A Modified Inhaler for Oral Vaccine Delivery

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A report detailing the prototyping and decision-making processes for creating the proposed oral vaccine delivery system.

Table of Contents

Executive Summary

Over the course of six months, the team was able to identify a market need, draft a number of possible solutions to address that need, select the most applicable design, and manufacture and test a number of different components in order to assess the functionality of such a device. Additionally, further work was done in assessing the production costs, life cycle assessments, and regulatory background regarding the proposed medical device and its status with regard to original intellectual property. As a result of all of this work, the team can successfully say that oral vaccine delivery systems like the one described in this report present a perfectly viable and painless alternative to traditional injection vaccines, while remaining safe, effective, and financially accessible. The team further believes that moving forward with the production process of this device would allow the company to profit from the tens of millions of Americans who refuse annual vaccinations due to fear of needles, while also increasing herd immunity and reducing needlestick injuries amongst healthcare workers and needle-based vaccine injuries amongst patients.

Mission Statement

Traditional injection vaccines are painful, scary, hard to transport, difficult to dispose of safely, and may not be suitable for people with certain bleeding disorders. Though the health effects conferred by traditional vaccines are desirable, their traditional route of administration has its flaws. Traditional injection vaccines are painful and frightening, so much so that approximately 16% of adult patients, 27% of hospital employees, and 18% of workers at long-term care facilities cite fear of needles as their reason for not getting the flu vaccine each year [1]. Further research also shows that needle phobia has more than tripled over the past 30 years, making it an increasingly modern problem [2].

Additionally, traditional injection vaccines can be difficult to dispose of safely. More than 1 billion needles are disposed of as sharps waste each year in the United States alone [3]. And each year, over 385,000 healthcare workers suffer accidental needlestick injuries [3]. The team believes that cutting down on sharps waste by transitioning away from standard vaccine administration technology could help to reduce that number by limiting the number of needles being added to waste streams each year.

Though some alternatives to the traditional needle-injection vaccine are currently available (like jet injection and intranasal spray vaccines) they remain expensive, invasive, uncomfortable, and incapable of self-administration, suggesting that there is still a need for additional products in this area to satisfy each of these concerns.

The target market for this device is the annual flu vaccination market, particularly focusing on marketing toward the 16% of adult Americans that cite fear of needles as their reason for refusing annual vaccinations. Additionally, the team believes this device may show promise in the field of disease eradication and disaster relief, as the device could be used to rapidly vaccinate larger groups of people when compared to traditional vaccines, making NGOs and international aid organizations a potential secondary market. Stakeholders would include vaccine manufacturers, public health experts and policymakers, local and regional health authorities, media representatives, and of course, customers from a range of demographics.

Through careful research, the team identified the following needs, ranked in order of importance, for the proposed device:

1. Safe and Effective Vaccine Administration
2. Painless Use
3. Extended Shelf Life
4. Easy to Use
5. Financially Accessible

The primary benefit of an orally inhalable vaccine delivery system would be increased vaccination rates, which would contribute greatly towards maintaining herd immunity in an era of anti-intellectualism and the rising tide of the anti-vaccination movement. Additional benefits include an increased and healthier lifespan for the consumer due to resistance to preventable diseases [4] (and increased productivity as a result [4]), the avoidance of needle-based vaccination injuries that cost billions of dollars every year [4], and the possibility of rapidly expanding disease eradication projects in the developing nations around the world [5].

The key business goals of this project are to capitalize on the fact that more than 33 million American adults cite their fear of needles as the reason for not getting the flu vaccine each year, and to increase public perception of the company through the device's waste-reduction efforts and support of disaster relief/disease eradication programs.

Some of the assumptions that the design team included throughout this process and in making this assessment include assuming a linearly decreasing pressure drop over the course of administering the multiple doses, assumptions around the manufacturing costs of certain materials, and assumptions relating to the aerosol dispersion mechanism of conventional asthma inhalers to that of the proposed design.

Some of the constraints or limitations identified during this project include the limit to a $200 budget, restrictions on the type of testing equipment and the times during which that equipment could be accessed, and the inability to gather in-person to assemble the individual components and test the performance as a singular device due to the COVID-19 virus.

Project Management Plan

When planning our production schedule, the team considered the time it would take to plan each prototype, collect the materials needed for building, build, test, and redesign each prototype. The team followed the course schedule given by the instructors, also taking into account the work done over the previous term. With a budget of only $200 and a lack of accessible lab space due to COVID-19, the team decided to focus primarily on mathematical and 3D computer models when developing the prototype of the device, meaning less time was spent on building the prototypes and more time was spent on development and testing.

Term Schedule

8 Jan - Project Prototyping and completion plans
13 Jan - Discuss manufacturing requirements
15 Jan - Manager Meeting
20 Jan - Discuss ethical considerations
22 Jan - Manager Meeting
27 Jan - Discuss intellectual property landscape
29 Jan - Manager Meeting
3 Feb - Economic analysis
5 Feb - Design Review Presentation
10 Feb - Work Session
17 Feb - Work Session
19 Feb - Manager Meeting
24 Feb - Work Session
26 Feb - Manager Meeting
3 Mar - Work Session
5 Mar - Manager Meetings
12 Mar - Final Design Reviews

The following Gantt Chart (Figure 1), shows the schedule of prototype development with corresponding class periods. The team planned carefully for the development of each prototype and was, therefore, able to stick to the schedule outlined in the chart. However, the testing and adjustment phases were intermixed at times, when adjustments that were made needed to be reevaluated. Throughout the term, the team generally split up tasks by prototype, with one person focusing on one aspect of the prototype at a time and reporting findings back to the team, allowing everyone to plan the next steps of development together.

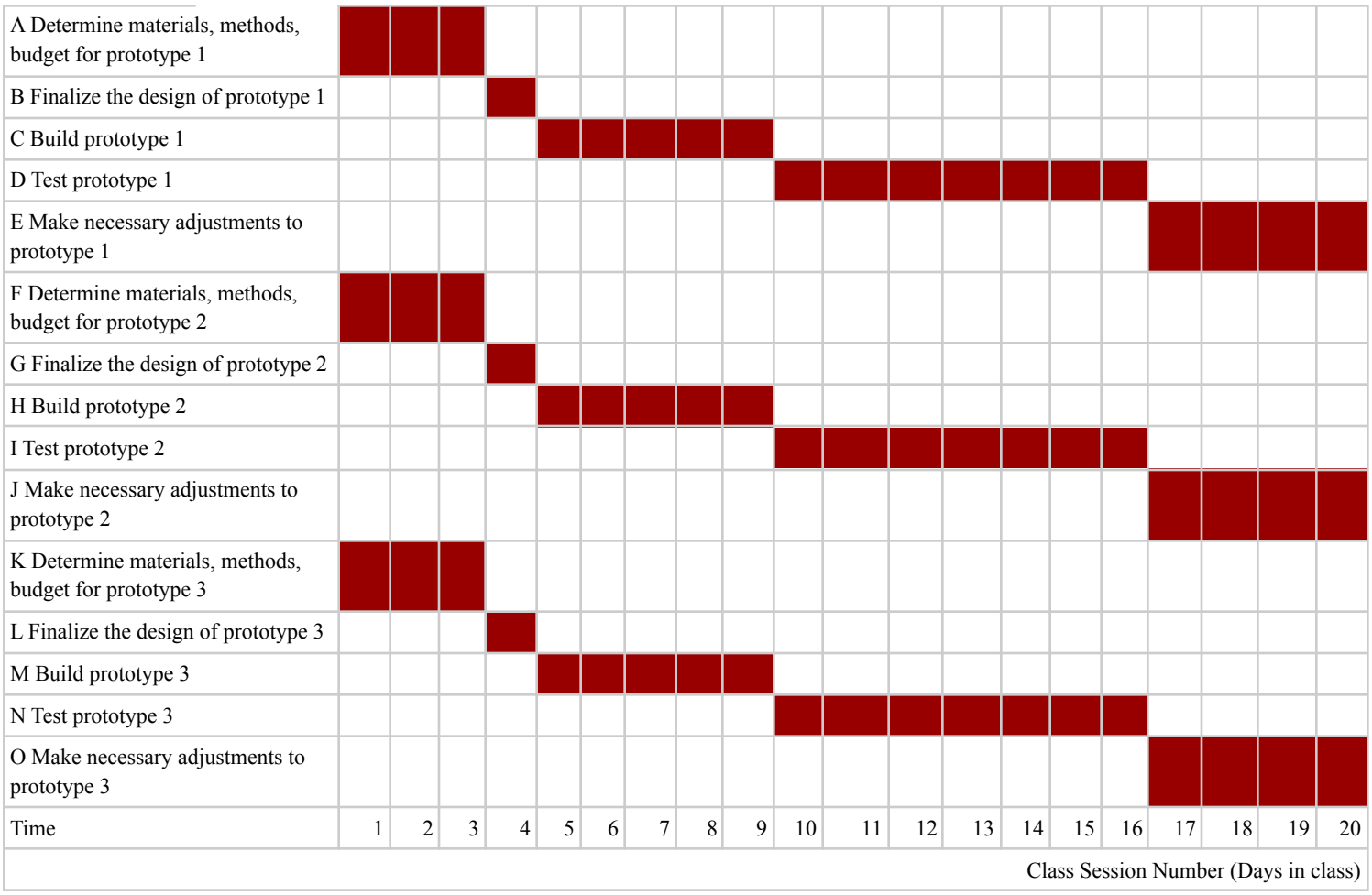

Figure 1: *Class session number in days vs prototype development*

Competitive Benchmarking

The two metrics suggested by Group 1 used to compare the product against potential competitors are vaccine type (liquid vs powdered) and the development of an autoclavable device, specifically, a powdered vaccine scheme and the development of an autoclave safe device are recommended. The following section details competing for products, recommendations, and final decisions of the team.

Compared with liquid vaccines, powdered vaccines would preclude the use of propellants by relying on patient inhalation for drug release [6]. Some data suggests that up to 50% drug deposition can be achieved using this method, reducing the amount of drug needed to properly vaccinate a patient [7]. However, data also suggests that children under the age of 8 have distinct difficulties using this method. If a powdered dose inhaler is not feasible, there is a more eco-friendly propellant known as Zephex 152a which was developed by Koura to reduce the carbon footprint of inhalers by up to 90% [8]. Due to the difficulties associated with the production and modeling of dry-powdered vaccines, as well as the lack of accessibility for young

children, a demographic especially endangered by the influenza virus, the group chose to use a liquid vaccine formulation, meaning that the recommended Zephex 152a propellant may be used as an alternative to HFA propellant.

An autoclave safe inhaler could prevent the necessity of complete teardown before sterilization or disposal of the device. Potential material choices are stainless steel, polypropylene, or polycarbonate. Stainless steel would make the most durable and environmentally friendly device, but would also be the most expensive. This method also requires clinics to have access to an autoclave, which may not be feasible. Furthermore, this method would require autoclave safe vaccine canisters, adding to the design burden on the team. Due to the costs and environmental impacts associated with autoclavable materials, the team decided against this recommendation, opting instead for a cellulose-based polymer -- a cheap and eco-friendly alternative -- and supplying single-use alcohol wipes to sterilize the mouthpiece before use. Disposable single-use plastic sleeves preventing contact between the product and the patient may also be an option, although the environmental impact and cost would be higher.

Metrics and Final Specifications

Initially, the needs for a vaccination process were identified and ranked based on importance. First, the vaccine needed to provide an immunological response, in other words, it must be effective, then the process of delivering the vaccine needs to be safe for both the healthcare professional and for the patient. The vaccine must also be painless and have a longer shelf life, and the device must be intuitive and easy to use. And all these must be achieved without compromising the financial aspect of the product, so it can have a reasonable price for the final customer. Then, the metrics were defined and assigned to the needs they satisfied, and some of the metrics identified and matched with multiple needs. Then a table of Metric x Needs (Table1) was created.

Metric → Need ↓	1 WBC Count/ antibody tests	2 Risk of misuse	3 Pain level	4 Temp of storage req.s	5 Mass, size	6 Amt. of add. training req'd	7 Cost of Production
1 Immune Boost	X						
2 Safe	X	X		X		X	
3 Painless		X	X				
4 Long Shelf Life				X	X		

5 Easy to Use		X	X			X	
6 Financially Accessible		X		X	X	X	X

Table 1: Metric and Needs table.

Design Solution Concepts Considered and Concept Selection

Concept → Need ↓	Inhalable Vaccine	Microneedle Patch	Edible Vaccine
1 Immune Boost	X	X	X
2 Safe	X	X	X
3 Painless	X	X	X
4 Long Shelf Life	X		
5 Easy to Use	X	X	X
6 Financially Accessible	X	X	

Table 2: Concept Selection matrix we used to consider which solution concept to select based on needs

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The table above shows the selection matrix we used to determine which concept we would move forward with depending on how the concept met the needs we outlined. We had to thoroughly consider what the shelf-life of the vaccine alternatives would be and how much it would cost to produce them and if they would be financially accessible by most people. We discussed how each concept addressed these needs and where they were lacking in order to get a clear idea of how we could further our concept into a model. Using feedback from the class and professors as well we determined that the inhalable vaccine had the most promise because it met most of the needs and had the potential to go in more than one direction as a model.

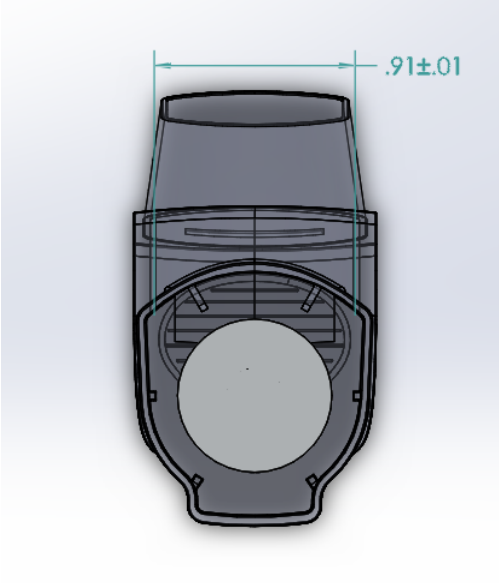
Thinking about how the product was going to be made, what materials would be used, and what mathematical models were needed to describe the mechanisms and details of our potential product really solidified the concept of inhalable vaccines for us. Edible vaccines proved difficult to maintain at the ideal temperature and were very costly. The microneedle patch vaccine

concept was going to be pursued by another group but we also thought that it was very dependent on the patient or user and the pressure they applied to the patch to deliver the microneedles effectively. We decided on modeling our inhalable vaccine after an asthma inhaler with changes made to the size and mechanism of the canister to accommodate for the difference in the drug. These differences and the way we could visualize the product made us confident in our choice of concept.

Final Project Concept

The final product would weigh approximately 25g, be about 3 inches tall, two inches long, and about an inch wide. The product is composed of a canister of the specified proportions containing the ingredients outlined in the preliminary patent portion of the report and a cellulose-polymer shell designed to be held comfortably with one hand with an integrated atomizer.

The .08 inch diameter canister tip shown in figure 3 is designed to fit into the atomizer pictured inside the shell in figure 4 (further pictured in Appendix Figure 1), where it must be pressed down to be administered. The canister will fit in the shell through the opening in the top of the shell, which is hollow. The shell (Figure 4) provides stability for the canister and protection to the internal mechanism while allowing the user to administer the vaccine with one hand. The nozzle also pictured in figure 4 is appropriately sized at .3 mm in order to produce our desired droplet size. Additionally, Appendix Figure 2 shows the 3D PLA prototype developed by the group.



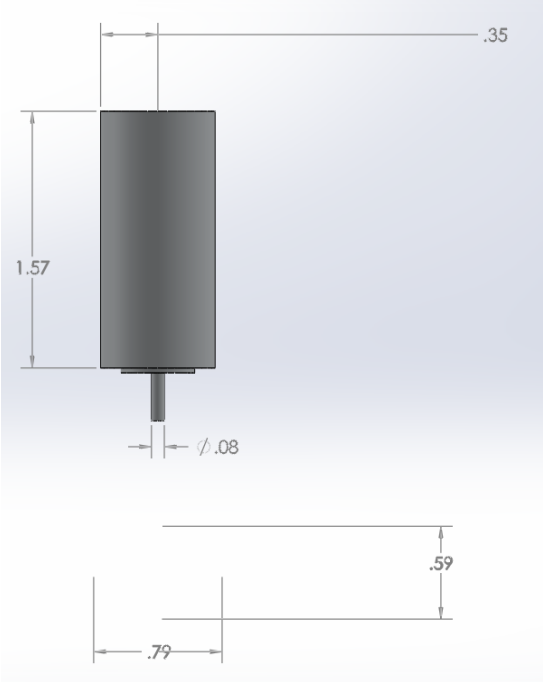


Figure 2: *Canister and shell with measurement of mouthpiece opening in inches*

Figure 3: *Canister with all relevant measurements in inches*

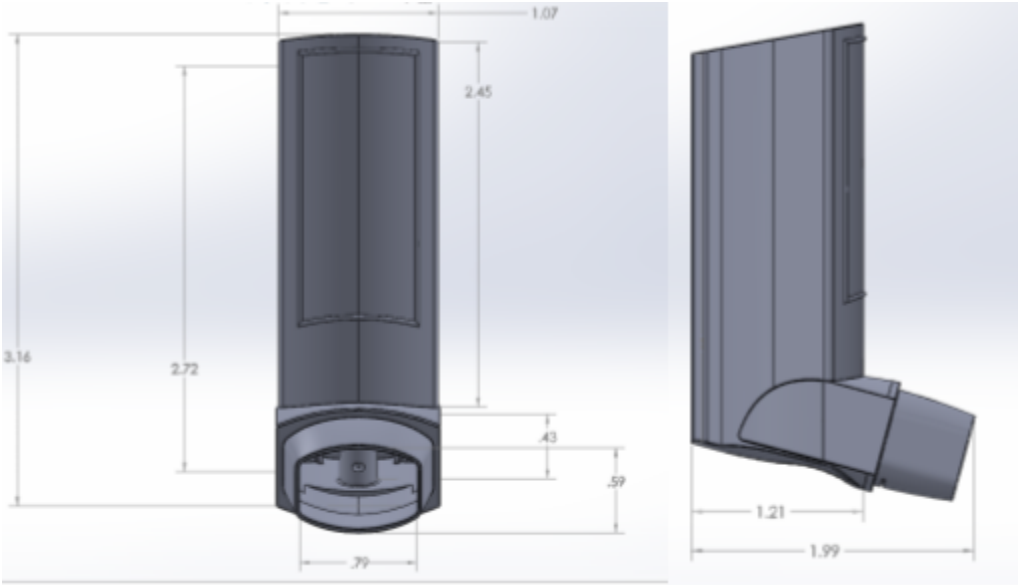


Figure 4: *Shell and integrated actuator with all relevant measurements in inches.*

The vaccine is administered by the patient fully exhaling and then depressing the canister into the actuator while inhaling with their lips fully sealed around the mouthpiece. When depressed, the canister dispenses the liquid formulation of the vaccine and the pressurized propellant into the chamber of the actuator, creating a mist of microscopic droplets and gas that is inhaled by the patient.

Engineering Analysis of Design/Prototyping Efforts

Model 1: The Canister

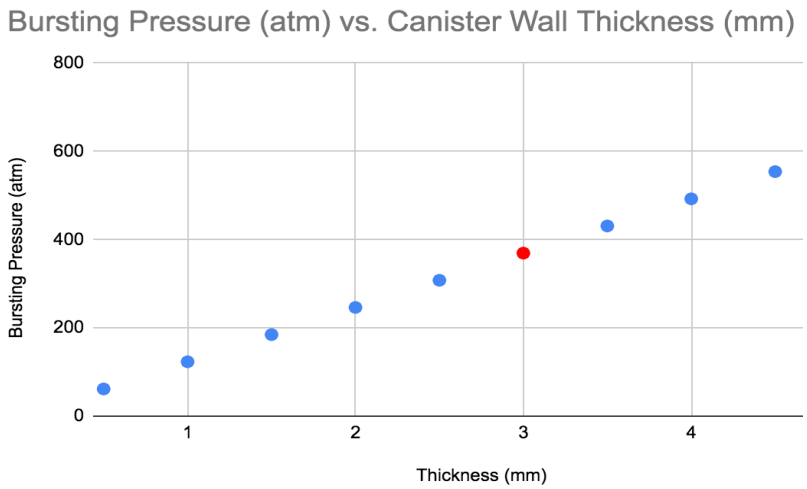


Figure 5: *Calculating the bursting pressure of an aluminum canister based on its thickness, using Barlow's Law.*

The team began working on the first model, the canister model, by determining the maximum amount of internal pressure the canister could withstand based on its thickness, as according to Barlow's Formula, listed here below:

$$P = \frac{2ST}{(OD)*(SF)}$$

Where P is the internal pressure (psi), S is the material strength/tensile yield strength (psi), T is the pipe wall thickness (in), OD is the pipe external diameter (in), and SF is the safety factor (which is 1.5 for general calculations, or 1 when finding the bursting pressure, as was done). We then substituted in our appropriate values to determine the bursting pressure and converted the final units of psi to atm.

$$\frac{2*(40{,}000psi)*(0.125in)}{(2.03in)*(1)} = P = 4926.108psi = 335.2atm$$

This means that the proposed 10mL canister, being 4cm high and having a radius of 0.89cm and a thickness of 3mm, should be able to withstand up to 335 atmospheres of pressure before bursting or experiencing permanent deformations. At these dimensions, it should also fit perfectly into the proposed shell geometry.

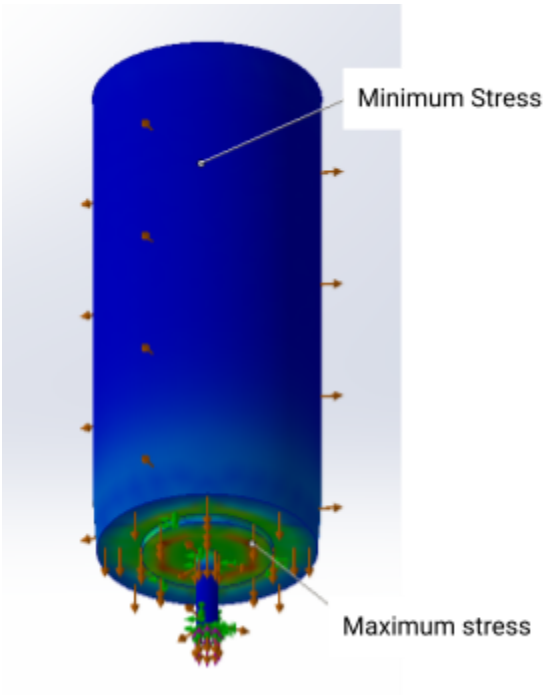


Figure 6: *Stress Profile of Pressurized Canister*

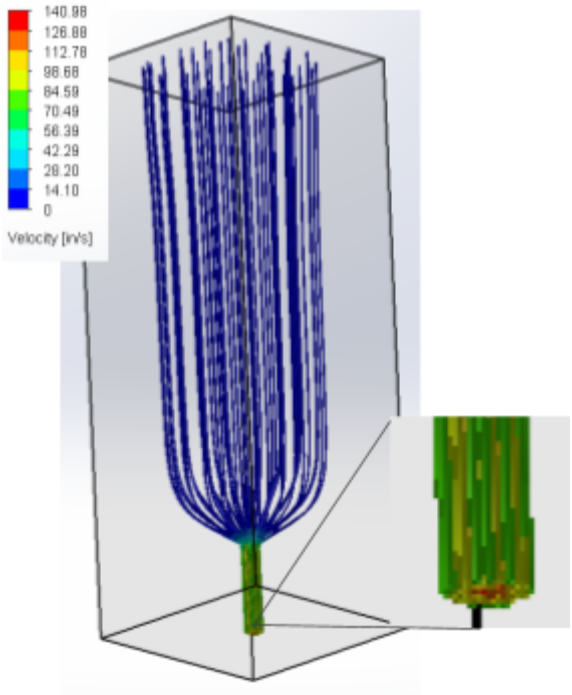


Figure 7: *Velocity profile of the first administered dose*

The figures above are stress and velocity profiles of the proposed canister, as generated by COMSOL.

On the left, Figure 6 shows that the canister is able to safely contain the vaccine and propellant mixture at all tested internal pressures, which ranged from 1-300 standard atmospheres of pressure. This proves that the proposed design will not burst or cause any damage during administration, thus ensuring safety for the consumers.

On the right, Figure 7 shows the velocity profile of the first of 15 administered doses. Since this is the dose that will be administered at the highest pressure, this is the one that is most critical to ensure safe administration. As one can see, the velocity is low throughout the canister until it reaches the actuator, where it increases but remains at a safe and usable point throughout the short time that it is activated.

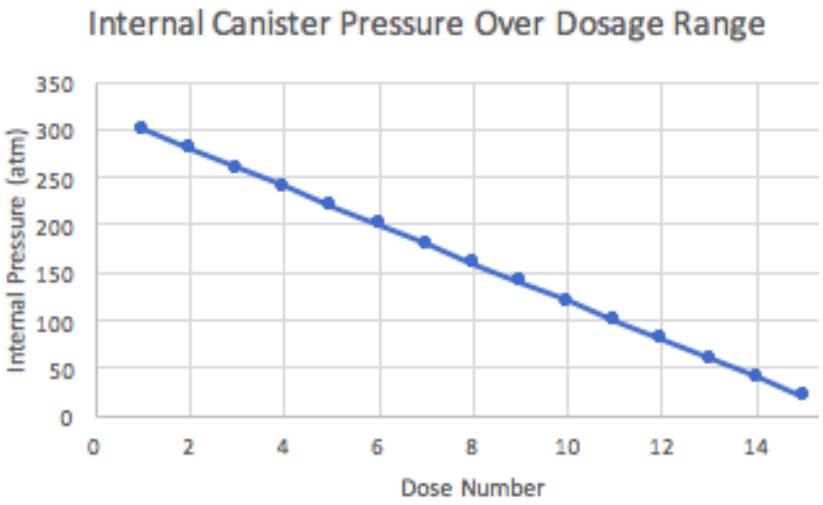


Figure 8. *The linear decrease in internal canister pressure as each dose is administered.*

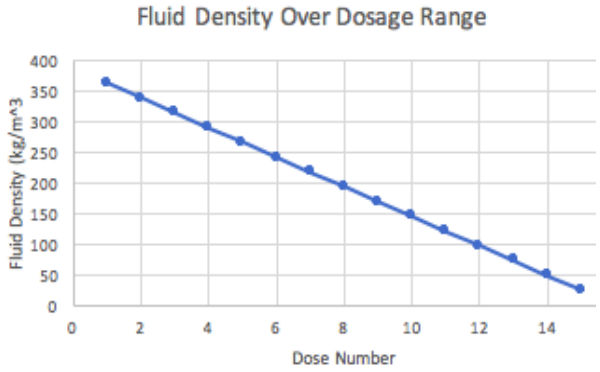


Figure 9. *Linear decrease in fluid density over time.*

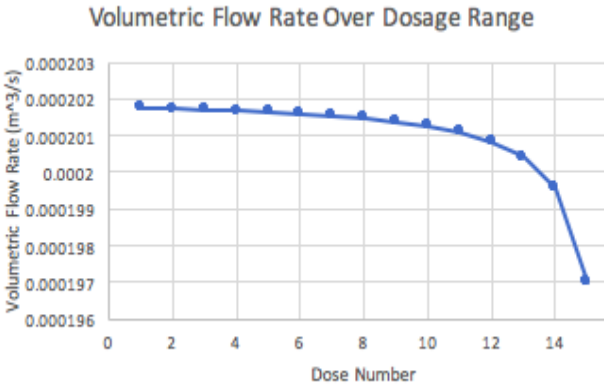


Figure 10. *Decreasing flow rate over time.*

Figure 8 above illustrates the linear decrease in internal canister pressure (as anticipated given the proposed dispersal mechanism) and Figure 9 shows how that trend is reflected in a linear decrease in fluid density.

One important thing to note is that the device retains a nearly constant volumetric flow rate and discharge time per dose. Though the drop in Figure 10 may visually appear to be significant, one can determine from the vertical axis that the decrease is only by about $4x10^{-6}$ cubic meters per second. Given the small magnitude of this decrease, the short time period over which the vaccine is administered, and the minimal volume of the proposed canister, the team came to the conclusion that this decrease would not have a significant impact on the performance or administration capabilities of the device.

Model 2: The Actuator: Droplets and their Dispersal

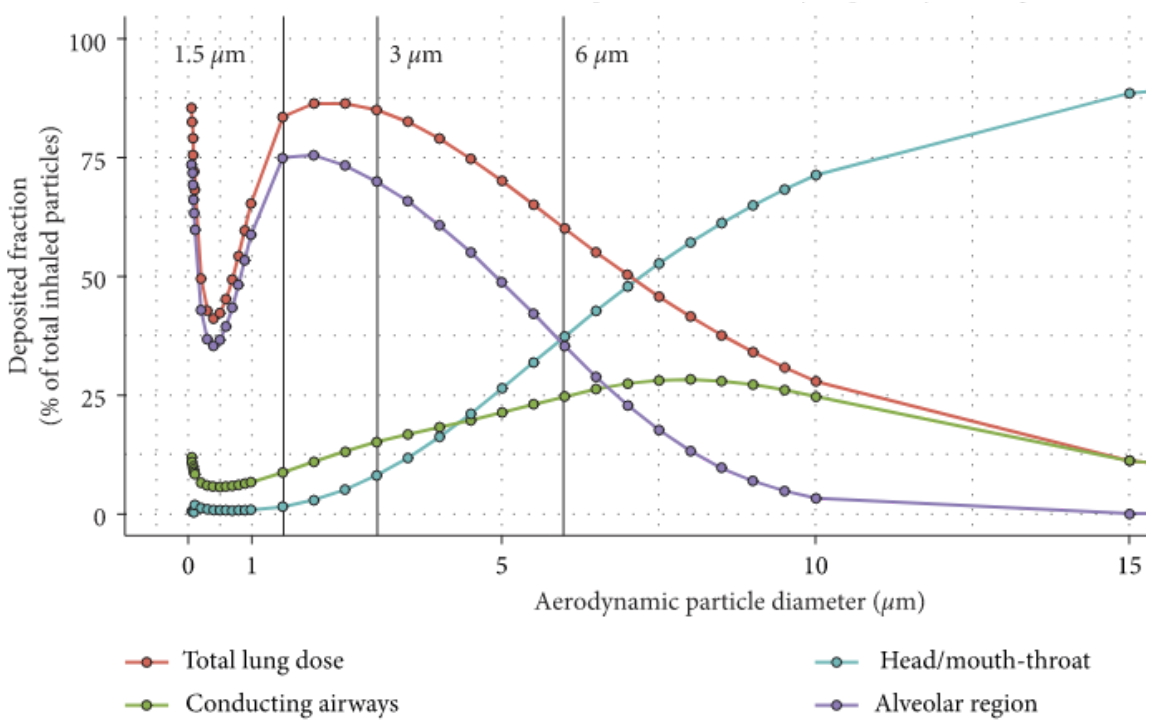


Figure 11: *Particle size-dependent deposition stratified by respiratory tract region [10]*

The size of the droplets that are formed by the actuator is significant for the application of an inhalable vaccine. This is because the droplet size must be large enough to be able to contain the live-attenuated virus particles that will evoke an immune response, but also be within the size range that can be appropriately deposited in the airways. According to literature values, approximately 20% of our dose volume must be deposited in the conducting airways or alveolar region of the lungs to provide a high enough concentration of the drug to be completely certain that it will be effective. As can be seen in figure 11, the ideal droplet size to ensure enough drug is adsorbed is about 1-10 microns, which is large enough to carry the viral components as well.

$$d_{max}=d(C_{ct}^{1/2})$$

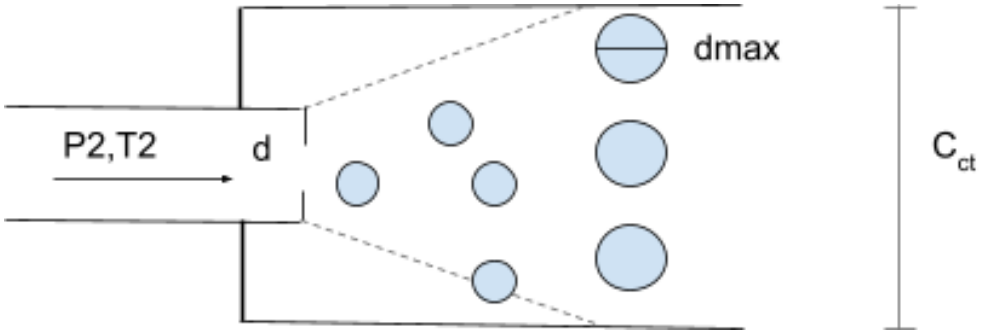


Figure 12: *Mathematical model using desired droplet size to find actuator nozzle diameter*

After finding the desired droplet size for maximum deposition in the airway, the equation seen in figure x: d_{max}=d multiplied by the square root of C_{ct}, (where d_{max} is the maximum desired droplet size, d is the diameter of the actuator nozzle, and C_{ct} is the effective diameter of the exiting jet) was used to solve for the required diameter of the nozzle, which was found to be .3 mm when using the desired droplet size of 5 microns. This is the size that we made the nozzle of our actual 3D printed actuator.

Measuring Droplet Size

Originally, the team attempted to determine the size of the droplets by spraying an inhaler onto a surface and visually measuring the size of the droplets. However, the team was unable to determine droplet size using this method since the mechanism sprays a consistent mist with no visible droplets. Various spray distances were attempted onto a colored absorbent surface to see the droplets but the results were not measurable, as seen below in Figures 13 and 14. The human eye cannot see anything smaller than 50 microns and we estimate our droplets to be 5 microns to be absorbed in the respiratory tract. This confirmed that the droplets are extremely small and cannot be seen by the human eye.

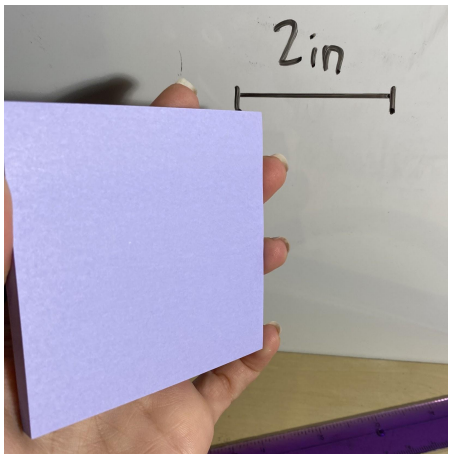


Figure 13: *Spray test with inhaler 2inches away.*

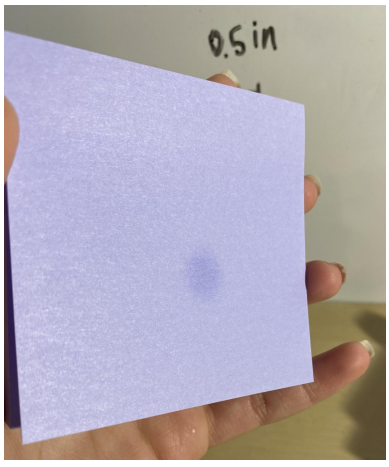


Figure 14: *Spray test with inhaler 0.5inches away.*

After the first spray test worked to confirm that our droplet sizes were on a microscopic scale as intended (<50 um), another test to more accurately measure the droplet size was devised. To

measure the droplet size, droplets were dispensed onto a hydrophobic surface and viewed under a microscope to measure their diameter using the captured image and the magnification settings.

Unfortunately, we were not able to use our actual 3D printed shell and actuator, as we did not have access to a canister that could fit in the printed shell, but were able to use a canister with an actuator with what looked to be the same nozzle diameter as the printed actuator, and with the exact same dimensions otherwise, so we can assume that the results of this test are applicable to our product.

The experiment was done by dispensing a dose from the inhaler onto a hydrophobic surface and then viewing the surface under a microscope, as pictured in figure 15. Using an objective of 4x and a magnification of 10x, the diameter of the field of view is 4 mm. With approximately 400 of the smallest sized, meaning not combined, droplets fitting across the diameter, the droplets can be estimated to be approximately 10 microns, which is reasonably close to our desired size of 5 microns given the somewhat high margin of error with this experiment, and is within the acceptable range of droplet sizes as researched by the team through literature review.

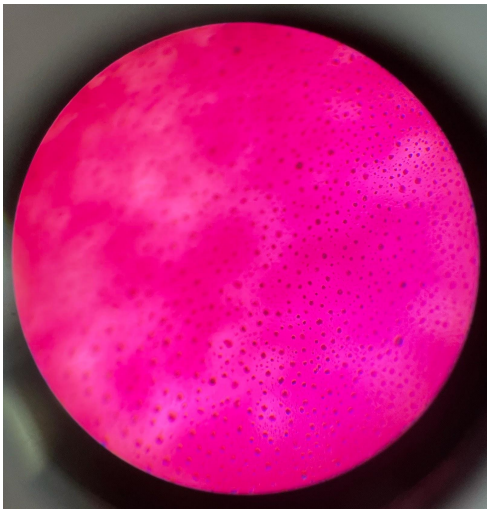


Figure 15: *Droplet Spray Test*

Human Factors Considerations

When thinking about human risk factors associated with the product, the group considered the severity of harm, the likelihood of risk, duration of exposure to the population, the possibility of false-positive/negative results, tolerable risk levels, failure modes, and risk factors for healthcare professionals.

The severity of harm of the inhalable vaccine most significantly includes the risk of adverse reactions to vaccine antigens or propellants. Common vaccine side-effects include fever, chills, headache, muscle and joint aches. There is also some concern over lung inflammation as part of the immune response to the vaccine antigens, potentially causing complications for some populations more than others; Patients with asthma or who are immunocompromised, for example, may experience more severe side-effects. Potential impacts on the lung microbiome are also not known. However, the duration of exposure to the population is low. The individual administering the vaccinations will have the greatest exposure to the product in terms of time, but will not be exposed to the risks associated with receiving the vaccine itself. The risk of needlestick injury and transference of blood-borne pathogens associated with traditional vaccines is also removed with this product and the smooth edges and comfortable grip design of the inhaler shell reduce the risk of injury caused by the product to the administrator. For the patient, the exposure will be a matter of seconds as they are being dosed.

Generally, the likelihood of risk for the general population is low, with most individuals experiencing no or mild systems. The likelihood of physical injury and allergic reactions to certain ingredients found in traditional vaccines is reduced with the inhalable vaccine as well. Despite the risks that do exist, the patients are generally tolerant to them, as vaccines are considered essential for preventing many potentially fatal illnesses. Due to the reduction in common risks associated with traditional vaccines, patients are expected to be more tolerant of the inhalable vaccine product than a traditional vaccine.

There is no risk of a false positive or negative with this product, since the product does not take any measurements. Potential failure modes that are applicable to the inhalable vaccine include faulty atomizer/actuator, overly pressurized canister, or incorrect storage of the canister containing the vaccine. Our product design addresses these failure modes by creating a development that will reduce the number of individual parts, have the most cohesive design, and reduce the likelihood of failure. This directly relates to the atomizer and our plan to have it integrated into the shell since it is a small piece. Thinking large scale, an automated system would be used to sufficiently pressurize the canisters at the same level. Labels with storage information and proper transportation storage will be blatantly stated to ensure the optimal shelf-life.

Design for Manufacturing

Our design plan for manufacturing revolves around keeping the parts simple and minimizing any moving parts to decrease labor costs. Reducing fragile and thin parts will also help to decrease labor costs and any other damage done during the manufacturing process. We decided that using a minimal number of materials will help us have a faster processor and make things simple. To decrease material cost we decided that buying the alcohol wipes, used to disinfect the

mouthpiece of the inhaler, in bulk. To minimize the number of components we manufacture, we decided that purchasing the vaccine and propellant as a mixture would help reduce cost and make things more simple. After creating the set of design for assembly rules for the product listed above, the estimated cost of the product is $27.52. The cost analysis is broken down below.

Design Economics and Costs Analysis

Our most up-to-date cost estimate breaks the individual components into two categories: catalog components (which are used exactly as purchased) and custom components (which cannot be purchased as-is from the market, and so must be assembled through alternative means). It is estimated that the final product will cost approximately $27.51 to produce. Of that, the team expects $11.98 to be spent on procuring raw materials, $14.36 to manufacture and process the custom components, and about $0.03 on labor costs. A more specific cost-breakdown analysis is included in the table below:

Catalog Components	**Retail Price/Unit**	**Qty/Unit**	**Component Cost**
Canister	$0.11	1	$0.036
Actuator	$2.50	1	$0.83
Alcohol Wipes	$0.03	15	$0.15
Custom Components	**Material**	**Mass (kg)**	**Cost**
3D Printed Shell	Cellulose-Based Plastic	<1	$2.38
Vaccine-Propellant Mixture	Vaccine, HFA Propellant	0.015	$11.34
Total Unit Values	**Manufacturing Cost**	**Price**	**Profit**
	$27.52	$50.00	$7.49*

*Note that other costs, like labor and transportation, eat into the profit without being explicitly listed in this table.

At the packaging size of 2.95 inches (75mm) long by 2.95 inches (75mm) wide and 1.97 inches (50mm) in height, the team has calculated that one shipping container of conventional dimensions should be able to ship 245,130 of these devices anywhere in the world. Given that each device contains 15 doses, this means that one shipping container can contain over 3.5 million doses of vaccine.

Regulatory Review and Strategy

Our device is defined as a medical inhaler for vaccine delivery, therefore it is categorized as Class II equipment according to the FDA standards, the Class II category comprehends all the devices that the general controls are not sufficient to provide assurance of the safety and effectiveness of the product. The modified inhaler, not only, is significantly more complex than any device classified as a Class I, but also its primary function is drug delivery, consequently, it is considered a combination product. A medical device is classified as a combination product if it requires another FDA-regulated product, in this case, the oral inhalable vaccines, in order to be fully operational. The combination products may also be subjected to further regulations set by the FDA's Office of Combination Product on a case-to-case basis.

Furthermore, the product would most likely require a 510(K) premarket notification, validating our modified inhaler as substantially equivalent to an already legally marketed device. In this case, our device must be compared to existing marketed inhalers and prove that it has an equivalent intended use, and that, even with differences, it is as effective and safe as the legally marketed product. Also, the product must be compared with other vaccination methods, such as traditional intramuscular injection and nasal inhalable, and prove to be equally effective and safe. If the product is not qualified as substantially equivalent it would be necessary to get a Class II designation via the De Novo classification process. And if a product is commercialized without its effectiveness and safety proven, it would be susceptible to a recall, recently, in 2020 approximately 600,000 Perrigo's albuterol inhalers were recollected due to possible clogging of the equipment, this problem caused patients not receiving the correct dosage of the medicine [9].

IP Review and Considerations

The existing patents that were identified by the team that remained relevant throughout development include patent 10,898,666 (January 26, 2021), AKA "Methods for generating and delivering droplets to the pulmonary system using a droplet delivery device". This patent is for a droplet delivery device and related methods for delivering precise and repeatable dosages to a subject for pulmonary use. The droplet delivery device includes a housing, a reservoir, an ejector mechanism, and at least one differential pressure sensor. The droplet delivery device is automatically breath-actuated by the user when the differential pressure sensor senses a predetermined pressure change within the housing. The droplet delivery device is then actuated to generate a stream of droplets having an average ejected droplet diameter within the respirable size range, e.g, less than about 5 um, so as to target the pulmonary system of the user. For the design being considered by our production team, a pressurized canister with a metering chamber is being considered, but the overall delivery method is extremely similar, including desired droplet size. The second relevant patent, patent 10,836,817 (November 17, 2020), AKA "Anti-Tau antibodies and methods of use", describes an invention that provides anti-Tau

antibodies and methods of using the product. This may relate to our product given the patent covers antibodies relevant to that vaccine being administered.

Taking existing patents and trademarks into account, the team came up with the following claims detailing the product for a preliminary patent:

A vaccine delivery system allowing for painless and effective vaccination via oral inhalation including:

1. a 10mL aluminum canister that is 40mm high, has a diameter of 17.8mm, a thickness of 3mm, able to withstand up to 335 atmospheres of pressure.
    a. Hydrofluoroalkane (HFA) propellant that will allow the spray mechanism to deploy the appropriate size droplets of 5 microns for each dose.
    b. Live-attenuated virus (various strains) in a solution including sucrose, dipotassium phosphate, potassium dihydrogen phosphate, gelatin (porcine, Type A), arginine hydrochloride, monosodium glutamate monohydrate, and water
2. A cellulose-polymer shell that is 80mm in height, 28mm in diameter, and approximately 3mm thick. Sized to house the canister described in section 1.
    a. Effervescent atomizer integrated into the outer shell that will hold the aluminum canister, which will plug into the atomizer to ensure the vaccine and propellant will be activated when appropriate. Nozzle size of .3 mm.
3. A set of alcohol wipes to sanitize the mouthpiece of the device between uses.

The oral inhalable vaccine device will operate by having the user shake the device, then depress the canister into the atomizer mechanism while inhaling, such that the droplets will flow through the mouthpiece that is integrated into the outer shell and into the user's respiratory tract.

Design for the Environment Considerations

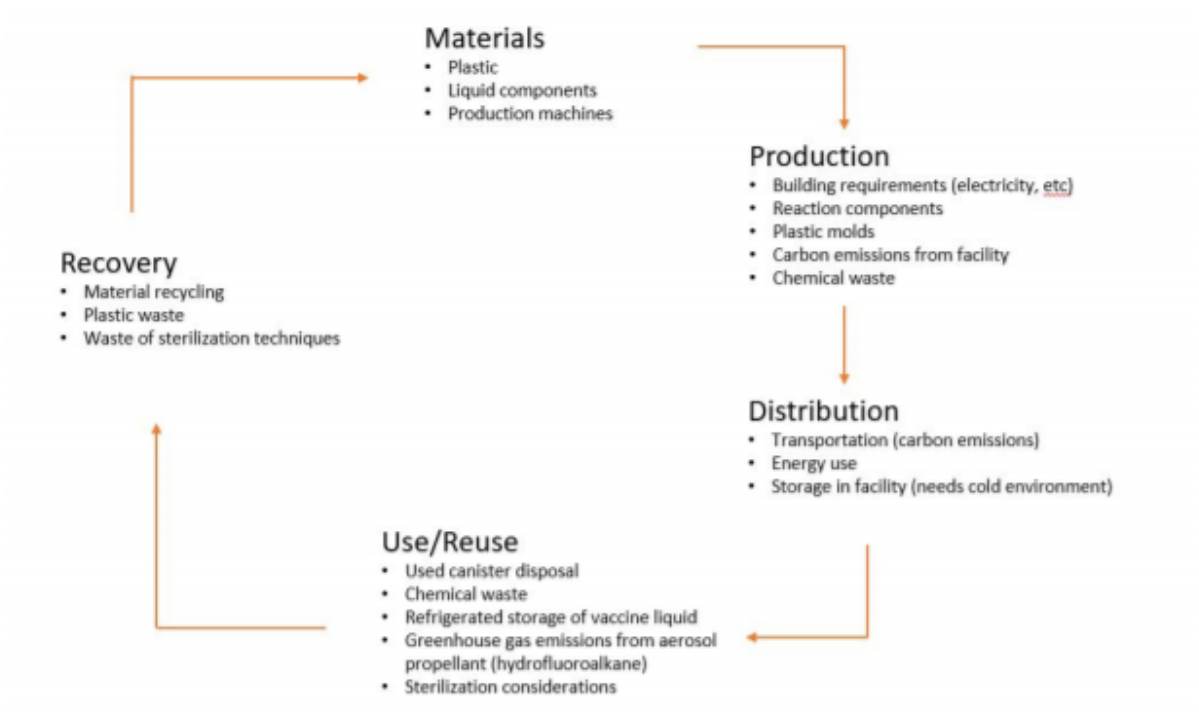


Figure 16. The life-cycle assessment of our inhalable vaccine provided by Group 1.

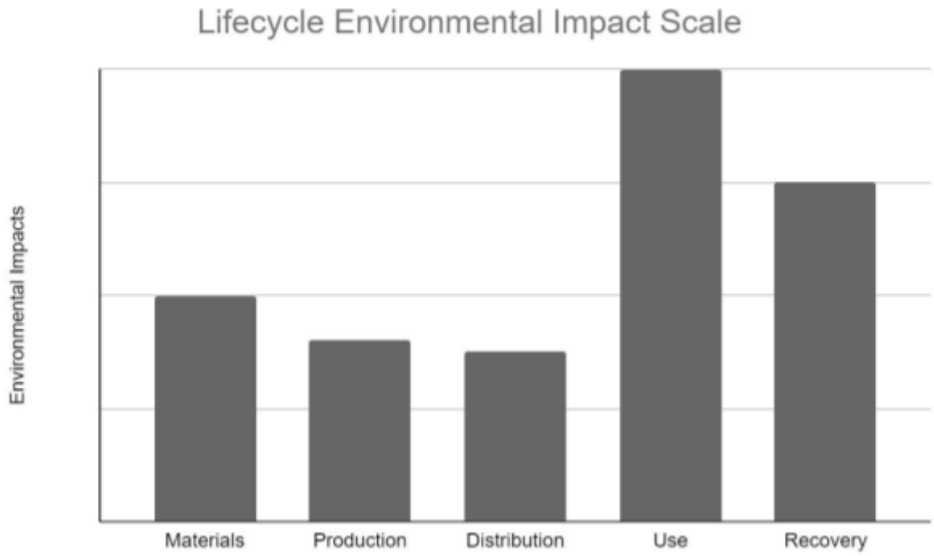


Figure 17. The environmental impact of the inhalable vaccine provided by Group 1.

Above, figures 16 and 17 show the life-cycle assessment and environmental impact of our concept, the inhalable vaccine, provided by our consultants - Group 1. We discussed how the use of a mechanism like an inhaler is detrimental to the environment because of the aerosol used as the propellant. This led our group to consider other options for a propellant but after carefully comparing our current method to others found we decided to keep our current propellant because other methods either did not meet our needs and specifications or had other obstacles such as not being able to be administered to a certain population. We tried using materials that are reusable or can be easily disposed of, which is how we decided to use a cellulose-based plastic for the outer shell that can be reused, it just needs to be cleaned with an alcohol wipe, and the canister is made from medical-grade metal to hold the right amount of doses to not go to waste. The recovery proved to be difficult for the canister since it is not refillable and cannot be recycled because of the drug particles inside.

Summary and Conclusions

In conclusion, the final design addresses all the issues identified that are associated with the traditional vaccination method, it can deliver the vaccine dose quickly, effortlessly and painlessly, while being financially accessible to the general public. It also eliminates the necessity of a healthcare professional to administer the vaccine, and it is not invasive nor uncomfortable like other techniques. The project had as inspiration the existing asthma inhalers, and after doing research on orally inhalable vaccines, specific modifications were proposed to the inhalers so they could be effectively used for vaccine delivery. Then, the three distinct models were created to analyze the performance of the newly altered device. The first model revealed what would be the necessary pressure inside the canister in order to deliver all doses of the vaccine and the wall thickness necessary to sustain that pressure. Then, another model was designed to determine the optimum size of the vaccine particles for deposition on the lungs and the required nozzle opening to achieve that size, and the actual size of the particle was found to be 10 microns, approximately twice the ideal size. Finally, the last prototype was a 3D printed shell and canister to assess the shape, fit of the canister, material, and user's ability to handle the product. The next stage would be making precise adjustments to the existing prototypes to improve the results and then creating a more comprehensive prototype to analyze how the device works as a whole.

<u>Individual Reflection Statements:</u>

Meagan: I think that, despite the unique challenges associated with remote learning, we were able to come together to creatively, logically, and effectively model a product that could realistically be produced. Considering I honestly didn't know how inhalers worked at all at the beginning of last term, I definitely feel as though we've come a long way since then. This term, we especially put a lot of effort into literature research and mathematical models to back up the dimensions and materials that we chose for our product. We were also able to further demonstrate these models physically, with our 3D printed model of the device, spray tests, and

Solidworks models. I also feel like our group did a good job of considering every aspect of the device, from the number of doses each canister should contain, what size/shape of shell should be for maximum comfort, materials of the shell and canister, dimensions of the actuator, etc.

Jacob: I was really proud of how we as a team were able to collaborate on this capstone project. It was difficult occasionally to find times that worked for all of us outside of class, work, research, and other significant obligations, but through lots of late hours we eventually made it through. I personally spent a lot of time and effort on the canister model (with a lot of success, I believe), but would have liked to have been better at the COMSOL piece of it, which I had a number of technical difficulties trying to access and a lot of issues getting to work how I wanted it to once I could access it. But as a whole I think we did a great job brainstorming solutions for every problem we encountered and delegating tasks according to our individual strengths.

Pedro: This project was a very stimulating experience, even though I believe some of the steps were rushed and I would've liked to have some more time to decide things. Also, I was really impressed with the amount of progress our team made since the beginning of the last term (considering that the past few terms were far from ordinary), at the start none of us knew anything about oral inhalable vaccines or inhalers, but we were able to come up with a design that we truly believe can solve the problems with the current vaccination methods.

Fabiola: I believe this term has been full of learning experiences that tested our ability to quickly adapt our concept to what we had available to us for our experiments. I believe we had good outcomes that came from our quick thinking and problem solving to achieve results. As a group we worked to honestly try and solve a problem we thought was pertinent to what we have been going through.

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Appendices

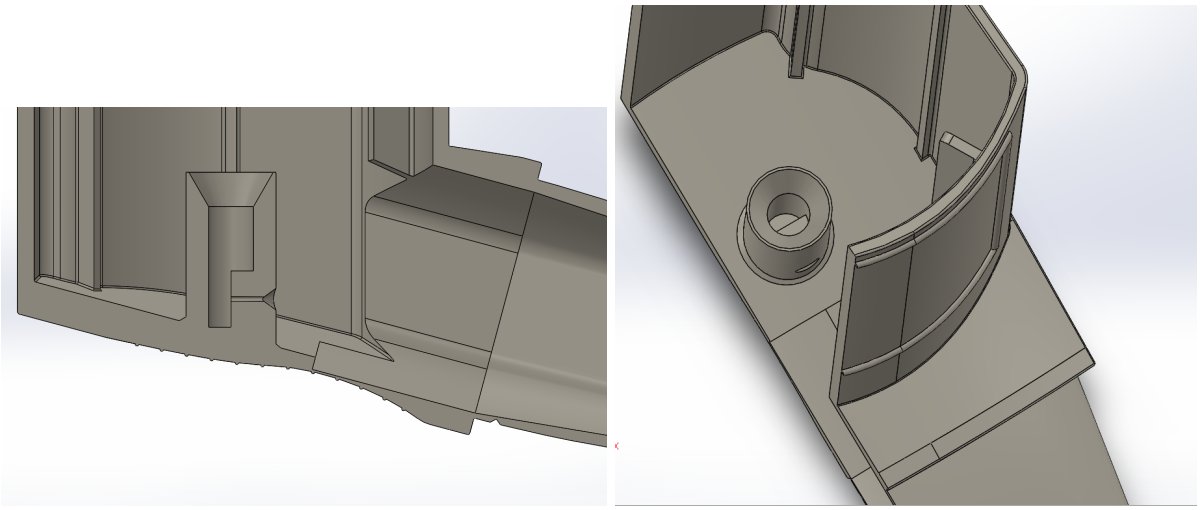


Figure 1: *Cross-sectional views of the integrated actuator in the outer shell.*

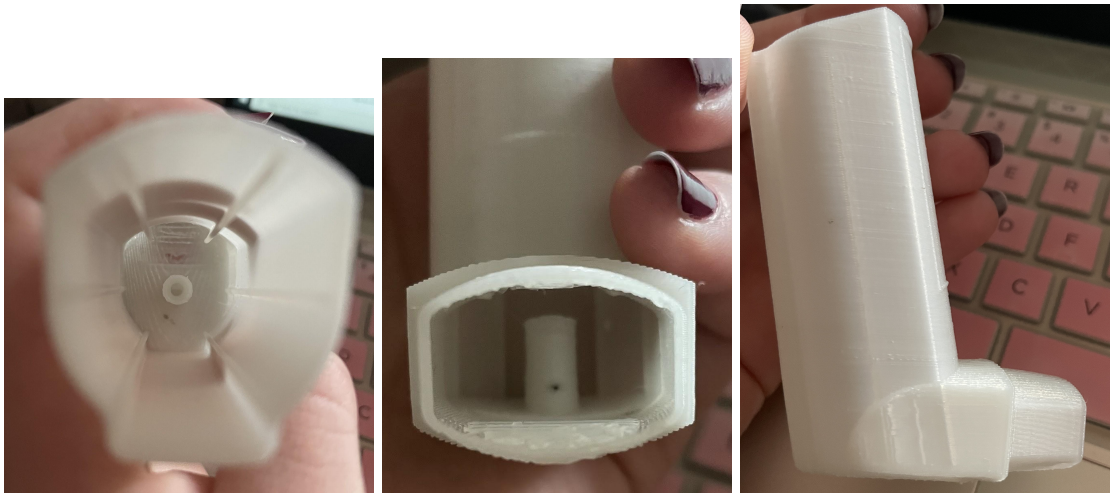
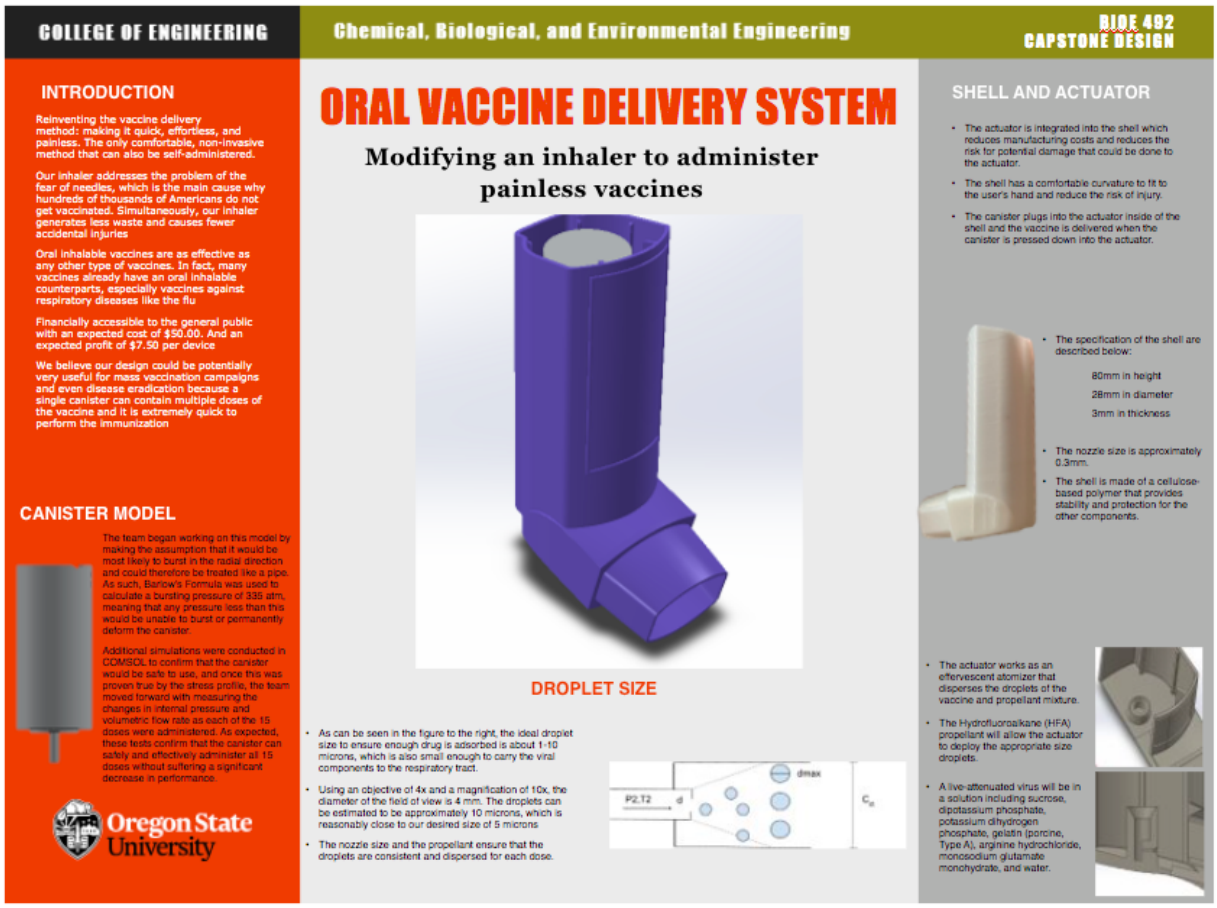


Figure 2: *3D printed PLA prototype of cellulose polymer outer shell with the integrated actuator.*

Poster:


COLLEGE OF ENGINEERING
Chemical, Biological, and Environmental Engineering
RIDE 492
CAPSTONE DESIGN
INTRODUCTION
Reinventing the vaccine delivery method: making it quick, effortless, and painless. The only comfortable, non-invasive method that can also be self-administered.
Our inhaler addresses the problem of the fear of needles, which is the main cause why hundreds of thousands of Americans do not get vaccinated. Simultaneously, our inhaler generates less waste and causes fewer accidental injuries
Oral inhalable vaccines are as effective as any other type of vaccines. In fact, many vaccines already have an oral inhalable counterparts, especially vaccines against respiratory diseases like the flu
Financially accessible to the general public with an expected cost of $50.00. And an expected profit of $7.50 per device
We believe our design could be potentially very useful for mass vaccination campaigns and even disease eradication because a single canister can contain multiple doses of the vaccine and it is extremely quick to perform the immunization
CANISTER MODEL
The team began working on this model by making the assumption that it would be most likely to burst in the radial direction and could therefore be treated like a pipe. As such, Barlow's Formula was used to calculate a bursting pressure of 335 atm, meaning that any pressure less than this would be unable to burst or permanently deform the canister.
Additional simulations were conducted in COMSOL to confirm that the canister would be safe to use, and once this was proven true by the stress profile, the team moved forward with measuring the changes in internal pressure and volumetric flow rate as each of the 15 doses were administered. As expected, these tests confirm that the canister can safely and effectively administer all 15 doses without suffering a significant decrease in performance.
Oregon State University
ORAL VACCINE DELIVERY SYSTEM
Modifying an inhaler to administer painless vaccines
DROPLET SIZE
As can be seen in the figure to the right, the ideal droplet size to ensure enough drug is adsorbed is about 1-10 microns, which is also small enough to carry the viral components to the respiratory tract.
Using an objective of 4x and a magnification of 10x, the diameter of the field of view is 4 mm. The droplets can be estimated to be approximately 10 microns, which is reasonably close to our desired size of 5 microns
The nozzle size and the propellant ensure that the droplets are consistent and dispersed for each dose.
dmax
P2,T2
d
SHELL AND ACTUATOR
The actuator is integrated into the shell which reduces manufacturing costs and reduces the risk for potential damage that could be done to the actuator.
The shell has a comfortable curvature to fit to the user's hand and reduce the risk of injury.
The canister plugs into the actuator inside of the shell and the vaccine is delivered when the canister is pressed down into the actuator.
The specification of the shell are described below:
80mm in height
28mm in diameter
3mm in thickness
The nozzle size is approximately 0.3mm.
The shell is made of a cellulose-based polymer that provides stability and protection for the other components.
The actuator works as an effervescent atomizer that disperses the droplets of the vaccine and propellant mixture.
The Hydrofluoroalkane (HFA) propellant will allow the actuator to deploy the appropriate size droplets.
A live-attenuated virus will be in a solution including sucrose, dipotassium phosphate, potassium dihydrogen phosphate, gelatin (porcine, Type A), arginine hydrochloride, monosodium glutamate monohydrate, and water.