A NOVEL METHOD TO COMMERCIALIZZE MEDICAL DEVICES INITIALLY DEVELOPED AT CALIFORNIA POLYTECHNIC STATE UNIVERSITY SAN LUIS OBISPO

A Thesis
presented to
the Faculty of California Polytechnic State University,
San Luis Obispo

In Partial Fulfillment
of the Requirements for the Degree
Master of Biomedical Engineering

by
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December 2020
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TITLE: A Novel Method to Commercialize Medical Devices Initially Developed at California Polytechnic State University San Luis Obispo

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ABSTRACT
A Novel Method to Commercialize Medical Devices Initially Developed at California Polytechnic State University San Luis Obispo
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California Polytechnic State University, San Luis Obispo is a university that encourages students to approach learning hands-on. As such, there is cutting-edge technology being developed by students in all departments on campus. Being that the university possesses an outstanding biomedical engineering department, there are groundbreaking medical devices that students are creating at Cal Poly SLO. These are devices that can better the lives of individuals suffering from ailments or fulfill needs in the medical industry. Subsequently, it is vital that these devices make it out of campus laboratories and into the hands of consumers. In order to move a product from ideation to the market, numerous steps must be completed and often times, especially with the challenges of commercializing medical devices, these efforts can result in failed product launches. As such, there is demand for a commercialization process to be created at Cal Poly SLO that will aid student created medical devices in reaching the market. This paper documents the progress made thus far on such a process at Cal Poly SLO.

Key Words: Commercialization Pathway, Medical Device, Tympanostomy
ACKNOWLEDGMENTS

I would like to thank my thesis advisor Dr. Michael Whitt for allowing me to be a part of this project and for his continual excitement, support, and positivity. I have thoroughly enjoyed this project and have been incredibly inspired by him through its entirety.

I would like to thank Dr. Roger Haring for sponsoring this project and making this project so enjoyable. I have learned so much from him this past year and am enormously thankful for his help and determination.

I would like to thank Dr. Thomas Katona for his help and guidance on this project and for being on my committee.

I would like to thank Dr. Robert Stewart for providing his clinical expertise and volunteering his time to assist with this project.

I would like to thank Grant Coe for his support and for 3D-printing prototypes for this project.

I would like to thank Vanessa Shaverdean for keeping me on track and supporting me through this process.

I would like to thank my family, mom, dad, sister and brother-in-law for their support and love on this project.
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Chapter 1

INTRODUCTION

1.1 Prevalence

At California Polytechnic State University San Luis Obispo numerous biomedical products are created in the College of Engineering (CENG) annually. These devices aim to better the lives of people through the advancement of medical technology.

Medical devices are uniquely challenging in respect to commercialization because these devices often require clinical trials and approval from the U.S. Food and Drug Administration (FDA). These challenges are in addition to the traditional difficulties surrounding new product development. To transform a medical device from prototype into marketable device can take years and requires a plethora of resources. New medical device production is most often completed by large medical device companies who possess the ability to nurture the commercialization of medical devices. As a result, cutting edge medical devices made by smaller parties often do not have the means or knowledge required to push a medical device into market. As such, current market needs are not being met and devices that can potentially enhance the quality of life of groups of our population, are not being offered.

It is desirable for a university such as California Polytechnic State University San Luis Obispo, which encourages innovation within its reputable Biomedical Engineering department, to possess a method to commercialize medical device innovation that is incorporated into coursework.
1.2 Product Development Fundamentals

Product development requires the completion of five general steps. For the proposed method of commercialization for medical devices at California Polytechnic State University San Luis Obispo, all five phases will also need to be completed. The fundamental five phases are as follows:

1. Idea Generation: Individuals search for ideas that can potentially be converted into products. This may include determining a gap in the current market where there is a need that has yet to be met. In this stage early prototyping may take place to demonstrate an idea.

2. Screening: The feasibility of proposed product ideas are evaluated in this step. This step aims to ensure that product ideas will only be supported if there is a viable chance of product success.

3. Concept Development: Research is conducted to determine the specifics of the proposed project. Aspects such as product strengths, products weaknesses, product market, and product competitors may be explored in this phase. This step may involve focus groups or surveying to determine what consumers require out of a potential product or to further understand the need that is attempting to be met. Designs are flushed out within this step.

4. Product Development: Designs for the product are created and tested. The specifics of a design are determined and optimized. Products may be introduced to groups of consumers in order to receive feedback on the product before it’s official launch. Testing and device optimization will occur in this step.

5. Commercialization and Rollout: A product is marketed to its target audience and launched into the market.
1.3 Current Medical Device Commercialization Pathway

There are numerous pathways that entities may take when working to commercialize medical devices. However, there are key steps that must take place in order to launch a medical device. Many steps of this process occur simultaneously or are revisited throughout a commercialization process.

1.3.1 Market Assessment

Once a need in the market is determined and a potential solution is created, it is necessary to investigate the market for this device. Determining the number of devices that would be used annually by researching the number of procedures or cases where such a device would be applicable is necessary to place a potential market value on the product. It is vital to determine the other companies and competitors that are addressing the same medical need and how large of a portion of the market each competitor possesses.

1.3.2 Intellectual Property Securement

When attempting to commercialize a product, entities must work to secure the intellectual property (IP) of their device to ensure that other entities do not sell their product or pilfer an idea. In order to be assigned intellectual property, a product must be useful, novel, and nonobvious. Companies often seek legal assistance to complete a prior art search in which active intellectual property of similar devices is researched to ensure that any newly created product does not infringe upon existing patents. In this phase, a company will discover if they are able to patent their idea or if they must complete a licensing agreement to essentially use existing intellectual property by paying the IP owner a fee. IP filing is especially important to complete early on in
commercialization because patents are now assigned to the individuals who file a patent first as opposed to who actually invented the device or idea.

1.3.3 Business Model Creation

Entities hoping to commercialize medical devices must determine how they hope to achieve this goal. In the medical device industry, it is common practice for individual inventors or physicians to transfer their ideas to larger biotech firms. These firms will go on to develop and commercialize the device and will compensate the inventor. However, many inventors chose to create their own startups to promote their inventions. Often in this phase, gaining access to key opinion leaders and determining potential manufacturing options also takes place. In this step, companies may want to begin securing funding to allow for attainment of the necessary resources and for the product launch later to come.

1.3.4 FDA Approval Securement

Medical devices fall under 3 different classes as listed in Table 1. Depending on the class in which a product is classified, a device will require specified testing and documentation in order to be FDA approved. Additionally, varying devices will require that varying approval paths be completed. It is vital that a company determine their device classification and approval submission route to ensure that the necessary documentation, validation, and clinical trials be completed. FDA approval can be an exceptionally time-consuming step in medical device commercialization.
Table 1. Medical Device Classification Chart

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<thead>
<tr>
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<td>Low</td>
<td>- Surgical Instruments</td>
</tr>
<tr>
<td></td>
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<td>- Pacemaker</td>
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<tr>
<td></td>
<td></td>
<td>- Cochlear implant</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Defibrillator</td>
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</tbody>
</table>

1.3.5 Research and Development

This phase will require a multidisciplinary team’s work to create a design that account for a device holistically. An R&D team must take into account a product’s manufacturability, product requirements, FDA regulation, financing, and intellectual property when flushing out a design. In this step, prototypes and beta models will be created to gain consumer and key opinion leader feedback. Throughout the R&D process a device will undergo numerous redesigns to ensure that the device has been optimized.

1.3.6 Device Launch:

Once a medical device has gone through all portions of the commercialization process, it can be launched. Previous to product launch, there must be a post-market surveillance system in place to collect data on product performance in market. Such data can be used to later alter devices as needed.
1.4 Purpose of Thesis

The purpose of this thesis is to document a novel commercialization pathway created for medical devices made at California Polytechnic State University San Luis Obispo. This document will outline the commercialization method.

1.5 Scope of Thesis

In order to create the novel method proposed, it is necessary to use a medical device as a trial run of the process. For the purposes of this thesis project, a tympanic tube device will be used to determine the commercialization process.
Chapter 2

PROJECT SPECIFIC GOALS

The overall objective of this project is to create a commercialization method for medical devices made at California Polytechnic State University San Luis Obispo. There are seven project specific goals that must be completed in order to achieve this objective.

The goals consist of the following:

**Device Optimization:** The medical device design will need to be optimized in order to meet the design requirements. The design will be frozen after optimization is complete.

**Intellectual Property:** A legal partner, specifically a registered patent attorney, must be secured which will work to complete the legal documentation require to move the product forward, most notably intellectual property assignment documentation.

**Manufacturing:** An ISO 13485 certified manufacturer partner must be secured which will produce the medical device.

**FDA Approval:** An FDA consultant must be secured in order to provide guidance on the FDA documentation process. This consultant will ensure that medical devices will be approved by the FDA speedily by ensuring that all documentation is correctly and completed filed.

**Funding:** A means of project funding must be secured to allow for the product continuation and support.

**Marketing Plan:** A marketing plan must be created to ensure that once a device is created, knowledge of said device reaches relevant parties.
Chapter 3

COMMERCIALIZATION LITERATURE REVIEW

3.1 Model University Processes

Certain U.S. universities have placed an emphasis on assisting students in the development and commercialization of products and the creation of businesses. In this section, universities which offer such programs will be discussed and function as potential templates from which certain elements may be beneficial towards the development of a unique commercialization method for California Polytechnic State University San Luis Obispo.

3.1.1 University of Notre Dame ESTEEM Program

The University of Notre Dame, located in South Bend Indiana, is home to the ESTEEM program. This is a graduate program that focuses on not only on the study of entrepreneurship in STEM fields but the application of entrepreneurship. Upon completion of the ESTEEM program, students are granted a Master of Science (M.S.) in Engineering, Science, and Technology Entrepreneurship. This program is open to students whom possess technical undergraduate degrees. The three-semester program is unique as it does not focus on course assignments but rather has a capstone project that students work on throughout the entirety of their three semesters. As concepts and skill sets are taught through courses, students must then apply these concepts to their capstone project in an actual effort to commercialize their project. Students are required to take business courses as well as technical electives in order to receive their graduate degree. Business courses cover topics such a business law, accounting, and leadership. Such topics are not generally taught in STEM undergrad programs and the inclusion of these courses allows for students to gain a holistic understanding of entrepreneurship in both the business aspects and the technical and innovative aspects.
The efforts made by ESTEEM students on their capstone projects will often result in the fruition of companies and products that will outlast a student’s time at Notre Dame. Projects offered through the ESTEEM program leave Notre Dame with a strong foundation to ensure success. This program allows students to nurture a product and gives graduates the tools they need to create successful, long-lasting businesses. By offering a means by which students do not have to separate creating product from academic work, the University of Notre Dame ensures that pupils graduate with far more than just the knowledge surrounding entrepreneurship.

3.1.2 Purdue University Burton Morgan Center for Entrepreneurship

Purdue University, located in West Lafayette, Indiana, has created the Burton Morgan Center for Entrepreneurship. This center functions to make commercialization tangible for students and alumni. There are numerous programs offered through the center that focus on a range of commercialization steps such as early stage product development to product launch. All programs allow for startup companies to acquire whatever resources they may need to become successful and reach their full potential. This center provides legal, funding, marketing, and manufacturing resources that students need for the successful launch of companies. This program allows MBA students to apply concepts acquired through coursework, to actual companies and products. Similar to the ESTEEM program, students are able to enroll in courses and programs that combine coursework and projects hosted by the Burton Morgan Center for Entrepreneurship. In this way students are able to learn and apply entrepreneurial concepts and create viable companies while also completing coursework.

The Burton Morgan Center for Entrepreneurship provides a unique opportunity for students to leave the university with a concrete business. Students are able to propose
their own product ideas and develop these ideas through course work that utilizes their own startup formation as course work.

3.1.3 Business Creation Program UCLA

The University of California, Los Angeles offers a business creation program as part of their full-time MBA programs. Students currently completing an MBA may choose to take part in the business creation program that aims to launch student companies while students are still attending university. In the first year of their MBA, students will submit project proposals to the business creation program and complete two prerequisite courses. Accepted proposals will begin work on their startup in their second year and will require two quarters to plan and launch. Through these two quarters, student startups are rapidly developed and nurtured, and each week one aspect of a student’s business is addressed. On average, 50% of student startups that participate in this program launch successful companies. This program is designed to take student ideas and use them to combine the theoretical and hands-on portions of entrepreneurship within the required ten units of coursework. Students within this program are encouraged to forge new ideas and combine technical fields with business concepts to develop new products and companies and transform these ideas into profitable careers.

3.1.4 Babson College MS in Entrepreneurial Leadership (MSEL)

Babson College housed in Wellesley, Massachusetts, is known worldwide for their entrepreneurial programs. They currently offer an MS in Entrepreneurial Leadership (MSEL) which aims to launch student startups as well as produce effective leaders in industry. This nine-month, full-time MBA program allows students to work on their own startup ideas and place their startups on the path to commercialization and long-term success. This program holds coursework at its core to teach students the necessary
skills to create and launch a business. Outside the classroom, students are required to apply this knowledge to a project to reinforce recently learned concepts. This program allows students to either bring in their own startup ideas or contribute to outside sponsor proposed projects. Because of the robust entrepreneurial community at Babson College, students have access to a plethora of resources and advisement. A unique aspect of this program is its focus on the leadership role necessary in business. Core classes provide students with skills they will need as leaders in a business including negotiation, effective communication, and talent recognition. Students within this program are able to grow their personal skillsets as well as launch a company while in university.

3.1.5 Cal Poly’s Center for Innovation and Entrepreneurship (CIE)
California Polytechnic State University San Luis Obispo is home to the Center for Innovation and Entrepreneurship which functions to support students with an interest in entrepreneurship and the world of start-ups. The CIE has helped students start over 120 successful companies and provides invaluable resources such as a project workspace, mentorship opportunities, and networking opportunities. Numerous students that become involved with the CIE are undergraduate entrepreneurship students however this organization welcomes students of all years and majors. Different programs to help start student-run companies include elevator pitch competitions and accelerator programs. The Cal Poly CIE has allocated manufacturing resources on campus, the space is known as Innovation Sandbox, to assist student run companies prototype their products. This program does a phenomenal job of supporting students and their entrepreneurial endeavors.
3.2 Unique Aspects of a Cal Poly Commercialization Method

The proposed commercialization pathway for medical devices will adopt aspects of commercialization pathways currently offered through other universities. However, there are two unique aspects to the pathway described in this document.

3.2.1 Ownership to Students and Sponsors

A major focus of the commercialization process to be created at California Polytechnic State University San Luis Obispo (Cal Poly SLO) will be to ensure that students and/or sponsors possess a majority of company ownership. Many institutions do not openly disclose what portion of ownership the institution will collect if a company is created through university programs and using university resources. The ambiguity of where ownership will fall can deter students and sponsors from approaching universities for assistance with entrepreneurial endeavors. However, the proposed commercialization pathway hopes to encourage individuals to consider Cal Poly SLO as a resource to reach their business goals. Typical projects that may use this pathway include senior projects sponsored by individuals who retain all intellectual property of the project, individual student projects, and faculty sponsored projects.

3.2.2 Specialization in Medical Devices

While this pathway would retain the capabilities necessary to commercialize non-medical devices, it will specifically target the commercialization of medical devices. The commercialization of medical devices can prove an exceptionally difficult process as previously mentioned. This commercialization pathway would be unique in that it offers students specialized support in producing viable medical devices and companies while students are in the university.
Chapter 4

TYMPANIC TUBE LITERATURE REVIEW

4.1 Otitis Media

Otitis Media, otherwise known as a middle ear infection, consists of swelling and inflammation of the middle ear. Fluid and pus buildup behind the tympanic membrane, also known as the eardrum, occurs and proper drainage of such fluid through the Eustachian is hindered\textsuperscript{14}. Figure 1 illustrates the differences between a normal middle ear and an infected middle ear. In most cases, the bacteria that cause Otitis Media are streptococcus pneumoniae, Moraxella catarrhalis, and non-typeable haemophilus influenza.

\textbf{Figure 1}. Normal vs. Otitis Media Inner Ear\textsuperscript{15}

Otitis Media can occur for a number of reasons. If an individual suffers from an upper respiratory infection (URI) such as a cold, sinus infection, or tonsillitis, the swelling that may occur as a result of such infections allows for bacteria to enter the Eustachian Tube\textsuperscript{16}. Changes in altitude and climate can also cause this type of infection. Otitis Media can also occur if an individual possesses a deformed, blocked, or dysfunctional Eustachian tube. Ears with more horizontally positioned Eustachian tubes are more likely to suffer from Otitis Media due to increased ease for bacteria introduction to the
middle ear\textsuperscript{14}. Those who smoke, are exposed to secondhand smoke or have allergies are at higher risk for developing Otitis Media as well. Individuals with immune dysfunction and over activity are at risk for Otitis Media because their bodies may produce excess amount of mucus and immune cells which may increase the inflammation and fluid buildup behind the eardrum\textsuperscript{17}.

Children are at the highest risk of suffering from Otitis Media. Individuals ranging from birth until seven years of age account for the largest population suffering from Otitis Media. Children have shorter, more horizontal Eustachian tubes as shown in Figure 2 and this allows for bacteria to enter the middle ear with ease. Children also possess enlarged adenoids which can block the Eustachian tube and cause a buildup of fluids which produces the ideal conditions for an ear infection to occur. Children who are not breastfed or who feed while laying down often suffer from middle ear infections as well as children who use pacifiers for prolonged periods of time\textsuperscript{18}. Recent studies have shown that children who receive the pneumococcal vaccination may be less likely to experience middle ear infections\textsuperscript{17}.

\begin{center}
\textbf{Figure 2.} Infant and Adult Eustachian Tube Orientation\textsuperscript{18}
\end{center}
4.2 Otitis Media Symptoms
Symptoms of Otitis Media include irritation and pain in the ears. Because of the nature of the infection, individuals may experience a loss of balance, loss of hearing, or headache. Vomiting, fever, and diarrhea may be present in patients as well. In severe cases, Otitis Media can cause Mastoiditis which is an infection of the bones in the skull which can be life threatening. Symptoms of Otitis Media can persist for months even after treatment.

4.3 Otitis Media Treatment Options
Currently there are a limited amount of treatment options for Otitis Media. One method of treatment may be an Ototopical antibiotic such as Ciprofloxacin or Ofloxacin. This treatment option proves successful for acute cases of Otitis Media.

Another treatment option is an antibiotic prescription. Amoxicillin is most commonly prescribed for this type of infection however in those allergic to the medicine, clindamycin, cephalosporins, and macrolide antibiotics can be used as a substitute. This may be paired with an analgesic to alleviate the pain experienced from the infection such as acetaminophen. Antibiotic treatments usually continue over a ten-day period for optimum results. If unsuccessful, an extended antibiotic treatment may be prescribed.

If an antibiotic treatment proves unsuccessful or if a large amount of fluid is still present in the inner ear after the infection dissipates, a tympanostomy tube may be recommended. These tubes allow for the fluid buildup of the infected middle ear to drain and can help prevent future middle ear infections from occurring.
4.4 Tympanic Tube Overview

Tympanic tubes are small tubes that are surgically implanted into the tympanic membrane. These tubes create a direct path between the middle ear and the ear canal. This pathway allows for the proper drainage of fluid in the middle ear as well as serves as a means to regulate pressure within the middle ear. Tympanic tubes were first introduced to the market in 1954 by Beverly Armstrong MD. Previous to their introduction, a hole was punctured in the eardrum and the fluid in the eardrum was drained via gravity. However, such drainage systems would seal rapidly as the body healed and the infection would not entirely dissipate or would return shortly. Today’s tympanic tubes are able to remain implanted anywhere from three months to two years.

Tympanic tubes today are most commonly made of medical grade silicon and metal. Although designs vary, tubes generally possess a cylindrical portion which functions as the connector piece between the middle ear and the outer ear. Most designs also possess flanges that function to keep the tube in place in the ear and prevent premature exit. Figure 3 demonstrates commonly used tympanic tube designs, the collar button (A), Triune (B), and t-tube respectively (C). The collar button and the t-tube are currently market lead devices and are manufactured by Summit Medical. The triune tube is not as popular as the aforementioned tubes, however it is still very prevalent in the market and is manufactured by Grace Medical.

![Commonly Used Tympanic Tubes](image)
4.5 Tympanic Tube Implantation

Tympanic tubes are implanted into patients by an Ear, Nose, and Throat physician (ENT) in a procedure called a myringotomy. This procedure is completed using either general anesthetic or local anesthetic. Once the proper anesthetic has been administered, the physician will slightly puncture the eardrum to create an opening for tube implantation. The built-up fluid within the ear will be removed as needed and an ear tube will be placed within the incision. The tube will create a connection between the middle ear and ear canal as the tympanic membrane heals itself around the tube. Directly after the procedure, the ears may be plugged to absorb excess blood. This outpatient procedure takes about 15 minutes and a patient can be in and out of the hospital within a few hours.

After the procedure, patients should be careful to avoid the introduction of outside fluids such as pool water, bath water, etc. into the ear canal as this may cause additional infections.

4.6 Issues with Current Tympanic Tube Designs

Since its invention, tympanic tubes have tremendously aided in alleviating Otitis Media in patients worldwide. Although this is true, such devices come with their own set of flaws. A major issue is perforation of the tympanic membrane. Perforation occurs when the eardrum is unable to heal properly after a tympanic tube is removed and as a result, the tympanic membrane is not uniform and possesses a gap. This can result in temporary or permanent hearing loss depending on the severity of the perforation. Depending on the model of tube used, a different level or perforation risk will be present. However, when tubes naturally extrude, there is a very low risk of perforation of about 4%. When tubes are surgically removed this risk increases to roughly 30%.
Another issue with current tympanic tube designs is tube blockage. Tubes may become blocked by Otorrhea, wax, blood, or foreign bodies\textsuperscript{27}. A physician may recommend eardrops to loosen the blockage. If unresolvable blockage occurs, a tube is no longer able to allow for pressure regulation or middle ear fluid drainage and will require removal. Because tympanic tubes expose the middle ear to the outside, the tube itself may actually cause middle ear infections. The same units that may be causing blockage in the tube may also be contributing to infections within the middle ear. As such, patients with tympanic tubes may be advised to wear earplugs when their ears may be in contact with water. Regular checkups every 3-6 months are necessary to assess a tube’s functionality\textsuperscript{28}.

Due to the nature of the tube, granulomas can also result from the implantation of a tympanic tube, although this is not common. A granuloma occurs when the deepest layer of the eardrum heals itself while the tube is implanted in the ear and blood vessels grow throughout the aperture of the tube\textsuperscript{29}. Figure 4 illustrates a small granuloma. When this happens, these blood vessels will often rupture and bleed out into the middle ear. In these cases, a tube will need to be surgically removed.

\textbf{Figure 4. Granuloma Visualization}\textsuperscript{29}
Cholesteatomas can also occur in patients who have experienced chronic otitis media and who have had a tympanic tube implanted. Cholesteatomas often present themselves in the form of cysts that grow behind the tympanic membrane. As these cysts grow, they can become massive and shed layers of skin inside the middle ear. This can result in damage to the bones within the middle ear\textsuperscript{30}. Patients who experience Cholesteatomas will often experience symptoms similar to that of patients with Otitis Media\textsuperscript{29}.

Tympanic tube patients also may experience Tympanosclerosis, which is the hardening of the tympanic membrane due to scarring. Tympanosclerosis can occur due to many of the aforementioned complications of tympanic tube implantation. This condition can result in conductive hearing loss\textsuperscript{31}.

\textbf{4.7 Device Market Need}

In the United States, it is estimated that one million tympanic tubes are implanted annually\textsuperscript{32}, representing a 90-million-dollar industry as of 2018\textsuperscript{33}. According to the Children’s Hospital at Vanderbilt, seven percent of all children in the United States will receive bilateral implantation of tympanic tubes by the age of three\textsuperscript{34}. Being that the insertion of ventilation tubes is the most common surgical procedure for children to undergo, there is an enormous market for this medical device\textsuperscript{35}. It is estimated that by 2025, the market will grow to a 102-million-dollar industry. Such growth allows for new devices to enter the market and provide for this growing need.
Chapter 5

METHODS

5.1 Device Optimization

Device optimization is a step in the commercialization process that will largely be completed by the creators of the device. Bench testing and validation must be completed to ensure that a suitable device has been created. A key part in this portion of the process is the identification of key opinion leaders. These are individuals who are experts in a certain subject matter. In the case of the tympanic tube, the project sponsor Roger D. Haring was the primary key opinion leader as he is a retired Ear, Nose, and Throat (ENT) physician. Additionally, Robert Stewart MD, who is a practicing ENT physician in San Luis Obispo was recruited as a key opinion leader. Both individuals have functioned as valuable sources of information in the subject matter. Their opinions and advice have helped to optimize the tube design. As such, it would be necessary for each device that utilizes the proposed commercialization pathway to pinpoint key opinion leaders in the niche of biotechnology that pertains to their project. The Biomedical Department at Cal Poly SLO has strong connections with French hospital and as such, key opinion leader securement should be tangible in this way.

There are hundreds of tympanic tubes on the market today with varying geometries, specialized uses and designs. In order to optimize a tympanic tube, a few design aspects must be taken into consideration to produce an effective tube with the specified capabilities. At the start of this project, there was a proposed design for the tympanic tube. Modifications have been made to this design in order to optimize its function and marketability.
5.1.1 Versatility

It was desirable for the tympanic tube design to be versatile in terms of the length of time the tube would be implanted in the eardrum. Tubes with longer flanges will remain in the eardrum for a longer period of time and the opposite is true for short flanges. In order to accommodate both timelines, notches were added to the flanges of the tympanic tube. These notches indicated where a physician could cut a tube’s flange to alter the length of time a tube remained implanted.

5.1.2 Absence of Premature Extrusion

Currently many tympanic tubes prematurely extrude themselves from the eardrum. This issue causes patients to have to undergo multiple surgeries to have the tubes re-implanted in their ears. To counter this, the once straight flanges were curved to ensure that the flanges provided grip without damaging ear drums when implanted for extended periods of time. Additionally, the flanges of the tympanic tube were left long. This will allow physicians to provide patients with a tube that will remain in the ear for an extended period of time without falling out.

5.1.3 Aperture Size

Aperture size is a vital dimension in any tympanic tube. Aperture size of a tympanic tube describes how large the pathway created between the middle ear and the ear canal will be. Larger aperture sizes allow for larger particulate to enter the ear yet also have the less likelihood of being blocked by ear fluid drainage. A major consideration with aperture size is that an aperture has to be large enough to allow for middle ear fluid drainage while also restricting the outside fluids and particulate that is able to enter the ear. Testing was conducted to determine the ideal aperture size by using a thin
elastomer sheet and varying aperture sizes. The specifics of this testing can be found in section 6.1 of this document.

5.2 Intellectual Property

To protect the tympanic tube design created through this project, it was necessary to secure the intellectual property of the design. A crucial factor considered was that this commercialization process had to be repeatable. As such, it was necessary to find a legal partner whom would agree to and have the capabilities to complete the legal work for all devices using the proposed commercialization process. Most universities in the United States offer patenting services to their students and faculty and have a set budget, that varies between institutions, for this purpose. California Polytechnic State University San Luis Obispo currently offers patenting to students as well. However, it was determined that this route would not fit the needs of this commercialization pathway because a large number of patents may be needed, and the university does not always accept student patent proposals.

It is also necessary that teams that use this commercialization pathway determine if extraordinary campus resources had been used in the product development. Extraordinary resources are any machinery or tools that are extremely specialized. General machine shop products and testing devices do not warrant extraordinary resource usage in general. If extraordinary campus resources have been utilized, the university will have a claim to the device and teams will need to approach the university before intellectual property is assigned.

At California Polytechnic State University San Luis Obispo, Ideally, this entity would be a university, as students of law as well as practicing lawyers are encouraged to work on
legal documentation while attending law school; because of this, it would be possible to allow for an agreement to be made where legal documentation could be traded for equity in a company and legal documentation completion experience for law students. Being that California Polytechnic State University San Luis Obispo does not bear a law school, an outside legal partner was required.

The most tangible option for acquiring a legal partner was utilizing an American based university that possessed a reputable law school. An agreement is to be made with this university where Cal Poly SLO products would receive legal support including non-disclosure agreements and utility patents applications. In return, the law school involved would receive a percent equity of each entity to which a patent application was completed as well as real-life legal documentation experience for students.

Due to the high volume of projects that may utilize the proposed pathway, another legal entity was needed. As such, two outside organizations that will be included in the proposed commercialization process were identified. Both organizations would be given equity of the company created around the legal work completed.

5.3 Manufacturing

Medical devices require that their manufacturer is International Organization for Standardization (ISO) 13485 certified. ISO 13485 outlines the quality management systems that must be in place for a manufacturer to produce medical devices. As such, it was necessary to locate a manufacturer that was ISO 13485 certified and also able to produce the tympanic tube. It was determined that injection molding would be used to produce the tympanic tube as it allows for a rapid and mass production of tubes.
Tympanic tubes are exceptionally small in size and it became evident that not all manufacturers were equipped to produce this type of device. It should be noted that within the field of medical devices, there is a huge range of products that will each require specialized manufacturers to be produced. Due to this factor, it is impossible to secure a single manufacturer to produce all devices that will utilize the proposed commercialization path. This portion of the path is therefore not standardized and each individual project group must locate a manufacturer that is able to meet their specific produce needs.

Future efforts will be directed to creating a Cal Poly SLO ISO 13485 manufacturing plant. Such a facility would allow for products on the proposed commercialization route to have access to a manufacturing plant. This facility would allow for the same manufacturer to be used on all medical device projects aiming for commercialization created at Cal Poly SLO.

5.4 FDA Approval

FDA approval is one of the largest hurdles when attempting to commercialize a medical product. In order to secure FDA approval, it was necessary to identify what approval path the tympanic tube would be required to complete. By using the FDA’s small business assistance helplines, it was determined that the device would require the 510(k) pathway. An initial draft of the 510(k) submission was completed. Often, entities are required to submit, revise, and resubmit their FDA approval applications; this can be a costly and time-consuming process. To minimize the possibility of the tympanic tube 510(k) application being rejected, it was decided that participating in the Q-Substitution program with the FDA would be the best course of action. The Q-Substitution program allows those hoping to receive FDA approval to meet with the team that will be
responsible for reviewing their application once submitted. Companies are able to receive feedback on their application and answer to specific questions. Participation in this program helps to better the likelihood of gaining FDA approval.

It was soon realized that because of the complexities surrounding FDA approval, possessing an FDA consultant would be vital to the rapid commercialization of the products on the proposed commercialization pathway. Onboarding an FDA consultant would assist in creating a repeatable commercialization process. In one embodiment of the commercialization plan, for her consulting, she would be given $10,000 and a portion of equity in the company for which she provided consulting for.

### 5.5 Funding

The tympanic tube device was initially funded through the Biomedical Engineering Department at Cal Poly SLO’s senior project program as well as through the company owner. Various pathways exist to secure funding means through the acquisition of investors. One potential route is the Cal Poly Center for Innovation and Entrepreneurship (CIE). This center works closely with Cal Poly SLO to assist students in advancing their entrepreneurial endeavors. Due to the already present relationship, including the Cal Poly CIE, would allow for this process to repeat and become a part of the proposed commercialization pathway.

An investor deck, that contained all relevant information about the tympanic tube and its market need, was created and will be presented to Cal Poly linked investors in order to secure funding for the continuation of the project.
5.6 Marketing Plan

The plan for the marketing of the tympanic tube design discussed in this document focuses largely on the use of medical device conferences. The American Academy of Otolaryngology, Medtech Live, 10x Medical Device Conference, etc. were all opportunities to market and showcase this device. Due to the COVID-19 situation and the early stage that the tympanic tube device was in, attending such conferences was not considered. However, in following years attending such conferences will be feasible. For future devices that will follow the proposed commercialization pathway, attending medical device conferences will serve as one means of marketing new medical devices created at Cal Poly SLO. However, differing devices will be most effectively marketed at conferences specific to the devices niche.
Chapter 6
TESTING, EVALUATION, AND DISCUSSION

6.1 Resistance to Flow Testing

6.1.1 Test Rationale and Description

A critical design choice for the cross-flange tympanic tube design was the internal aperture diameter. Because tympanic tubes are exposed to fluids other than inner ear fluid, it is vital that the aperture prevents as much inflow of outside fluids as possible to protect the middle ear. The aperture must also be large enough for middle ear fluid to exit without clogging.

Figure 5. Flow Within the Implanted Tympanic Tube

This was tested by using five different aperture sizes and three different fluid types. The apertures were placed across the opening of a length of tubing which was filled with fluid. The amount of water present in the line after one minute was recorded.

6.1.2 Methodology

In order to determine the needed aperture size, five potential aperture sizes were tested using three different types of fluid to reveal which aperture size was best able to resist

the flow of each fluid type. The five aperture sizes were as follows: .5 mm, 1 mm, 1.27 mm, 1.5 mm, and 2 mm. It should be noted that the most common industry standard for the internal diameter of tympanic tubes is 1.27 mm. The three liquid types used to test the apertures were room temperature tap water, soap water with a 16:1 ratio, and salt-water with a 4:1 ratio.

In order to create the varying aperture sizes, leather cutting tools and a syringe head were used to cut the appropriately sized aperture into an elastomer film. Figure 6 illustrates the 5 different tools that were used to create the apertures.

![Figure 6. Tools Used to Create Apertures and an Elastomer Sheet.](image)
Each elastomer sheet was placed at the end of a vertically oriented tube. 200 ml of fluid was poured through a funnel into the tube and once pouring was complete, a one-minute timer was started. The height of the fluid present in the tube after the one minute had passed was recorded. This process was repeated 5 times for each aperture size with each of the different fluid types resulting in 75 data points. Statistical analysis was conducted on the data using an ANOVA and Tukey post hoc to determine if there were significant differences in the yielded results.

### 6.1.3 Results and Discussion

A summary of results from the aperture testing can be seen in Table 2. The full dataset can be seen in Appendix I.

<table>
<thead>
<tr>
<th>Medium</th>
<th>0.5</th>
<th>1</th>
<th>1.27</th>
<th>1.5</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tap Water (mm)</td>
<td>11.6 ± 3.51</td>
<td>10.6 ± 1.34</td>
<td>8.2 ± 1.1</td>
<td>3 ± 1</td>
<td>3.6 ± 0.55</td>
</tr>
<tr>
<td>Salt Water (mm)</td>
<td>15.8 ± 2.95</td>
<td>7.2 ± 1.79</td>
<td>9.4 ± 1.14</td>
<td>5.6 ± 1.52</td>
<td>3.6 ± 1.52</td>
</tr>
<tr>
<td>Soapy Water (mm)</td>
<td>1.6 ± 1.52</td>
<td>0.8 ± 0.84</td>
<td>0.2 ± 0.45</td>
<td>0.6 ± 0.89</td>
<td>0 ± 0</td>
</tr>
</tbody>
</table>

**Table 2. Average Height in mm of Water Present in Tube.**
To determine the differences between the flow resistance between aperture sizes, a repeated measures ANOVA with a Tukey post hoc test was performed and the results are show in Table 3. The complete statistical analysis can be found in Appendix II.

**Table 3.** Tukey Post Hoc Data for the Fluid Height Compared to Aperture Size

<table>
<thead>
<tr>
<th>Aperture Size</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.50</td>
<td>15</td>
<td>9.66667</td>
<td>A</td>
</tr>
<tr>
<td>1.00</td>
<td>15</td>
<td>6.20000</td>
<td>B</td>
</tr>
<tr>
<td>1.27</td>
<td>15</td>
<td>5.93333</td>
<td>B</td>
</tr>
<tr>
<td>1.50</td>
<td>15</td>
<td>3.06667</td>
<td>C</td>
</tr>
<tr>
<td>2.00</td>
<td>15</td>
<td>2.40000</td>
<td>C</td>
</tr>
</tbody>
</table>

*Means that do not share a letter are significantly different.*

Through the statistical analysis, it was found that of the five different aperture sizes, there were three distinct groups in respect to fluid height recorded in the tube. The 0.5 mm aperture was able to hold the greatest amount of fluid overall and it held significantly greater millimeters of fluid than all other aperture sizes. The 1.00 mm and 1.27 mm apertures held the second greatest amount of fluid and these apertures did not perform significantly different from one another. These two aperture sizes were able to hold a significantly less amount of fluid than the 0.5 aperture and significantly more than the 1.5 mm and 2.0 mm apertures. The 1.5 mm and 2.00 mm apertures held the least amount of fluid and did not perform significantly different from one another.

As a result of this analysis, it was clear that choosing the 0.5 mm aperture would allow for the least amount of fluid to enter the aperture. Another viable choice was either the
1.00 mm or 1.27 mm aperture sizes because these apertures held the second greatest amount of fluid and are more comparable to current industry standards.

6.2 Tympanic Membrane Natural Frequency Testing

6.2.1 Test Rationale and Description
An area of concern with the cross-flange tympanic tube design created was that it might impede on the natural vibrational patterns of the tympanic membrane. There is currently limited data that explores the effects of tympanic tubes on the tympanic membrane’s vibrational pattern. As such, it was necessary to explore how a competitor tube effects the tympanic membrane and assess how the newly designed tube compares to the competitor tube.

The test used to explore the vibrational patterns of the tympanic membrane is commonly known as a pop-test\textsuperscript{36}. This test requires that the membrane of interest be stretched under pressure and then popped. A pressure transducer used was to record how the pressure changed as the membrane popped. This data was to be used to describe the vibrational properties of the membrane. A Fast Fourier Transform (FFT) was be applied to the pressure data and the frequency response was determined as well as the energy associated with the vibrations.

6.2.2 Methodology
To create the experimental setup, a hard-plastic container was used to create a pressure chamber. The Utah Medical Deltran\textsuperscript{®} Disposable Pressure Transducer was attached to the chamber as well as a hand pump and pressure gauge. The pressure transducer was connected to the BioPac MP160 data acquisition system. The experimental setup can be seen in Figure 8.
The membrane that was used to mimic the tympanic membrane was saran wrap. The membrane was stretched over the main opening of the pressure chamber. In order to insert the tympanic tube, a pin was used to create a small opening in the membrane and the tube was inserted using small grips. In order to help seal the chamber, glue was used to attach the tube to the membrane and a small piece of saran wrap was used to seal the internal aperture of the tympanic tube.
Once the membrane was in place, the data acquisition system was setup to gather pressure data from one channel. The reading was calibrated using the pressure gauge connected to the chamber to ensure that the correct pressure was reported. 125 ml of water was placed inside the plastic container and pressure was applied to the system using the attached handpump. Once the system reached 20 mmHg, a pin was used to pop the membrane.

![Figure 10. Membrane Stretch as Pressure is Applied.](image1)

This test was conducted with three different membrane treatments. The membrane without any tube inserted (natural response), the membrane with the competitor tube inserted, and the membrane with a 3D printed prototype of the cross-flange tympanic tube.

![Figure 11. 3D-Printed Cross Flange Tube Utilized During Pop-Testing.](image2)
6.2.3 Results and Discussion

A sample of raw pressure data and FFT data acquired from the BioPac system is shown in Figure 12 below. A summary of results from the aperture testing can be seen in Table 4.

Figure 12. Raw Pressure (Top) and FFT Data (Bottom) From Pop-Test.
Table 4. Pop-Test Data and Calculated Averages.

<table>
<thead>
<tr>
<th>Sample</th>
<th>Natural Response</th>
<th>Competitor Response</th>
<th>Cross-Flange Response</th>
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<tbody>
<tr>
<td></td>
<td>Frequency (Hz)</td>
<td>Energy (mmHg-Hz)</td>
<td>Frequency (Hz)</td>
</tr>
<tr>
<td>1</td>
<td>6.25</td>
<td>1.438</td>
<td>3.125</td>
</tr>
<tr>
<td>2</td>
<td>4.687</td>
<td>1.137</td>
<td>4.687</td>
</tr>
<tr>
<td>3</td>
<td>4.687</td>
<td>2.071</td>
<td>3.125</td>
</tr>
<tr>
<td>Average</td>
<td>5.208</td>
<td>1.549</td>
<td>3.646</td>
</tr>
</tbody>
</table>

To determine the differences between the frequency response and vibrational energy between different membrane treatments, a repeated measures ANOVA with a Tukey post hoc test was performed and the results are shown in Table 5.

Table 5. Pop-Test Statistical Analysis.

Comparisons for Energy (mmHg-Hz)

**Tukey Pairwise Comparisons: Membrane Treatment**

<table>
<thead>
<tr>
<th>Grouping Information Using the Tukey Method and 95% Confidence</th>
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<tbody>
<tr>
<td>Membrane Treatment</td>
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<tr>
<td>Natural Response</td>
</tr>
<tr>
<td>Cross-Flange Response</td>
</tr>
<tr>
<td>Competitor Response</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.

Comparisons for Frequency (Hz)

**Tukey Pairwise Comparisons: Membrane Treatment**

<table>
<thead>
<tr>
<th>Grouping Information Using the Tukey Method and 95% Confidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Membrane Treatment</td>
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<tr>
<td>Natural Response</td>
</tr>
<tr>
<td>Cross-Flange Response</td>
</tr>
<tr>
<td>Competitor Response</td>
</tr>
</tbody>
</table>

Means that do not share a letter are significantly different.
Through the Tukey comparison, it was revealed that none of the membrane treatments had a significantly different Frequency response. However, when looking at the averages it should be noted that the Cross-Flange tube had a higher frequency response than the competitor tube. Additionally, it can be seen that the Cross-Flange tube had a significantly similar vibrational energy to the natural response as well as the competitor response. A successful vibrational energy response, with a tympanic tube implanted in the membrane, would either be equal to or greater than the natural response. It was revealed that the competitor tube had a significantly lower vibrational energy than the natural response.

These frequency results are promising for the Cross-Flange tympanic tube. Because this newly designed tube had a similar frequency response to that of the competitor tube and natural membrane, the new design does not significantly affect the frequency response of the membrane. Theoretically, this would mean that the newly designed tube would not significantly alter the hearing of a patient with a tympanic tube. The vibrational energy results are also promising. The Cross-Flange design had a vibrational energy not statistically different than that of the natural membrane further illustrating that the new tube does not significantly affect the vibrations of the membrane. The Cross-Flange design actually out-performed the competitor tube, which had a significantly different vibrational energy than the natural membrane. Overall, from this testing it is clear that the Cross-Flange tube is a design that will not negatively affect the vibrations of the tympanic membrane.
Chapter 7

COMMERCIALIZATION METHOD DESCRIPTION

7.1 Device Optimization

Students and groups whom are producing medical devices at Cal Poly will largely be responsible for identifying and performing the necessary testing to ensure a quality device. These individuals will have access to Cal Poly SLO laboratories and equipment as needed to complete said testing as well as be able to connect with key opinion leaders through Cal Poly faculty and French Hospital that will assist in identifying product testing. The project’s FDA consultant, described in greater detail below, will also be at the creator’s disposal to assist in determining the necessary qualifications of a device to ensure it is able to be FDA approved.

7.2 Intellectual Property

The intellectual property of medical devices created at Cal Poly that are brought down this pathway will be granted with the assistance of a newly created patent clinic. This patent clinic will function to create a reliable and repeatable process, allowing for Cal Poly SLO students as well as individuals in the community to seek legal assistance. The patent clinic will receive a percent equity of each of the projects that become involved with the clinic. Such revenues would be recycled back into the surrounding community to create jobs, provide community funding, and help those in need in a community. An entity shall be created surrounding the patent clinic and the necessary legal team will be established. Lawyers completing the legal documentation may be students seeking experience or currently practicing patent lawyers.
7.3 Manufacturing

Devices that use the proposed commercialization pathway will seek manufacturing services from a certified ISO 13845 facility. It is impossible to assign one manufacturer to all devices on this pathway as different manufacturing facilities specialize in different types of production. However, as more projects utilize this pathway, agreements between manufacturers and Cal Poly SLO can be created to produce a list of potential manufacturers that form an alliance with Cal Pol SLO. Eventually it is hoped that Cal Poly SLO will possess its own manufacturing plant where such products can be produced.

7.4 FDA Approval

FDA approval is generally one of the largest hurdles a medical device must overcome to become commercialized. Medical devices that used the proposed pathway will be evaluated by an FDA consultation to ensure that devices are given the best possible chance of receiving FDA approval as possible. The consultant will provide their expertise to determine the necessary approval route that needs to be taken as well as be available to assist with the completion of the approval application. The consultant will help to determine what testing might be necessary as a part of the approval process as well. Overall, the consultant will function as a means to understand the complexities of applying for FDA approval in reference to a project’s specific needs.

After the FDA consultant’s evaluation and advice has been incorporated into the FDA approval application, a Q-sub meeting will be scheduled by the device creators. The Q-sub meeting serves as a means for those hoping to receive FDA approval to seek advice and knowledge from the direct FDA team that will evaluate their approval application. A template Q-Sub meeting request form can be viewed in Appendix III.
7.5 Funding

Medical devices that go down the proposed pathway will gain funding through investors. The device creators will create an investor deck which will depict their ideas to investors in the hopes of encouraging interest in the device. An investor deck outline is included in Appendix IV of this document.

Various pathways exist for Cal Poly to secure equity, two options are as follows:

1) Cal Poly is given first bid on company ownership. Students will present their investor deck to Cal Poly representative’s first and Cal Poly will have the first opportunity to invest and secure equity.

2) Cal Poly will receive equity in the company. This percentage would be equal for any and all devices that use the proposed commercialization method.

7.6 Marketing Plan

Student created medical devices that choose to use the proposed commercialization pathway will attend relevant medical conferences. Funding acquired from investors will fund the attendance of such conferences.
Chapter 8

SUMMARY AND CONCLUSION

8.1 Work Relevance

This project helps to lay the foundation in creating a process that allows medical devices made at Cal Poly SLO to be commercialized. California Polytechnic State University San Luis Obispo’s Biomedical Engineering Department presents numerous opportunities where students can combine their efforts with faculty and industry needs to create valuable medical technology. However, many of the student created medical devices never make it into the global market due to the challenges surrounding the commercialization process. The devices created at Cal Poly SLO are often cutting-edge technology that can have the potential to change the lives of many for the better. Creating a process to assist in the commercialization of medical products made at Cal Poly SLO will help to grow the world of biotechnology and place student devices in the market.

8.2 Project Limitations

The most limiting factor of this project was the timeline. The time required in creating agreements between parties and drafting and finalizing contracts is enormous. Due to the COVID-19 situation, certain timelines were extended and as a result, not all aspects of this process were finalized.

8.3 Future Steps

Through the efforts put into this project, potential commercialization pathways were explored. Due to the nature of the formation of this type of pathway, not all aspects of the process were determined, and finalization of certain aspects are needed before this pathway is able to support a large influx of student created devices.
A major step that will need to be taken is further development of the patent clinic. It will be necessary to secure a set legal team in order to ensure that access to a legal team become a repeatable and reliable portion of this process. It will be necessary to form an entity surrounding the patent clinic to continue its development.

Although the securement of manufacturers for proposed devices is easily attained through the numerous ISO certified manufacturers available, a long-term consideration may be for Cal Poly to create its own manufacturing plant. This would create student and community jobs and provide a way for Cal poly to move manufacturing capabilities in-house. A potential cite for this plant may be the Diablo Canyon ex-power plant as this is an enormous facility that currently has no use.

Marketing was an aspect of this process that was largely underdeveloped. It would be necessary for future work to create a robust marketing plan to ensure that created devices are given as much exposure as possible.
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# APPENDICES

## A

<table>
<thead>
<tr>
<th>Aperture Size (mm)</th>
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<tbody>
<tr>
<td></td>
<td>0.5</td>
<td></td>
<td>1</td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td><strong>Tap Water</strong></td>
<td><strong>Salt Water</strong></td>
<td><strong>Soapy Water</strong></td>
</tr>
<tr>
<td><strong>Fluid in Line After 1 Minute (mm)</strong></td>
<td>11</td>
<td>15</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>12</td>
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</tr>
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<td></td>
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<td>1</td>
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<td></td>
<td><strong>1.5</strong></td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td><strong>Tap Water</strong></td>
<td><strong>Salt Water</strong></td>
<td><strong>Soapy Water</strong></td>
</tr>
<tr>
<td><strong>Fluid in Line After 1 Minute (mm)</strong></td>
<td>8</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>11</td>
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<tr>
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<td>9</td>
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</tr>
<tr>
<td></td>
<td>10</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td><strong>Average Values</strong></td>
<td>8.2</td>
<td>9.4</td>
<td>0</td>
</tr>
<tr>
<td><strong>Aperture Size (mm)</strong></td>
<td><strong>2</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Medium</strong></td>
<td><strong>Tap Water</strong></td>
<td><strong>Salt Water</strong></td>
<td><strong>Soapy Water</strong></td>
</tr>
<tr>
<td><strong>Fluid in Line After 1 Minute (mm)</strong></td>
<td>3</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td><strong>Average Values</strong></td>
<td>3.6</td>
<td>3.6</td>
<td>0</td>
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</tbody>
</table>
## Comparisons for Fluid Height

### Tukey Pairwise Comparisons: Aperture Size

<table>
<thead>
<tr>
<th>Aperture Size</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.50</td>
<td>15</td>
<td>9.66667</td>
<td>A</td>
</tr>
<tr>
<td>1.00</td>
<td>15</td>
<td>6.20000</td>
<td>B</td>
</tr>
<tr>
<td>1.27</td>
<td>15</td>
<td>5.83333</td>
<td>B</td>
</tr>
<tr>
<td>1.50</td>
<td>15</td>
<td>3.06667</td>
<td>C</td>
</tr>
<tr>
<td>2.00</td>
<td>15</td>
<td>2.40000</td>
<td>C</td>
</tr>
</tbody>
</table>

*Means that do not share a letter are significantly different.*

### Tukey Pairwise Comparisons: Medium

<table>
<thead>
<tr>
<th>Medium</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
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<tbody>
<tr>
<td>Salt Water</td>
<td>25</td>
<td>8.32</td>
<td>A</td>
</tr>
<tr>
<td>Tap Water</td>
<td>25</td>
<td>7.40</td>
<td>A</td>
</tr>
<tr>
<td>Soapy Water</td>
<td>25</td>
<td>0.64</td>
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</tbody>
</table>

*Means that do not share a letter are significantly different.*

### Tukey Pairwise Comparisons: Aperture Size*Medium

<table>
<thead>
<tr>
<th>Aperture Size*Medium</th>
<th>N</th>
<th>Mean</th>
<th>Grouping</th>
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</thead>
<tbody>
<tr>
<td>0.50 Salt Water</td>
<td>5</td>
<td>15.8</td>
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<td>0.50 Tap Water</td>
<td>5</td>
<td>11.6</td>
<td>B</td>
</tr>
<tr>
<td>1.00 Tap Water</td>
<td>5</td>
<td>10.6</td>
<td>B C</td>
</tr>
<tr>
<td>1.27 Salt Water</td>
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<td>B C D</td>
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<tr>
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<td>5</td>
<td>7.2</td>
<td>C D</td>
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<td>D E</td>
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<td>E F</td>
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<tr>
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<td>E F</td>
</tr>
<tr>
<td>1.50 Tap Water</td>
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<td>E F G</td>
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<tr>
<td>0.50 Soapy Water</td>
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<td>1.50 Soapy Water</td>
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<td>F G</td>
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<tr>
<td>2.00 Soapy Water</td>
<td>5</td>
<td>-0.0</td>
<td>G</td>
</tr>
</tbody>
</table>

*Means that do not share a letter are significantly different.*
DEVICE NAME (Q-Sub)

Contact Information:
Best way the FDA can contact you

Company Name:
If no entity has been created, do not list

Address:
Company address or contact person’s address

Contact Persons:
List those who will be attending the Q-sub meeting from your group

Phone numbers:
Emails:

Q-Sub Type:
Meeting types include: Pre-submissions, Submission Issue Requests, Study Risk Determinations, Information Meetings, and Other Q-submission types. If you are unsure what type of Q-sub meeting required, contact the FDA small business helpline at 301-796-7100.

Draft Agenda:
A draft agenda proposing the topics to be presented and the estimated time for each agenda item.

Meeting Format:
Specify if a Teleconference or an in-person meeting is requested.

Proposed Dates:
List dates three months in advance of anticipated application submission, provide at least 3 dates.

Planned Attendees:
List everyone on project team, FDA consultant, and project advisor if applicable.

Requested FDA Staff:
Contact FDA helpline and request the names of individuals who are experts on the device you are presenting. This will ensure a productive meeting.

Questions:
List 3-4 questions/topics that the FDA will be able to cover in an hour's time. Make questions as clear as possible so that FDA is able to prepare answers beforehand.
D

Investor Deck Outline

Team Members & Contact Info
Include relevant team member information and if applicable, expertise relevant to the project

Indications for Use (IFU) & Device Background
Give context to the device and its usage, assume audience has a minimal knowledge of device

Product Renditions
Provide product visualizations and if possible, prototypes

Product Market Analysis
Present the current market value of device

Market Advantage
Highlight unique aspects of product that make it a competitive product

Required Funding
Provide a breakdown of the necessary costs that will be required for the project

Future of Device
Include the next steps the device will need to undergo and future goals