two weeks). Upon initial inspection of the folding mechanism, our design successfully operated as intended. However, our prototype was too small. We then realized that our model's barrel diameter was only half of the intended barrel diameter. Figure 7 displays the new prototype we ordered with correct dimensions, requiring a slight redesign.

After the completion of the prototype, a notable patent was discovered. Previous patent searches for foldable syringes turned up some syringes with the needle and cap hinged and not the plunger (Patent No. US8038654B2, 2011), syringes with the body folding for drug loading (Patent No. US2871858A,

1959), and syringes with collapsible chambers that fold along specific lines (Patent No. CA1057150A1, 1979). One particular patent, "Hypodermic syringe with articulate plunger," came into question "This syringe looks similar in design with a folding plunger, but has several key differences. Mainly, the syringe does not have a quarter-lock mechanism to lock the plunger in place when it extends. When the plunger is folded upwards, the plunger starts to depress through the plunger, indicating drug release during the folding mechanism. The Stringent Syringes' design allows the plunger to be fully extended and depressed before drug delivery can ensue, similar to current syringes used on the market. We created a product more within the range of the user's comfort levels. Also, this articulate plunger design does not fold into the thumb grips but rather surpasses them. To lock the plunger, this syringe has a clamp fastened fully around the barrel, extending the overall size and limiting maneuverability. This syringe also folds the material itself instead of rotating around pins, creating a weakness in the system (Patent No. US4011868 A, 1977). Overall, Stringent Syringes notices the design similarity, but we believe our design to be a significant addition to the current market.

Manufacturing

Stringent Syringes did not have the funds or means to pursue practical manufacturing. However, the product was designed with future manufacturing in mind. The original designs for our product contained up to nine individual parts that had to be assembled into the final product. By incorporating the pins into the other components, we were able to decrease the total number of components down to seven. Fewer parts are typically easier for manufacturing. However, because the pins used in our design are small, it may be difficult to design a manufacturing process that can assemble the parts. Thus, the nine-component system may prove to be a more manufactural model. Additionally, in order to decrease costs, our current system used polyethylene for the incorporated pins. The mechanical stabilities of the pins and of the overall design could be improved by using stainless steel pins. However, stainless steel pins could only be incorporated by either 1) making the parts incorporating the pins out of stainless steel, or 2) increasing the total number of parts to nine.

Other considerations include the addition of the second cut under the finger grips. The symmetry on both sides of the syringe allows for easier manufacturing when the part is not directionally oriented. The parts were also designed in a fashion similar to syringes currently on the market. A manufacturer would make minimal changes to incorporate the folding plunger into the system.

Performance Testing

Functional Testing

Using our prototype, we confirmed that our folding mechanism works as designed. The plunger audibly clicks into the side of the syringe, and once the plunger is extended, the quarter lock turn locks the system in place before depression. The plunger depresses fully through the syringe barrel. We also confirmed that the dimensions were correct based on the volume the syringe could potentially hold, 3 mL for this particular design. However, the syringe dimensions could be adjusted for a wide range of volumes.

In Silico Mechanical Testing

Because the prototype could not be 3D printed using polyethylene due to material options through Shapeways and 3D printed models are known to be very brittle, we performed mechanical testing in SolidWorks. In order to develop our model, we assumed that we would be injecting patients with a volume of 3 mL. We assumed that the time for the injection to occur would take somewhere between 1.25 and 10 seconds. We also assumed a worst case scenario; the injection would be intravenous such that the pressure resisting the injection of fluid would be equal to blood pressure. The value used for standard blood pressure was assumed to be 120 mmHg, which is approximately 16 kPa. To calculate the pressure required to inject 3 mL of fluid within 1.25 seconds, we first calculated the necessary volumetric flow rate according to the equation:

$$Q_1 = V/t \qquad \textbf{(Eq. 1)}$$

where Q_1 is the volumetric flow rate (m^3/s) through the needle, V is the volume of the fluid to be injected (m^3), and t is the time required to inject (s). As stated above, we assumed that V was 3 mL and that t was

between 1.25 and 10 seconds. The volumetric flow rate through the needle (Q_1) is equal to the volumetric flow rate out of the syringe body (Q_2):

$$Q_1 = Q_2 \quad \textbf{(Eq. 2)}$$

The velocity of the fluid could then be calculated using the equation:

$$Q_2 = A_2 v_2 \quad \textbf{(Eq. 3)}$$

alternatively arranged as:

$$v_2 = \frac{Q_2}{A_2} \quad \textbf{(Eq. 4)}$$

where Q_2 is the volumetric flow rate out of the syringe body, A_2 is the cross sectional area of the syringe body, and v_2 is the straight-line velocity of the fluid out of the syringe body. Using the straight-line velocity of the fluid, we calculated the pressure required to move the fluid according to Bernoulli's Equation:

$$P_1 + \frac{1}{2}\rho v_1^2 + \rho g h_1 = P_2 + \frac{1}{2}\rho v_2^2 + \rho g h_2 \quad \textbf{(Eq. 5)}$$

where P_1 is the pressure at the outlet of the needle, P_2 is the pressure at the outlet of the syringe body, ρ is the density of blood (assumed to be 1035 kg/m^3), v_1 is the velocity of the fluid exiting the needle, v_2 is the velocity of the fluid exiting the syringe body, g is the gravitational constant 9.81 m/s^2, h_1 is the height of the needle, and h_2 is the height of the fluid in the syringe. The density of blood was used instead of the density of water because the density of blood is presumably closer to the density of injectables, which may contain proteins, cells, small molecules, or even drug delivery systems. By assuming that the syringe is held horizontally during the injection, $h_1 = h_2$, Eq. 5 simplifies to:

$$P_1 + \frac{1}{2}\rho v_1^2 = P_2 + \frac{1}{2}\rho v_2^2 \quad \textbf{(Eq. 6)}$$

Solving for P_1:

$$P_1 = P_2 + \frac{1}{2}\rho v_2^2 - \frac{1}{2}\rho v_1^2 \quad \textbf{(Eq. 7)}$$

Written alternatively as:

$$P_1 = P_2 + \frac{1}{2}\rho (v_2^2 - v_1^2) \quad \textbf{(Eq. 8)}$$

The results were calculated for times ranging from 1.25 to 10 seconds. The results are shown in Table 2 with pressures ranging from 0.13 – 7.58 MPa. The calculated pressures, in units of Pascals, were used in the SolidWorks simulation. The simulation was designed as follows: all parts of the syringe were assembled into an assembly file, and mates were added to align the parts in the correct order. The needle of the syringe was designed from AISI 321 Annealed Stainless Steel. The plunger was designed to be made from polyisoprene. All other components were designed from low density polyethylene. The mechanical properties for AISI 321 Annealed Stainless Steel are provided in SolidWorks. The mechanical properties of polyethylene and polyisoprene were defined manually. All mechanical properties used in the simulations are reproduced in Table 3.

The mechanical testing simulations were performed using the Simulation add-in within SolidWorks. To build the simulation, the syringe body grip and the top surface of the plunger shaft were "fixed" in space, which makes them rigid and unable to move or deform. These surfaces were chosen as the fixation points because they are the points at which the syringe will be held. Presumably, the pressure exerted by the human hand will limit movement at the top of the shaft and at the gripper. Pressures were then applied to all surfaces within the syringe body, according to the values provided in Table 1. Placements of the fixation surfaces and of the applied pressures are shown in Figure 8. A solid mesh based on curvature with four Jacobian points was applied to the body. Using that mesh, 108107 nodes were defined with 67221 connections. For a visualization of the meshing, please refer to Figure 9.

The simulations were run using different time parameters, and the minimum factor of safety was determined. A power regression was fit to the data, which had a R^2 coefficient of determination equal to 0.9997. As shown in Figure 10, the minimum factor of safety was 14. Using the regression, the time of injection required to reach a factor of safety of 2 was 0.447 seconds, and the time of injection required to reach a factor of safety of 1 was 0.313 seconds. These data suggest that, in order for our current design to fail, a patient with normal blood pressure would need to be injected with 3 mL of fluid within 313 milliseconds, an extremely fast injection rate.

To determine where the syringe is most likely to fail, the stress and strain intensities were calculated. As shown in Figure 11, the maximum stress occurs within the walls of the syringe body, indicating that the rupture of the syringe body would be one likely mode of failure. If higher pressures are required, the syringe body thickness could be increased to withstand the additional stresses. Stress is also relatively high within the core of the shaft. Importantly, most of the stress is carried by the core of the shaft and not by the shell. This means that the quarter locking system (which is relatively delicate) does not bare much of the stress and is therefore unlikely to be the cause of system failure. Stress risers are apparent in the corners of some of the notches cut for the quarter lock systems. Those risers could likely be decreased by rounding those corners.

The maximum strain intensity was also calculated, and it is displayed in Figure 12. The maximum strain occurs in the plunger, largely due to the fact that it is made from non-rigid polyisoprene. Polyisoprene was used in our design because it has been used elsewhere for plungers. Two design changes could dramatically decrease strain in the plunger. Firstly, the polyisoprene could be changed to a more rigid material, such as rubber, another commonly used plunger material. Secondly, the plunger could be made of a more rigid material, such as low density polyethylene, with a small band of polyisoprene providing the seal.

Future Directions

Due to time and funding constraints, Stringent Syringes could not continue testing beyond simulation and simple verification and validation testing. Assuming we had the opportunity, this syringe would be placed under a multitude of testing procedures before becoming a usable product. First, working prototypes would be created with ideal features such as the proper polymer, polyethylene, and the proper size needle. Other features could be added to the syringe in accordance with user and FDA standards such as proper labeling and graduation lines, color coordinated parts, and user instructions (Guidance for industry and FDA staff: Medical devices with sharps injury protection features, 2005).

To use this syringe, it would need to pass ISO testing. Specifically ISO/TC 76, used for all transfusion, infusion and injection, and blood processing equipment for medical and pharmaceutical use (ISO, 1951). ISO 11040 consists of various standards for prefilled syringes including glass cylinders, plungers, disks, and aluminum caps for dental local anesthetics. This standard also tests for glass barrels, plungers, and plastic barrels for injectable (ISO, 2015).

Other considerable standards include ISO 7886-1 for sterile hypodermic syringes for single use (ISO, 2015) and ISO 8537 for sterile single-use syringes, with or without needles, for insulin which may be useful if insulin is reconsidered (ISO, 2015).

Bionix is not an ISO testing facility, so if these tests were continued, the syringe could be sent to a testing company such as Smithers Pira who tests prefilled syringes using some of the previously mentioned ISO standards. Smithers Pira analyzes syringe dimensions including the barrel, stopper, plunger, label, and graduation lines. Syringe performance, integrity, and resistance is determined based on various forces to inject and break with the dosing accuracy and residual volume. System compatibility is determined based on the assembly and deploying mechanism and ease of use. Shelf-life is determined with real time and accelerated aging in environmental conditions. Finally different syringe transport situations are simulated for vibration, pressure, and temperature (SMITERS GROUP, 2015). Syringes that can withstand and perform adequately under these conditions are considered mechanically safe.

After mechanical testing was complete, the biological response would be analyzed with ISO 10993. In this standard evaluation, genotoxicity, carcinogenicity, and reproductive toxicity would be tested. Other tests would include interaction with blood, in vitro cytotoxicity such as viability and proliferation studies, local inflammatory effects, sterilization processes, degradation products, skin sensitivity, and systemic toxicity (ISO, 2015).

After the bench testing is completed, clinical studies would need to be completed. Because the components of the syringe that contact the patient and the drug are not novel, it might be possible to bypass much of the testing with an FDA 510k exemption.

Additional

Standardized functional requirements are displayed in Table 4, and constraints and limitations are displayed in Table 5.

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Appendix

Table 1: Results of surveys showing the percent of people surveyed responding yes to each question displayed.

Question	% Answering Yes
Do you use a prefilled syringe?	88.9
Is the prefilled syringe an autoinjector?	55.6
Do you ever need to travel with the syringe?	88.9
Have you encountered a time when it was difficult to bring your syringe?	44.4
Do you find your syringe is too big or not portable enough?	22.2
Is your syringe conspicuous or embarrassing to use?	55.6
Does your syringe require temperature specific environments?	100.0
Do you appreciate color-codes?	77.8
Does your syringe ever malfunction?	55.6
Does your syringe ever accidentally deploy?	11.1
Have you ever accidentally stuck yourself with the needle?	44.4
Does your syringe require lots of dexterity?	22.2
Do you ever struggle to deploy your syringe?	22.2
Does your syringe require a specific injection site?	88.9

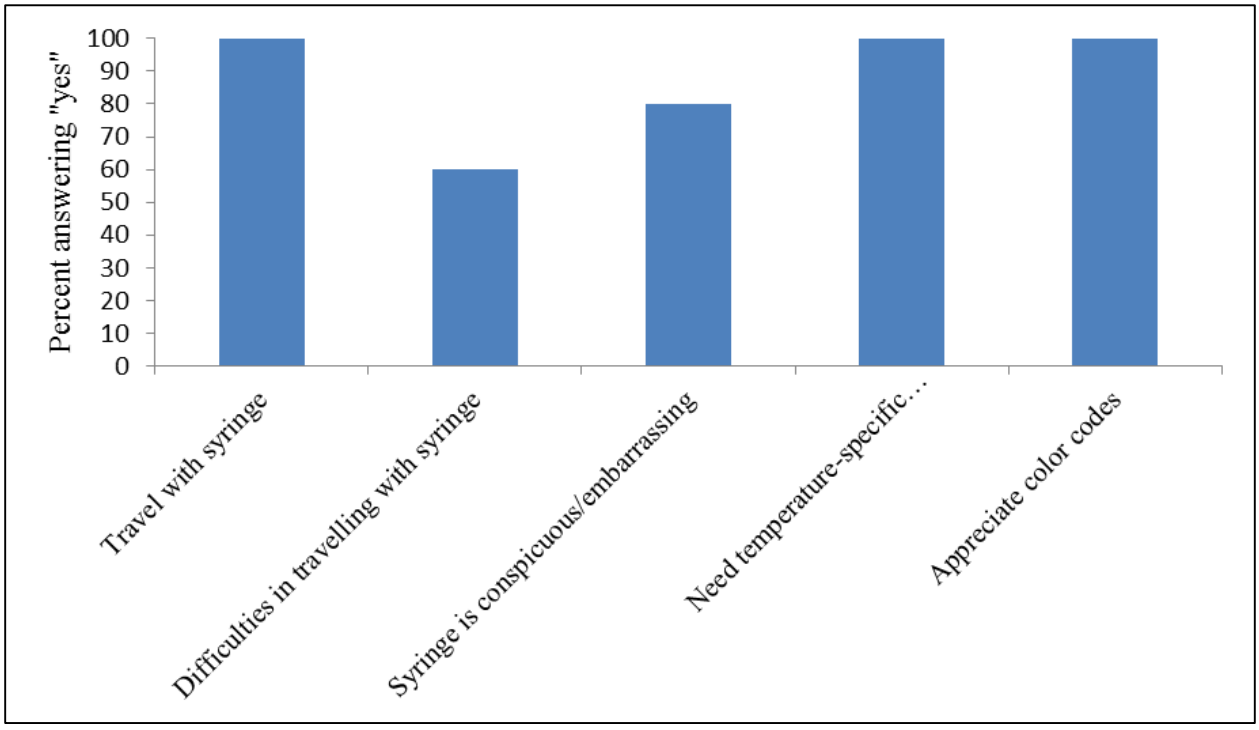

Figure 1: Bar chart showing the most prominent results from the prefilled syringe user survey.

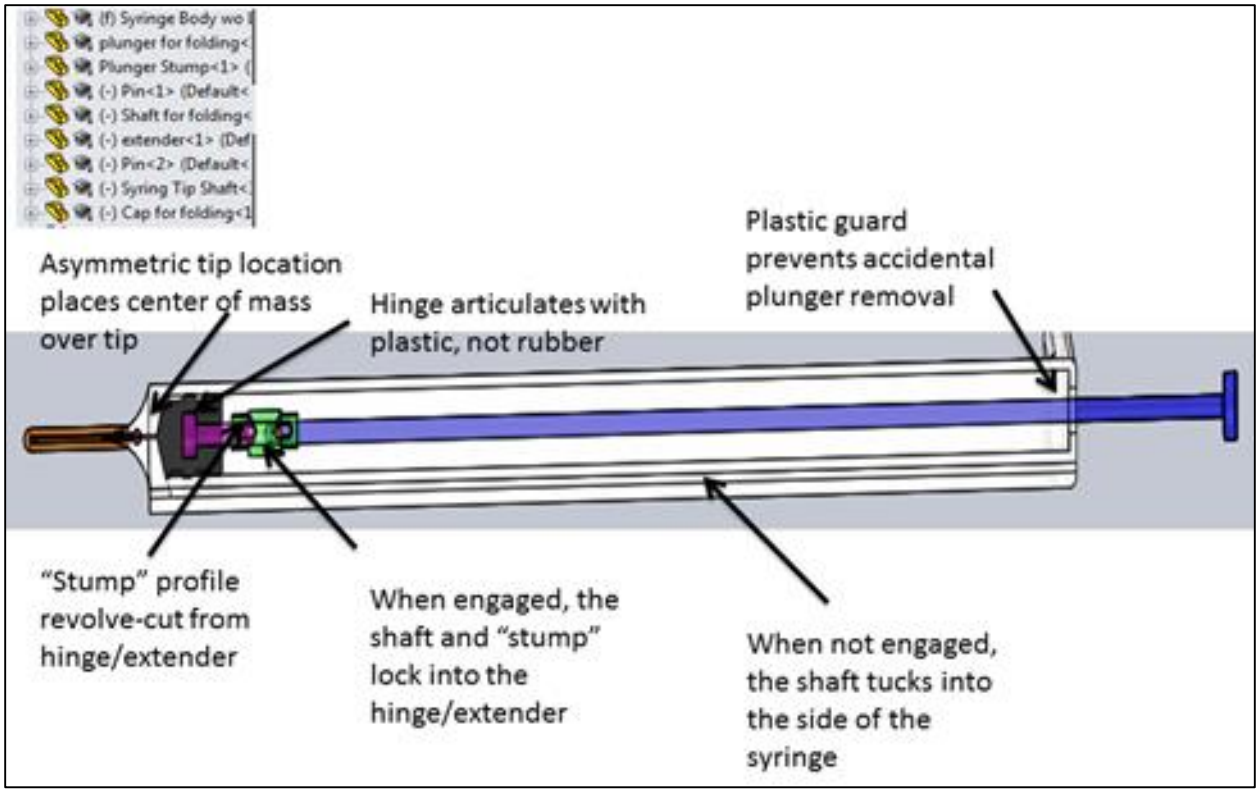

Figure 2: SolidWorks model showing the basic concept for our first design that was considered, the prefilled syringe with folding plunger.

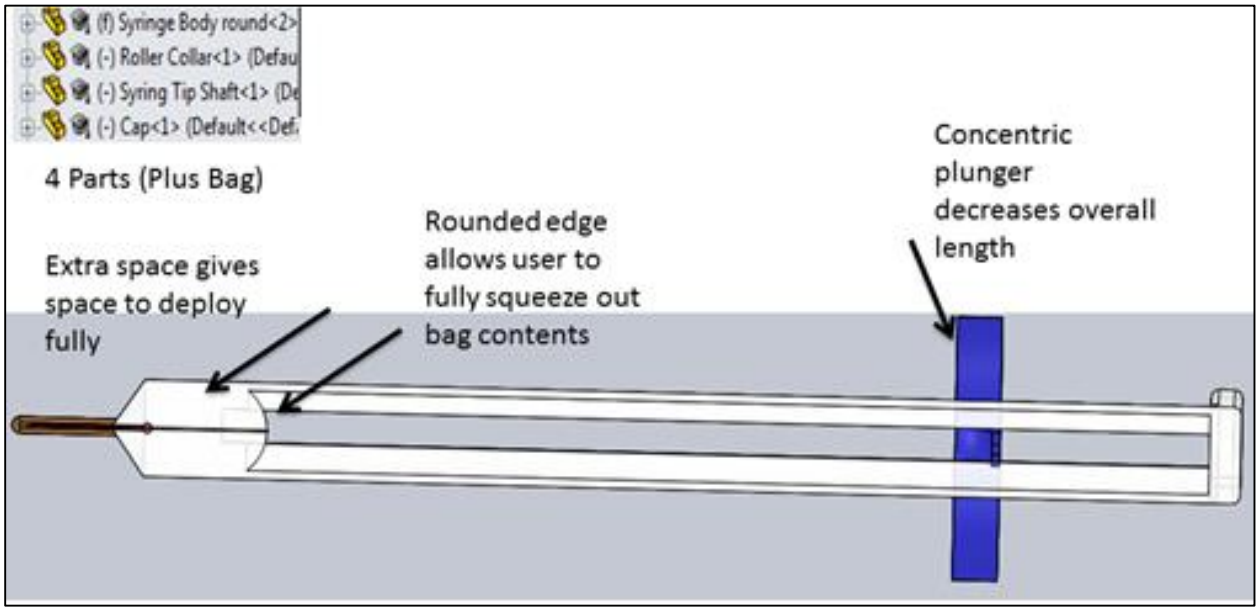

Figure 3: SolidWorks model showing the basic concept for the second design that was considered, a prefilled syringe with telescoping plunger component.

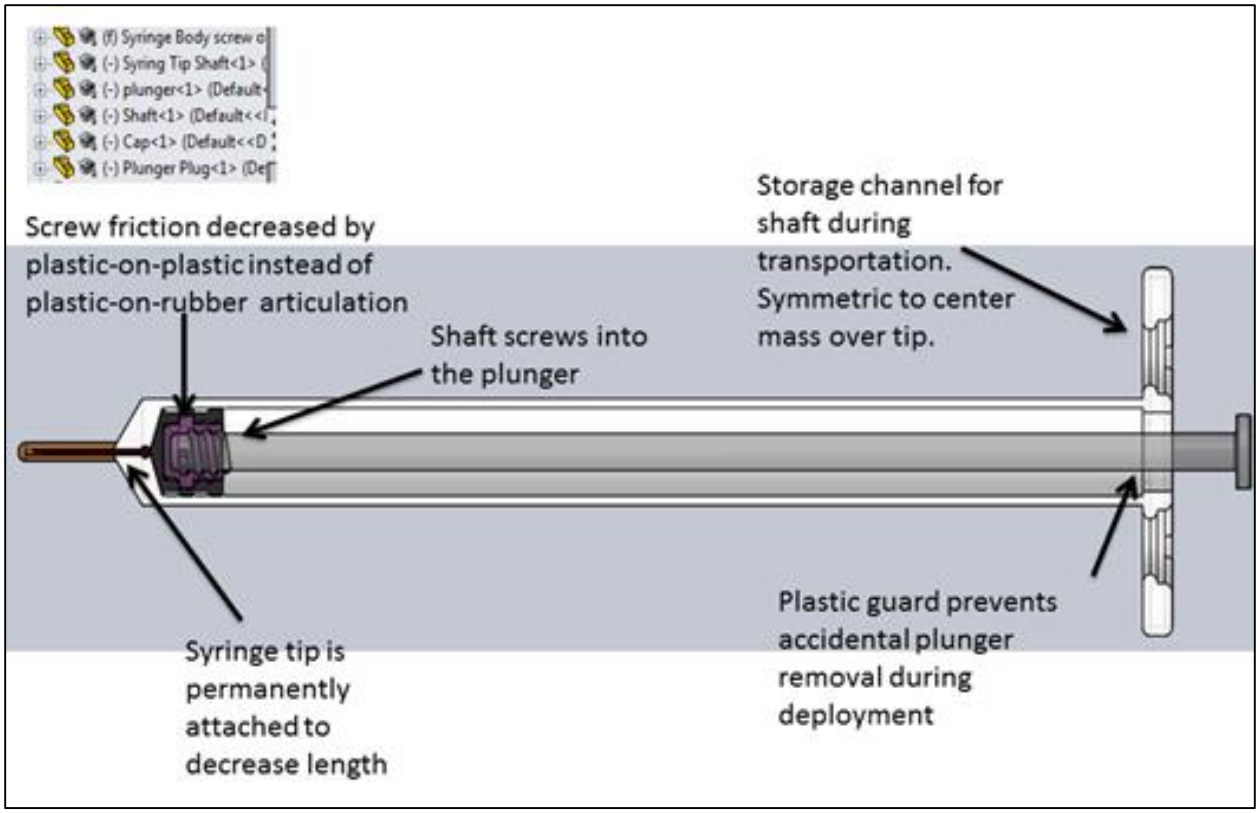

Figure 4: SolidWorks model showing the basic concept of the third design that was considered, a prefilled syringe with a separate screw-on plunger.

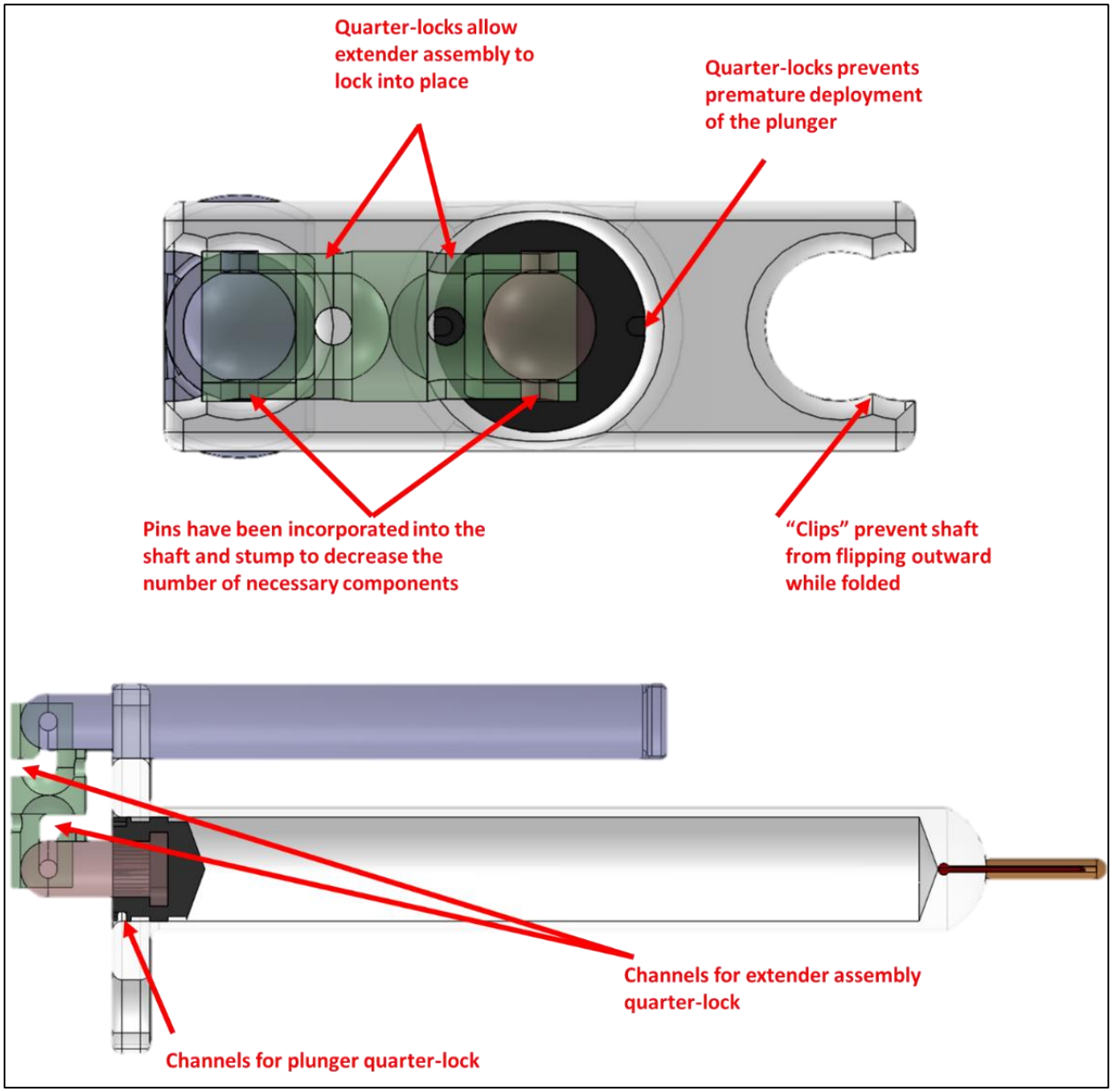

Figure 5: SolidWorks models showing two views of the preliminary folding syringe design with the added features of quarter-locks, the incorporation of pins, and clips to prevent premature syringe deployment.

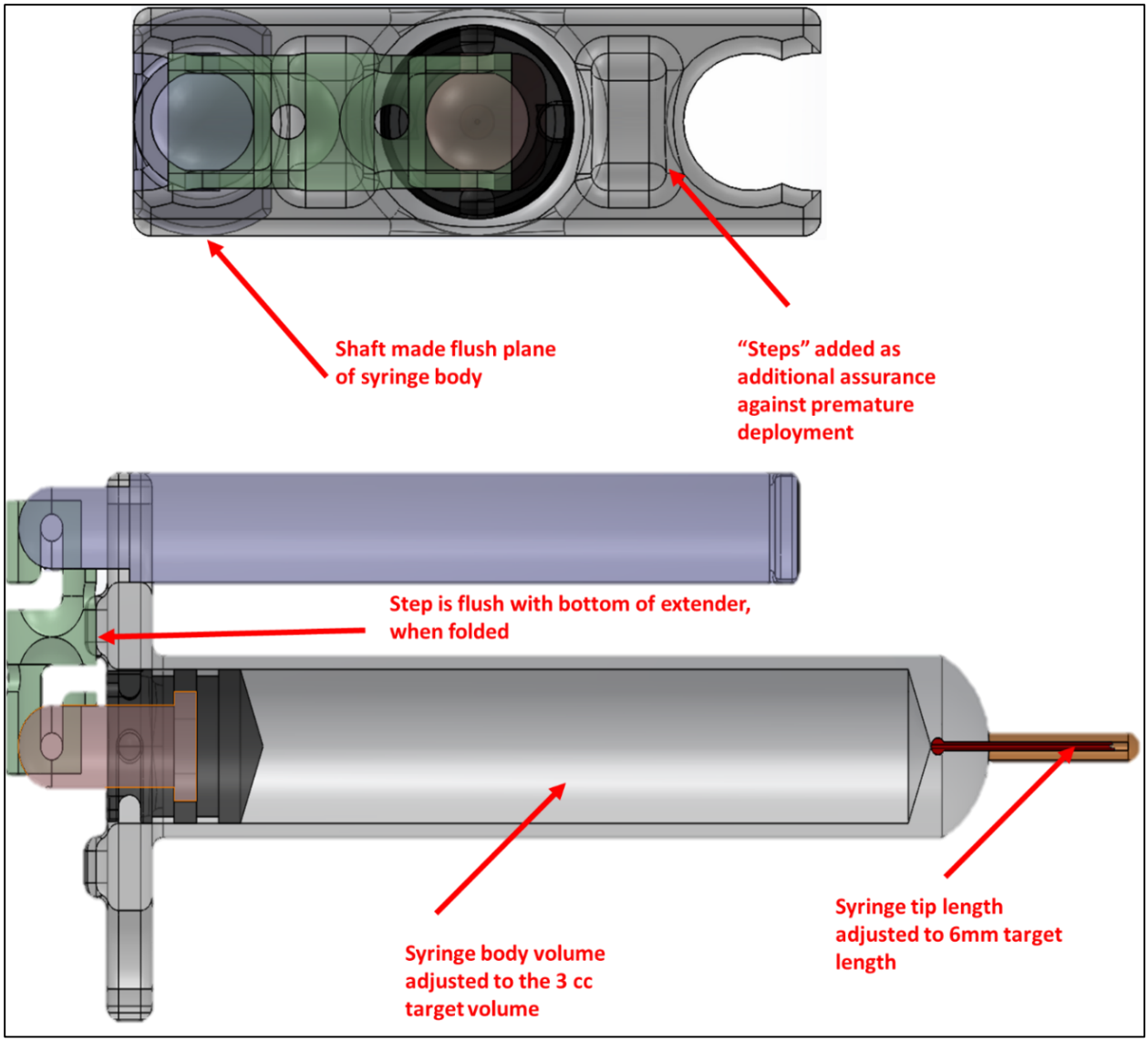

Figure 6: SolidWorks models showing first syringe prototype, including step to prevent premature deployment.

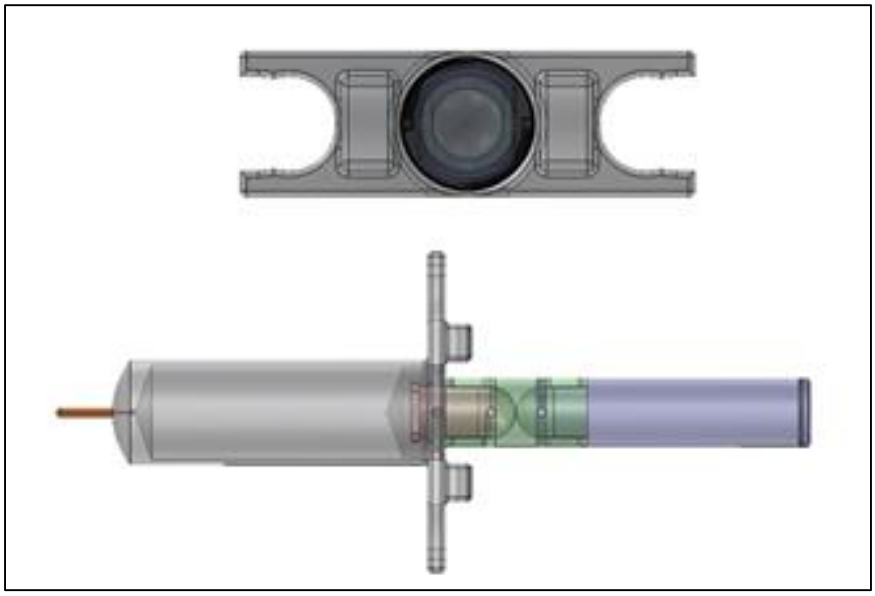

Figure 7: SolidWorks model showing the final prototype that was considered and ordered with correct dimensions.

Table 2: Pressure calculations used to determine appropriate forces that would be applied to syringe for mechanical simulations.

Time (s)	Q (mL/s)	P_1 (MPa)	P_1 (atm)
1.25	2.4	7.58	75.8
2.5	1.2	1.91	19.1
5	0.6	0.49	4.9
7.5	0.4	0.23	2.3
10	0.3	0.13	1.3

Table 3: Assumed mechanical properties that were used for SolidWorks simulations.

	AISI 321 Annealed Stainless Steel	Low-Density Polyethylene	Polyisoprene	Units
Elastic Modulus	1.93×10^{11}	3.00×10^{11}	1.15×10^{9}	Pa
Poisson's Ratio	0.27	0.45	0.50	(Unitless)
Shear Modulus	-	2.25×10^{11}	3.82×10^{8}	Pa
Mass Density	8000	919	906	kg/m^3
Tensile Strength	6.20×10^{8}	1.00×10^{10}	2.00×10^{10}	Pa
Compressive Strength	-	1.00×10^{10}	2.00×10^{10}	Pa
Yield Strength	2.34×10^{8}	1.75×10^{10}	5.00×10^{9}	Pa

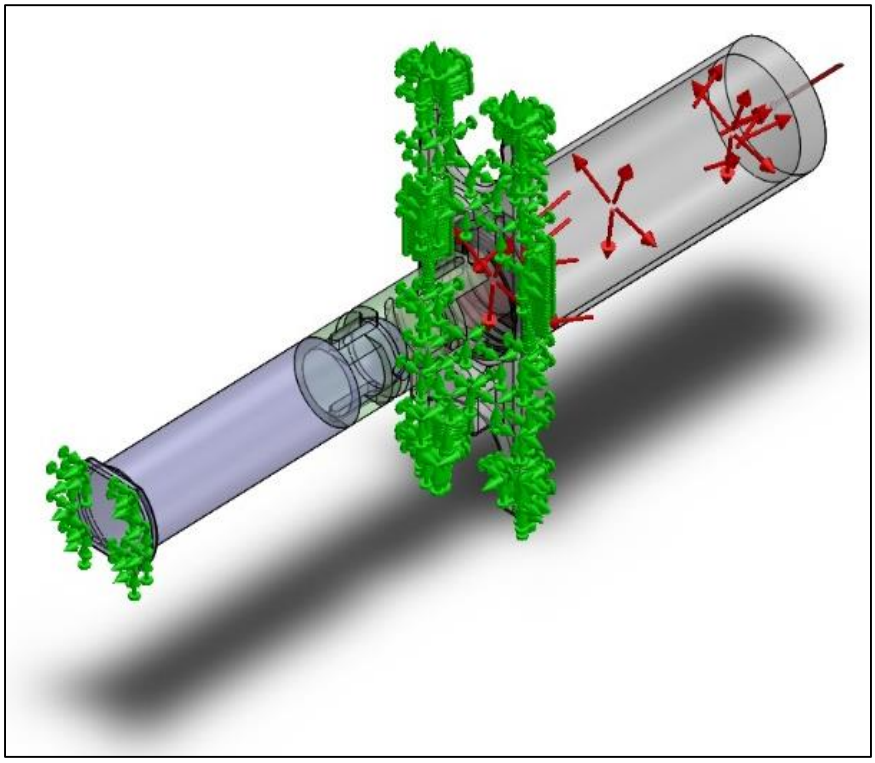

Figure 8: The assembly used for the mechanical testing is shown. The long, red arrows demonstrate where the pressures are begin applied. The clusters of short, green arrows demonstrated which faces were "fixed."

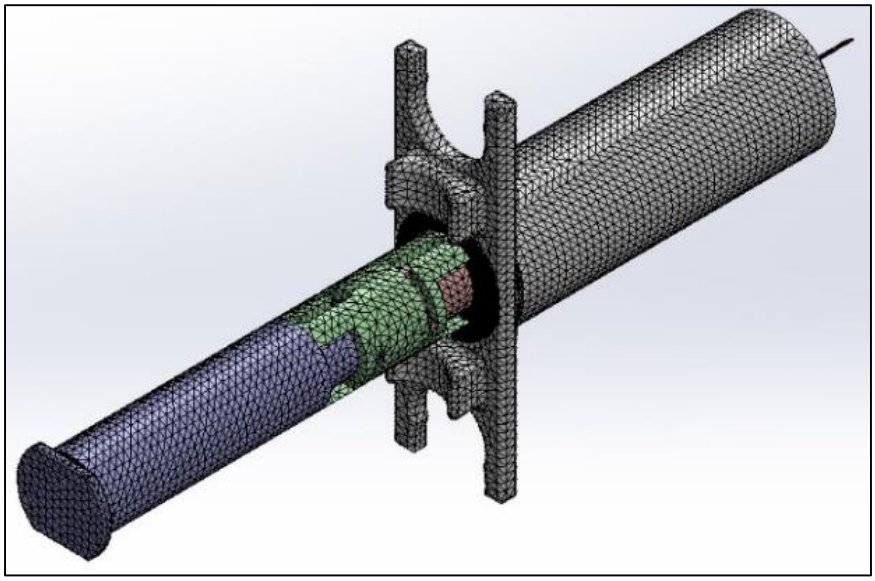

Figure 9: Visualization of the nodes used in the mechanical testing simulation.

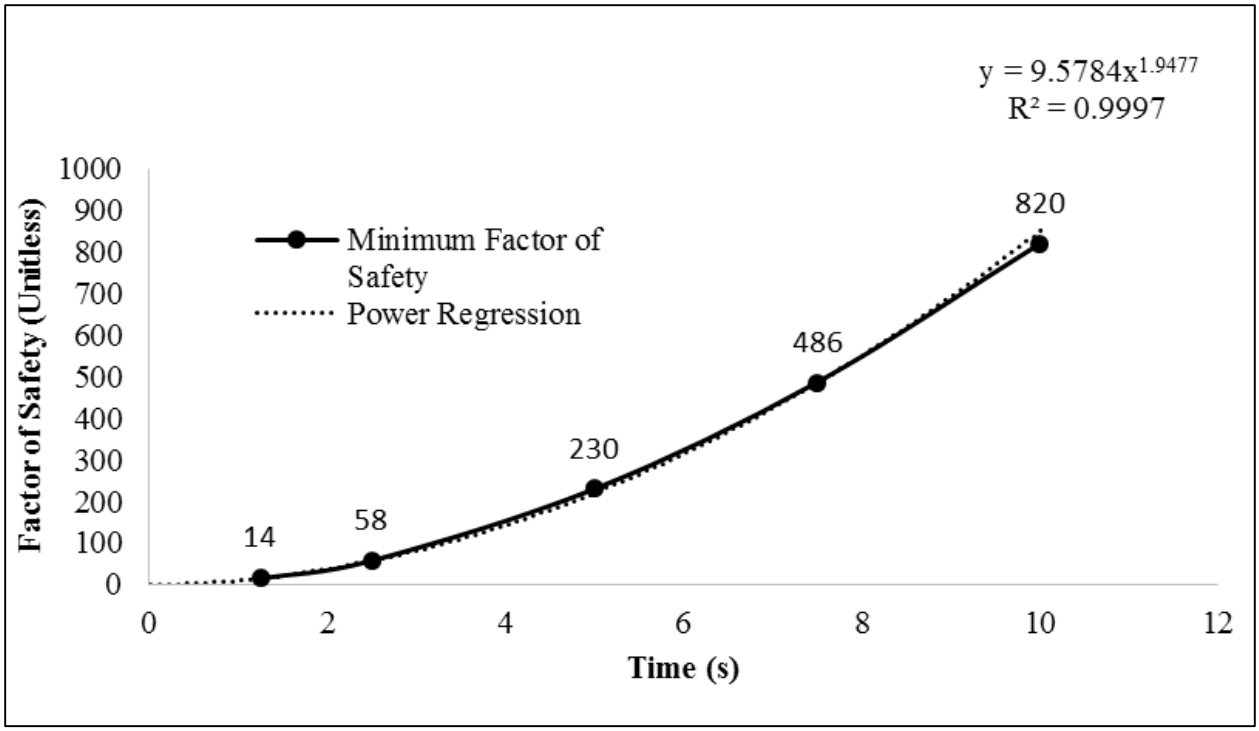

Figure 10: The factor of safety has been plotted as a function of the time that it takes to inject 3 mL of fluid into a patient with normal blood pressure. The minimum factor of safety was 14 at t = 1.25 seconds.

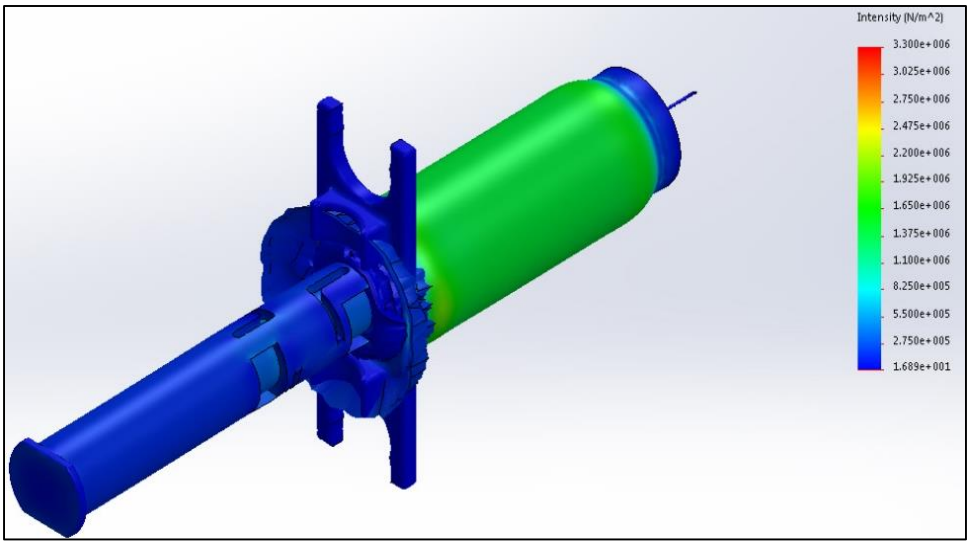

Figure 11: The maximum stresses occur along the syringe body (indicated by the green color). Additional high-stress areas occur along the center of the shaft and as stress concentrations in the corners of the notches in the shaft.

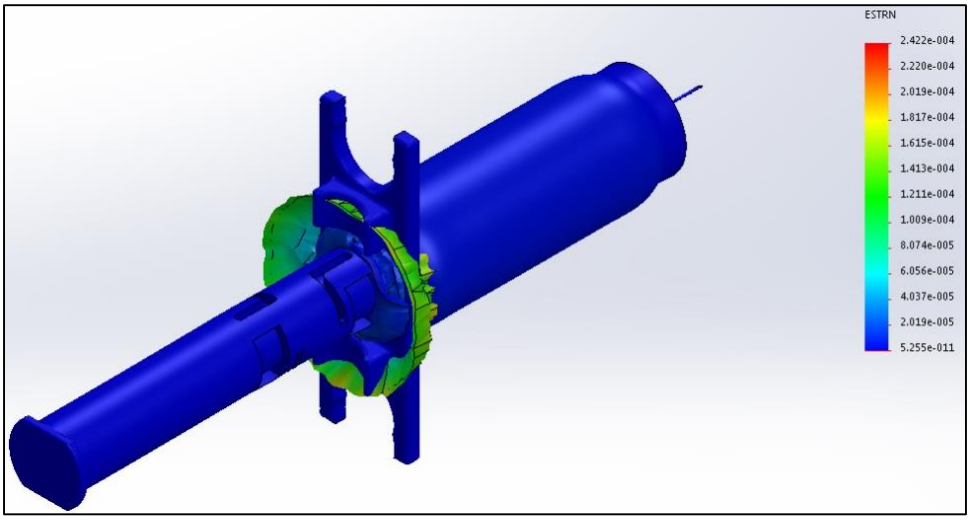

Figure 12: Strain intensities within the syringe assembly. The maximum strains occur primarily within the plunger.

Table 4: Functional requirements for the prefilled syringe. * Indicates that, although first determined to be a functional requirement during team brainstorming, this functional requirement was further considered by evaluating the results of our survey distributed to users of prefilled syringes.

Functional Requirement	Reasoning
Biocompatible material	3 members of the team have recently completed the Advanced Biomaterials course, which forced strategies for reducing foreign body response to our syringe and needle into our minds. If the syringe causes a negative response when in contact with the body, it cannot be used for its intended purpose.
Material does not absorb drugs	This requirement was also developed as a response to the above mentioned course. If the drugs absorb (stick to) the walls of the syringe body, it cannot be delivered through the needle.
Lightweight*	Our literature searches looked deeply into reasons as to why patients who use prefilled syringe products often stray from their treatment regimen. Difficulty carrying prefilled syringes on his or her person was a reason patients are dissatisfied with current products, and as a result we intend to account for this with our new design.
Withstand differences in storage temperature*	This requirement was developed in response to pursue an insulin delivery device. Insulin, and other drugs, often require refrigeration or specific storage temperatures. Therefore, the material used to create our device must be capable of being transported between these conditions.

Withstand mechanical forces without breaking	Varying amounts of force will be applied to the syringe, particularly the plunger and syringe body, during use. This force will be dependent on the context in which the syringe is used and the physique of the user. The syringe must withstand the largest amount of pressure that can reasonably be applied during use.
Reliable dosage*	With drugs such as insulin, which often require varying doses per user, it is important that the syringe is able to be tuned to deliver the correct amount.
Stores a consistent volume	Similar to dosing, the syringe must be able to store all of the required volume of drug without taking up unused space.
Dispenses a consistent volume	For a single-dosing syringe, it is crucial that the device dispenses the required amount of drug or vaccine.
Inconspicuous*	One prominent reason why patients do not always maintain their treatment as directed is that they are embarrassed or uncomfortable to use their prefilled syringe to administer drugs in public. We will make our syringe inconspicuous as to make users more comfortable.
Easy to dispose of	For a single-use syringe, the device must be easy to dispose of and not contain harmful components.
Compliant with regulations	Use and disposal of such syringe devices must comply with institutional regulations as well as those put forth by the FDA.
Design Feature	**Reasoning**
Molded pins	If pins are molded into other components, number of total parts decreases.
¼ turn locks	Including ¼ turn locks in the device ensures that the person completes this step before using the device, preventing accidental deployment.
Snap piece	In folded position, the plunger snaps into the syringe body for safe storage.

Step piece	Inclusion of the step piece, as requested by Bionix, prevents accidental deployment.

Table 5: Constraints and limitations for the prefilled syringe.

Customer Constraints	
Customer Constraint	**Reasoning**
Bionix	Bionix has requested that we develop this product and as a result we are constrained by the criteria they provide for this project.
Prefilled syringe users	People with diabetes, allergies, or other conditions mandating drug delivery via injection must be able to use this product safely and effectively.
Healthcare personnel	Doctors, nurses, pharmacists, and emergency medical technicians must know how to safely and effectively administer emergency medications and vaccinations using this product.
Parents and caregivers of children	People taking care of children, including teachers, babysitters, and school nurses, must be able to use this product in order to provide children with their medications.
Military personnel	Military personnel must be able to quickly administer medications in emergency situations.
Retirement and assisted living facility personnel	People caring for elderly individuals must be able to help them administer insulin and other drugs.
Design Constraints and Limitations	
Constraint/Limitation	**Reasoning**
Injection time	For use in emergency situations, we should design the device in such a way that drugs can be administered quickly.

Cost of device	The device must be as inexpensive as possible for the manufacturer(s) to make, drug companies to purchase for filling, and for customers to purchase.
Structure of device	The device must be lightweight to facilitate being easy to travel with, but must withstand pressure and temperature changes during travel, storage, and use.
Dispensation	The device must dispense the appropriate amount of drug for either a single-use or multiuse application.
Decreased plunger/button/trigger size	Bionix has requested that we decrease the overall size of the syringe and we decided this will be best accomplished by decreasing the size of the plunger/button/trigger.
Inconspicuous	The device should be inconspicuous to facilitate patient compliance.
Regulatory compliance	The device, its use, and its disposal must comply with both institutional and FDA regulations.
Color codes	For multiuse in insulin delivery applications, users reported via our survey to appreciate color coded dials to change the delivery.

Timeline

Stringent syringes hit many major milestones throughout the project from October 2014 through April 2015. Throughout the process, the notebook was continually assembled. The team information was developed during October. The literature was preliminarily reviewed during November. During this review, the definition of the problem, problem statement, objective tree, and functional requirements were determined and revised in November. The group developed a survey to help define customer opinions, an anonymous survey was conducted and analyzed starting in October and was continued through the end of February. Starting in January, Stringent Syringes began detailing design options. In January, the preliminary concepts were approved with Bionix, specific design parameters and materials were more thoroughly researched, SolidWorks models were created, and a final design concept was chosen. In February, testing methods and similar patents were researched for future use. By the middle of March, a prototype was

ordered from a 3D printing company, Shapeways. In tandem with the prototyping, simulation testing was performed on the finalized SolidWorks design. During this process, Stringent Syringes regularly met with Bionix every other week and we met with our advisor three times (corresponding with three progress reports). Table 6 shows Stringent Syringes' Gantt chart as a detailed schedule throughout the design process.

Table 6: Detailed timeline of Stringent Syringes design process as task list of the Gantt chart.

	Task	PIC (blank = all)	Start Date	Finish Date
1	Team Information		14-Oct-14	11-Nov-14
1.1	Team Introductions		14-Oct-14	11-Nov-14
1.2	Create team name		14-Oct-14	14-Oct-14
1.3	Decide that Doodle pools are best way to plan meeting days and times		14-Oct-14	14-Oct-14
1.4	Coordinate meeting times	Katie	11-Nov-14	11-Nov-14
1.5	Write team member expectations		20-Oct-14	6-Nov-14
1.6	Define team mission statement		20-Oct-14	6-Nov-14
1.7	Define group goals		20-Oct-14	6-Nov-14
2	Literature review of topic		16-Oct-14	21-Nov-14
2.1	Primary literature review		16-Oct-14	6-Nov-14
2.2	Independent literature mini review on cost of syringes	Katie	4-Nov-14	21-Nov-14
2.3	Independent literature mini review on design of syringes	Cale	4-Nov-14	21-Nov-14
2.4	Independent literature mini review on design of syringes	Sarah	4-Nov-14	21-Nov-14
2.5	Independent literature mini review on uses of syringes	Jen	4-Nov-14	21-Nov-14
3	Connect with Bionix		16-Oct-14	1-May-15
3.1	Come up with questions for customer		16-Oct-14	20-Oct-14
3.2	Preliminary literature search before meeting with customer		16-Oct-14	20-Oct-14
3.3	Meet with customer		20-Oct-14	20-Oct-14
3.4	Send 1st (fall) progress report to Bionix	Katie	6-Nov-14	5-Dec-14
3.5	Meet with Bionix every other week for updates (spring)		20-Jan-15	27-Apr-15

3.6	Send Spring Progress Report I	Sarah	2-Feb-15	6-Feb-15
3.7	Revise Gantt Chart for Progress Report II	Katie	23-Feb-15	27-Feb-15
3.8	Send Spring Progress Report II	Sarah and Katie	2-Mar-15	6-Mar-15
3.9	Revise Gantt Chart for Progress Report III	Katie	30-Mar-15	3-Apr-15
3.10	Send Spring Progress Report III	Cale	6-Apr-15	10-Apr-15
3.11	Send Final Report	Katie	27-Apr-15	1-May-15
4	Fall semester reports and notebook		13-Oct-14	2-Dec-14
4.1	Assemble preliminary notebooks and turn in to Dr. V.	Katie	13-Oct-14	6-Nov-14
4.2	Complete Fall Progress Report I	Cale	13-Oct-14	5-Dec-14
4.3	Assemble, complete, and turn in final fall project notebooks to Dr. V.	Sarah	14-Oct-14	2-Dec-14
5	Preliminary definition of problem and requirements		20-Oct-14	6-Nov-14
5.1	Develop preliminary definition of problems and requirements		20-Oct-14	6-Nov-14
5.2	Define problem statement		20-Oct-14	6-Nov-14
5.3	Develop preliminary objective tree		20-Oct-14	6-Nov-14
5.4	Develop preliminary list of functional requirements		20-Oct-14	6-Nov-14
6	Revise preliminary notebook		18-Nov-14	21-Nov-14
6.1	Revise functional requirements	Cale	18-Nov-14	21-Nov-14
6.2	Finalize objective tree	Sarah	18-Nov-14	21-Nov-14
6.3	Revise team member expectations	Katie	18-Nov-14	21-Nov-14
6.4	Revise agendas and minutes	Sarah	18-Nov-14	21-Nov-14
7	Customer survey		14-Oct-14	27-Feb-15
7.1	Create customer survey	Katie	14-Oct-14	13-Nov-14
7.2	Distribute customer survey (round 1)	Jen	13-Nov-14	28-Nov-14
7.3	Analyze results from customer survey	Sarah	28-Nov-14	2-Dec-14
7.4	Redistribute customer survey	Jen	20-Jan-15	24-Feb-15
7.5	Analyze final results from customer survey	Sarah	24-Feb-15	27-Feb-15
8	Define client and engineering constraints and limitations		29-Oct-14	2-Dec-14
9	Revise fall notebook		7-Jan-15	30-Jan-15
9.1	Determine spring meeting time for group	Katie	7-Jan-15	12-Jan-15

9.2	Determine spring meeting time for Bionix	Katie	7-Jan-15	12-Jan-15
9.3	Review notebook and report comments	Cale	13-Jan-15	13-Jan-15
9.4	Revise team member expectations	Katie	13-Jan-15	30-Jan-15
9.5	Revise agendas and minutes	Katie	13-Jan-15	30-Jan-15
9.6	Revise Gantt Chart for Spring Progress Report I	Katie	13-Jan-15	30-Jan-15
10	Develop prototype		13-Jan-15	20-Mar-15
10.1	Determine our design options for Bionix	Jen	13-Jan-15	13-Jan-15
10.2	Approve preliminary concepts with Bionix	Cale	13-Jan-15	20-Jan-15
10.3	Research specific design parameters and materials	Sarah and Katie	20-Jan-15	3-Feb-15
10.4	Develop SolidWorks models	Cale	20-Jan-15	3-Feb-15
10.5	Approve final concept with Bionix	Sarah	20-Jan-15	3-Feb-15
10.6	Research and develop testing methods	Sarah	3-Feb-15	3-Mar-15
10.7	Research ISO testing	Katie	10-Feb-15	17-Feb-15
10.8	Research similar patents	Sarah	10-Feb-15	17-Feb-15
10.9	Research prototyping companies	Jen	10-Feb-15	24-Feb-15
10.10	Finalize SolidWorks model with Bionix	Cale	3-Feb-15	17-Feb-15
10.11	Finalize SolidWorks model	Cale	3-Feb-15	24-Feb-15
10.12	Create prototype 1	Jen	24-Feb-15	14-Mar-15
10.13	Mechanical testing in SolidWorks	Cale	9-Mar-15	13-Mar-15
10.14	Revise prototype and order new one	Cale and Jen	17-Mar-15	31-Mar-15
10.15	Test the prototype	Katie and Sarah	31-Mar-15	10-Apr-15
10.16	Analyze test results	Katie	18-Mar-15	10-Apr-15
11	Spring semester reports and meetings		12-Jan-15	1-May-15
11.1	Submit Spring Progress Report I	Sarah	30-Jan-15	2-Feb-15
11.2	Progress Report Meeting I	All	2-Feb-15	6-Feb-15
11.3	Submit Spring Progress Report II	Jen	27-Feb-15	2-Mar-15
11.4	Progress Report Meeting II	All	2-Mar-15	6-Mar-15
11.5	Submit Spring Progress Report III	Cale	3-Apr-15	6-Apr-15
11.6	Progress Report Meeting III	All	6-Apr-15	10-Apr-15

11.7	Assemble and complete spring notebook (with fall notebook)	Katie	12-Jan-15	1-May-15
11.8	Prepare final presentation	All	8-Apr-15	1-May-15
11.9	Submit Final Progress Report, notebook, presentation, and team evaluations	Katie	27-Apr-15	1-May-15
12	Honors College deadlines		20-Mar-15	17-Apr-15
12.1	Submit full version of Honors Research Project Report to Sponsor	Katie	20-Mar-15	1-Apr-15
12.2	Respond to Sponsor revisions and edits		7-Apr-15	9-Apr-15
12.3	Submit full version of Honors Research Project Report to two Readers	Sarah	9-Apr-15	10-Apr-15
12.4	Respond to Readers revisions and edits		13-Apr-15	15-Apr-15
12.5	Obtain Sponsor and Readers signatures for the report	Jen	15-Apr-15	17-Apr-15
12.6	Submit the final version to the Department Chair for signature	Jen	15-Apr-15	16-Apr-15
12.7	Final submission of abstract and report to Honors College with one page summary of individual work	Cale	16-Apr-15	17-Apr-15

Budget

Our allotted budget was used to create the design prototypes. The prototype was determined a significant part of the process, allowing us to determine function and validation as well as demonstrate these features. Our design was sent to a 3D printing company, Shapeways, made out of ultra-detailed frosted plastic. Our first model was $29.06. Upon arrival, a dimension error was noted, corrected, and the model was reprinted with the same material. The second model was $39.64. Given these costs, we are well within our budget for this project.