PNEUMONIACHECK: A DEVICE FOR SAMPLING LOWER AIRWAY AEROSOLS

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PNEUMONIACHECK: A DEVICE FOR SAMPLING LOWER AIRWAY AEROSOLS

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SUMMARY

The pathogens causing pneumonia are difficult to identify because a high quality specimen from the lower lung is difficult to obtain. A specimen collection device, named the PneumoniaCheck, was previously designed to collect aerosol specimens selectively from the lower lung generated during deep coughing to aid in the diagnosis of specific pathogens causing pneumonia. The device also includes several specially designed features to exclude oral contaminants from the sample, and a filter to collect the aerosolized pathogens. The objective of this thesis is to develop tests to verify the functionality of the device, called the Design Inputs.

Nine verification tests were performed to demonstrate the ability to collect lower airway aerosols separate from upper airway aerosols, successful exclusion of oral contents, and capture of pathogens in the filter. Further, the PneumoniaCheck was tested for proper sampling of the lower airway aerosols during deep cough at a very low volumetric flow rate to simulate patients with severe restrictive lung disease and with mal-positioning to simulate incorrect patient placement.

Verification testing of the PneumoniaCheck demonstrates effective separation of upper airway gas from the lower airway gas ($p<0.0001$) and exclusion of both liquid and viscous oral material ($p<0.0001$) from the collection chamber. Testing also demonstrated the selective sampling of the lower airway, even during low volumetric flow rates or incorrect positioning of the device.

The complex shape of the PneumoniaCheck presents a manufacturing challenge. Making the device from a solid and then drilling out the tubes would be difficult because

the outer channels do not align with the inner channel. Rapid prototyping, vacuum molding, and injection molding are all manufacturing options. Rapid prototyping is slow, and usually only economic for small numbers of parts. For vacuum molding or injection molding, the PneumoniaCheck would need to be cut in half and molded, and then the halves connected with fasteners, glued, or welded. Vacuum molding is inexpensive, but there would be a lip at the connection that may be uncomfortable for patients. If the lip is on the inside of the device, it may interrupt air flow through the device. Injection molding is inexpensive and fast. The PneumoniaCheck could be injection molded in halves, and then glued or sonically welded together. Injection molding would be an efficient and economical way to manufacture the device.

Verification tests were developed and performed, and the results demonstrate that the PneumoniaCheck successfully collects lower airway aerosols separate from upper airway aerosols, excludes oral contents, and captures pathogens in the filter, even during non-ideal conditions. After considering three different manufacturing options, injection molding was recommended for the device.

CHAPTER 1: INTRODUCTION

Pneumonia, or an inflammation of the lungs (Figure 1), is a leading cause of morbidity and mortality worldwide (Figure 2). In 2002, there were 451 million lower respiratory infections reported to the World Health Organization. Worldwide, pneumonia accounts for nearly 30% of all deaths in children under the age of five, killing more children than AIDS, malaria, and measles combined (Figure 3) [1]. In the United States, there were an estimated 1.4 million hospitalizations and 59,000 deaths due to pneumonia in 2002. Pneumonia can be caused by a variety of bacterial and viral pathogens, including *streptococcus pneumoniae*, *mycoplasma tuberculosis*, influenza viruses, respiratory syncytial virus, parainfluenza, adenovirus, rhinovirus, human bocavirus, influenza, *Mycoplasma pneumoniae,* hantavirus, and cytomegalovirus [2].

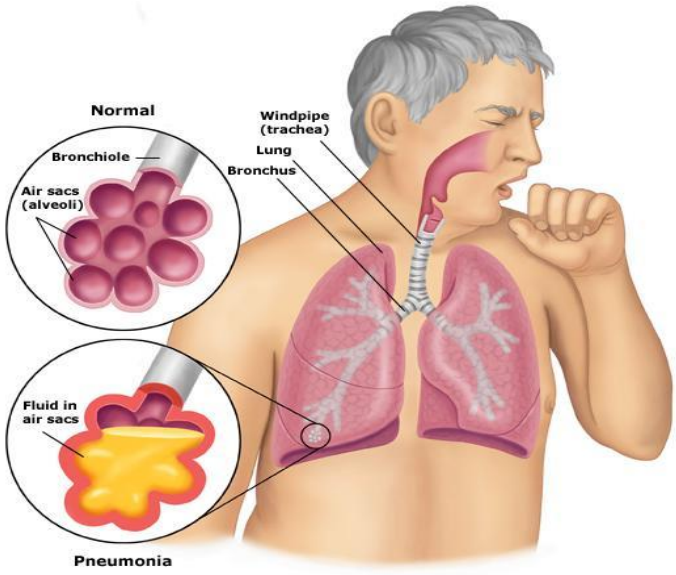
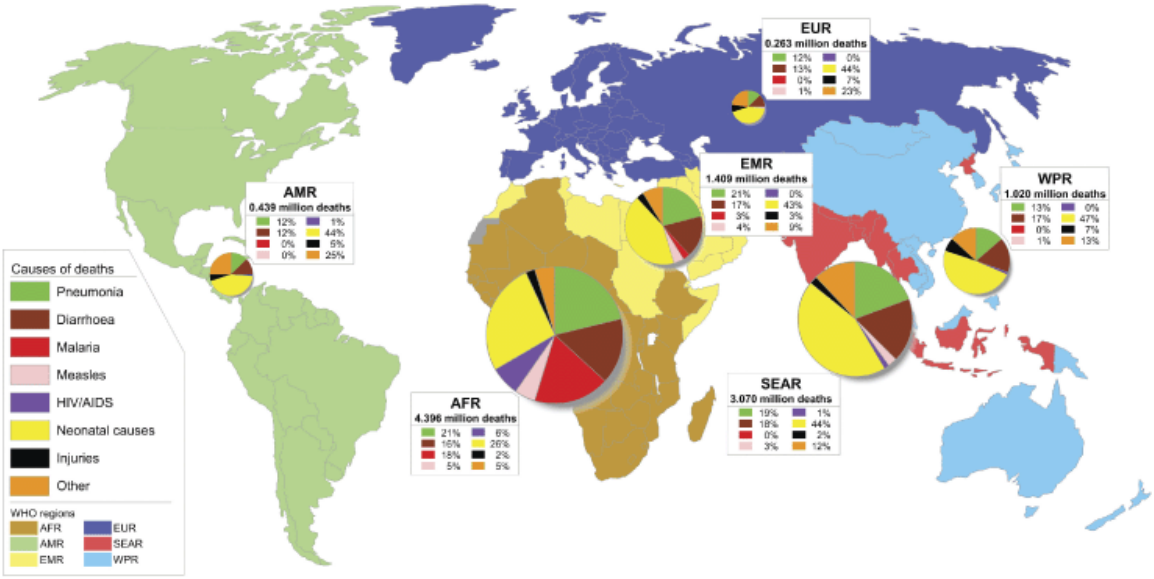


Figure 1. Pneumonia. Normal alveoli compared with the fluid-filled alveoli in a pneumonia patient.
(http://www.uptodate.com/online/content/images/id_pix/Pneumonia_anatomy.jpg, 01/09)

Fig. 2. **Distribution of deaths from pneumonia and other causes in children aged less than 5 years, by WHO region**



AFR, African Region; AMR, Americas Region; EMR, Eastern Mediterranean Region; EUR, European Region; SEAR, South-East Asia Region; WPR, Western Pacific Region.

Figure 2. Deaths from pneumonia in children under 5 years old.
(Epidemiology and etiology of childhood pneumonia)

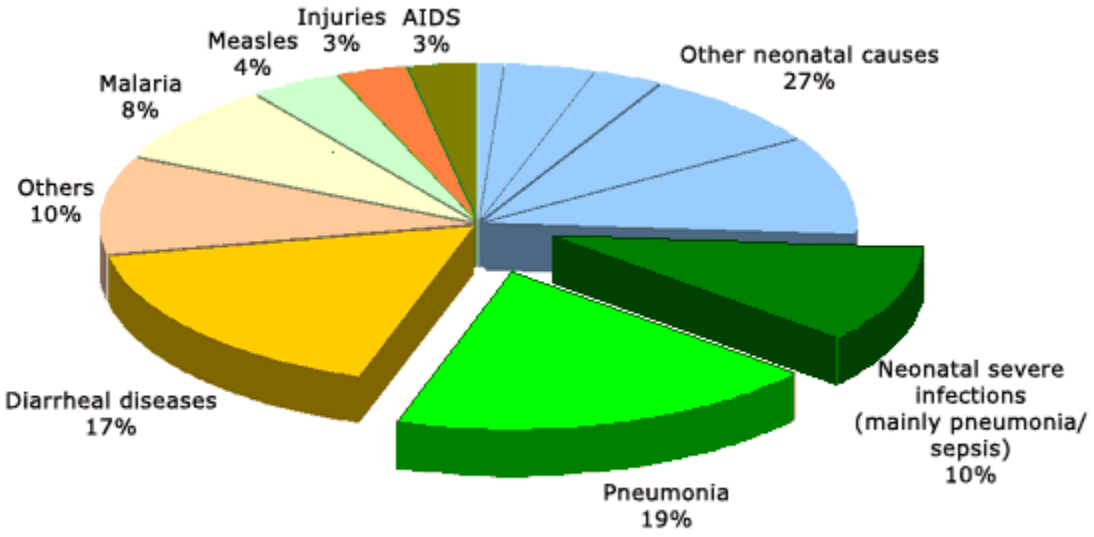


Figure 3. Global distribution of cause-specific mortality among children under five, 2000-2003. Pneumonia accounts for almost 30% of childhood deaths worldwide.
(Child Health Epidemiology Resources Group (CHERG), with additional data from UNICEF)

Detecting a pathogen and linking the pathogen to pneumonia can be difficult. The Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) have established guidelines for community-acquired pneumonia diagnosis [3]. A chest x-ray is required for all patients with suspected pneumonia. Other diagnostic tests are recommended for patients with different circumstances. The recommended diagnostic tests include sputum culture, blood culture, urinary antigen test, thoracentesis, and bronchoalveolar lavage. Though these tests are recommended, they are optional, and it is the physician's responsibility to determine whether or not to perform the tests.

The diagnosis of pneumonia is by "demonstrable infiltrate by chest radiograph or other imaging technique." Unfortunately, in most cases, the chest x-ray is not pathognomonic for determining the infectious pathogen. Thus, other diagnostic tests are necessary to determine how the pneumonia should be treated.

A sputum culture may identify oral bacteria with a gram stain by a microbiology lab. A sputum sample is obtained by a patient coughing into a cup (Figure 4). The sputum sample is then cultured to determine which, if any, bacteria are present. Many people harbor pneumonia-causing bacteria in their upper airway even when they are healthy, as these bacteria are only harmful when in the lower airway (Figure 5). A common sputum sample or nasopharyngeal swab is usually contaminated by organisms harbored in the oral cavity of carriers that may or may not be associated with the disease even when the specimen is of high quality (Figure 6). One study estimates the inaccuracy of sputum gram stain test for pneumococcal pneumonia as 57% sensitivity and 97% specificity in comparison with the final diagnosis [4]. Another study highlights the fact

that many people cannot give a good sample where only 54% of the collected sputum samples were of good quality, and only 14.4% returned a predominant morphotype [5].

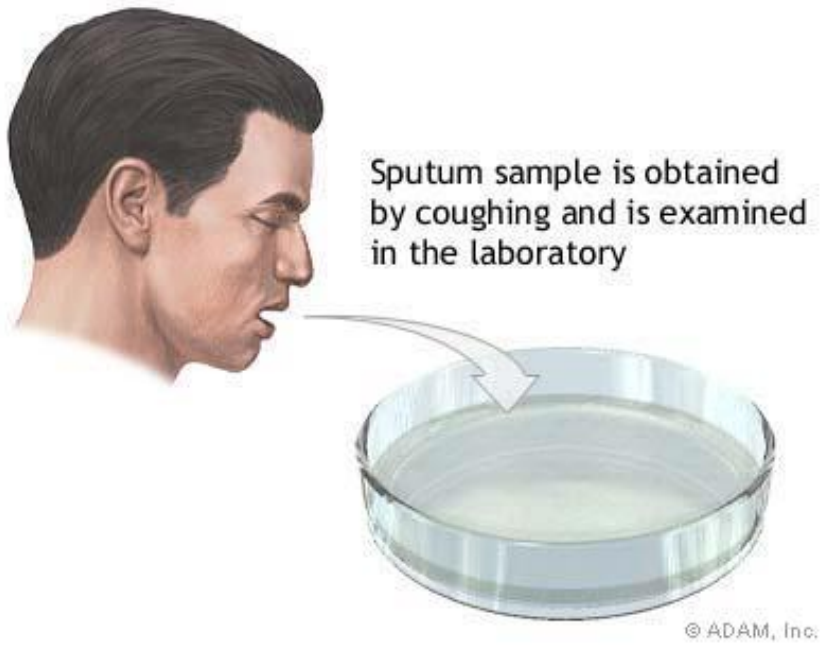


Figure 4. Sputum sample. To collect a sputum sample, the patient coughs into a cup. The sputum is then cultured to see if bacteria are present. *(http://www.nytimes.com/imagepages/2007/08/01/health/adam/9945Sputumtest.html, 02/09)*

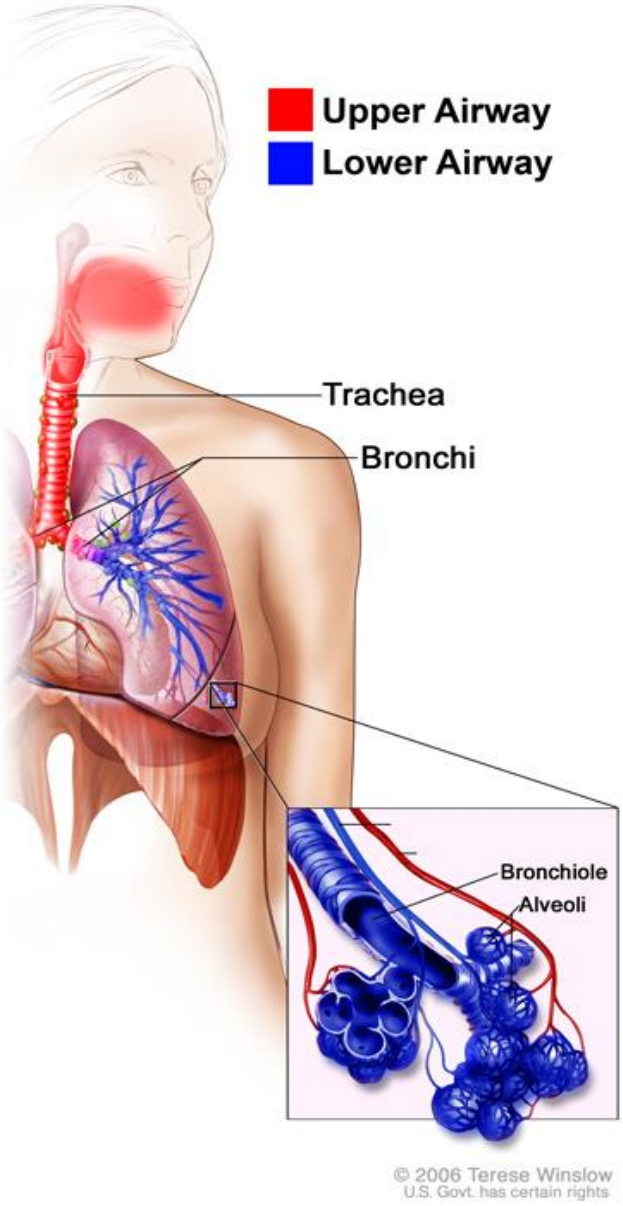


Figure 5. Upper and lower respiratory spaces. The red represents the upper airway, or mouth and trachea, and the blue represents the lower airway, or the alveoli. *(National Cancer Institute)*

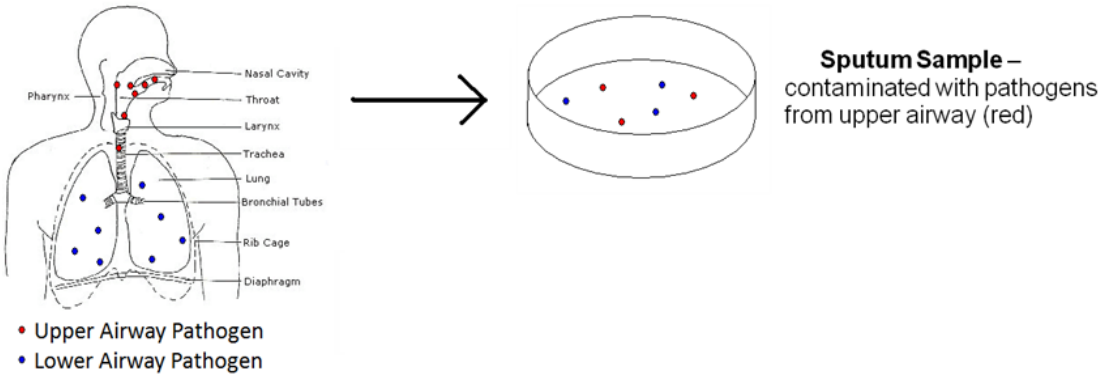


Figure 6. Pathogens collected in a sputum sample. The patient has contaminating bacteria in his upper airway (red), and a different pathogen causing his pneumonia in his lower airway (blue). He coughs into the sputum cup, and the sample includes contaminating bacteria from his upper airway.

Blood cultures are another diagnostic test for pneumonia. The patient's blood is taken and cultured in media, and then, if bacteria are present, it is tested to determine the type of bacteria. However, often in patients with pneumonia, the pathogen has not caused septicemia, so the blood culture's use is limited. One study found that the usefulness and yield of blood cultures increased with Pneumonia Severity Index grade: I-5.3%, II-10.2%, III-10.3%, IV-16.1%, V-26.7% [6]. In another study, only 5.7% of the pneumonia patients had significantly positive blood culture results, and only 1.97% of patients had a change of therapy due to blood culture results [7]. Almost as often as a pathogen is identified from a blood culture, a blood culture is contaminated, resulting in a false positive in 4.8% of pneumonia patients [8]. This can lead to longer hospital stays, and thus increased costs.

Urine antigen and antibody presence is correlated with disease in about 50% of pneumonia cases, but many false positives occur. In one study, the sensitivity and specificity of the urine antigen test in children with pneumococcal pneumonia were 86.7

and 62.9%, respectively, for non-concentrated urine, and were 100 and 11.7%, respectively, for concentrated urine [9]. More often than not, sputum cultures, blood cultures, and urine antigen tests do not return a definitive pathogen for treatment, so the physician is faced with treating the pneumonia without microbiological identification. The widespread use of empirical broad-spectrum antibiotics may not provide proper treatment of many pathogens and is a major cause of the development of resistant bacteria [10].

Specimens obtained directly from the lung, e.g. bronchoalveolar lavage (BAL) (Figure 7), transtracheal aspirates, thoracentesis (Figure 8), or needle biopsy, may identify the etiology of the pneumonia. One study found the sensitivity and specificity of BAL to be 80 and 66%, respectively. The same study found that the BAL results and results from a lung culture taken immediately after death of the patient were completely in agreement 57% of the time [11]. These invasive procedures are difficult and costly to perform and present a risk to the patient.

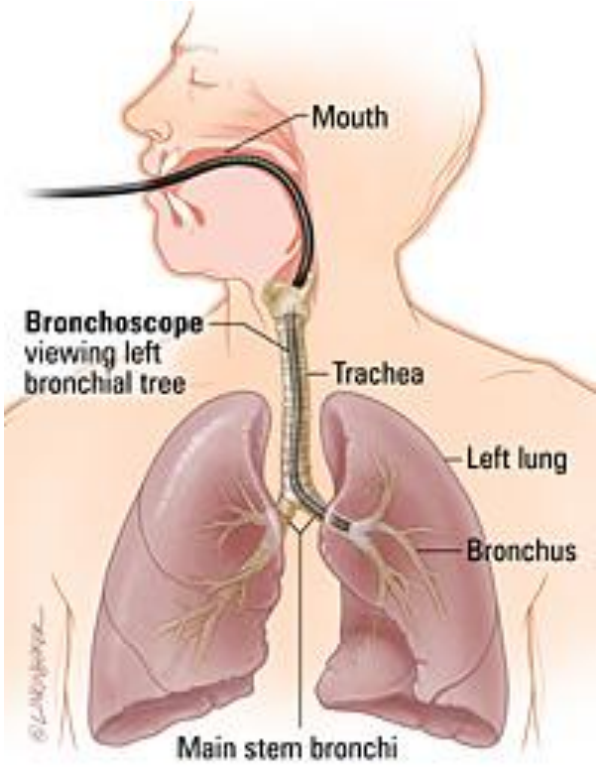


Figure 7. Bronchoalveolar lavage.
(http://www.hopkinscf.org/main/research/researchaz.html, 03/10)

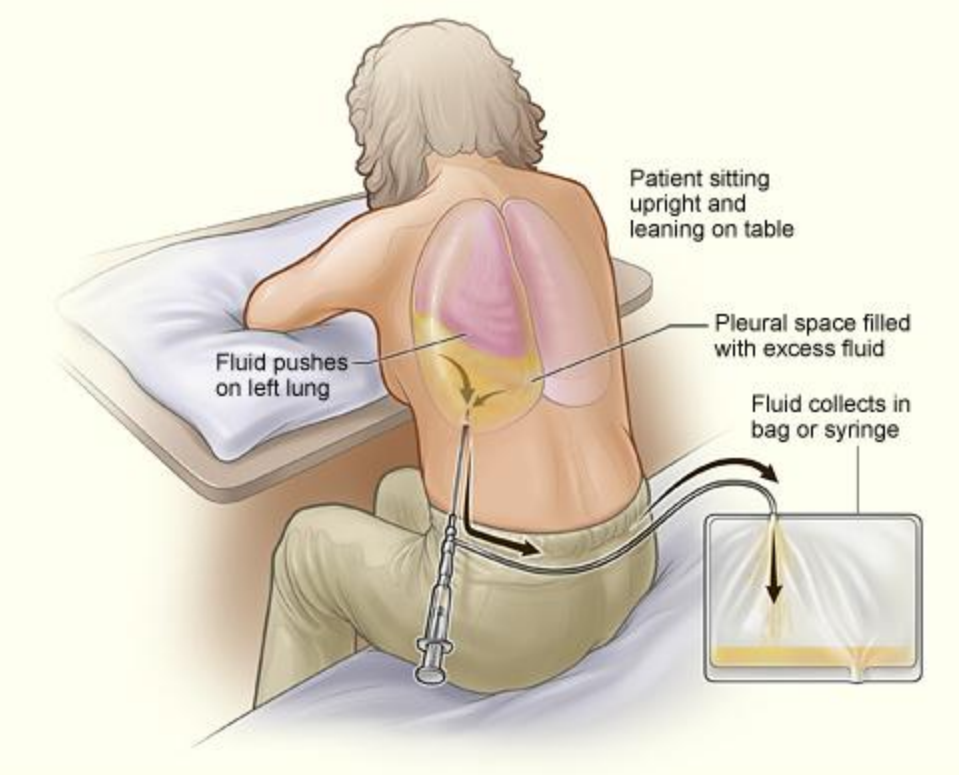


Figure 8. Thoracentesis.
(http://www.nhlbi.nih.gov/health/dci/Diseases/thor/thor_during.html, 02/09)

Diagnosis of some viral causes of pneumonia, e.g. influenza and RSV, may be obtained from an upper respiratory tract specimen such as a throat or nasopharyngeal swab or aspirate. Yet even in patients with positive viral indicators, bacterial super-infection remains an important problem.

Previous studies have demonstrated that lower lung pathogens can be aerosolized during deep coughing while deep exhalation is not as productive [12]. A specimen of the lower lung aerosols during deep coughing could improve treatment of pneumonia, as well as improve our understanding of the epidemiology of the disease. One study suggested that a diagnostic test for acute lower respiratory infections that can be performed with

minimal infrastructure that is 95% sensitive and 85% specific could save the lives of more than 405,000 children under the age of 5 worldwide every year [13]. Each percentage point increase in sensitivity would save an additional 14,000 lives, while each percentage point increase in specificity would save another 8,000 lives [13]. A readily available diagnostic test would have an enormous, global impact on the number of lower lung infection-related deaths in children.

Other devices have been described with the goal of separating the upper airway air from the lower airway air. U.S. patent number 3,544,273, issued to McConnaughey in 1970, describes a T-shaped device which separates the alveolar breath by using a pressure-triggered one-way valve [14]. The pressure-triggered valve will cause the cost of this device to be significantly higher than the cost of the PneumoniaCheck.

U.S. patent number 3,734,692, issued to Lucker in 1973, describes a device comprised of a single input mouthpiece with two outputs which are connected to two non-communicating compartments of a single inelastic bag [15]. The downfall of this design is that both chambers are at the same elevation, allowing for the possibility of liquid matter from the mouth and lungs to contaminate the alveolar sample.

In U.S. patent number 3,858,573, issued to Ryan in 1975, a flow-through device is described in which the entire breath passes through a chamber, but only the last 100 ml is captured [16]. U.S. patent number 5,211,181, issued to Delente in 1993, employs a similar principle, where the upper and lower airway air pass through the collection chamber [17]. Neither of these methods separate the upper airway material from the lower airway material and are thus subject to contamination. U.S. patent number 5,361,772, issued to Murnick in 1994, is a similar flow-through device whose entrance

and exit are shut by the user [18]. This device requires user-interaction, so there is the risk of the user not shutting the entrance and exit at the proper time, allowing upper airway air and aerosols to contaminate the sample.

In U.S. patent number 6,582,376, issued to Baghdassarian in 2003, a device is described which analyzes the carbon dioxide concentration during exhalation to determine when an alveolar sample is being obtained [19]. Similarly, U.S. patent number 4,248,245, issued to Kempin in 1981, uses a temperature sensor to discern when alveolar air has entered [20]. Both methods use sensors, which would increase the cost of the device compared to the PneumoniaCheck.

Many of the above devices utilize complicated valves and sensors. Others require user-interaction. In many of these devices, liquid and solid matter from the mouth can contaminate and overwhelm the lower airway aerosol sample. Some devices claim to sample only the lower airway air yet pass all the upper airway aerosols through the collecting chamber, potentially contaminating the sample.

Currently, there is no sensitive, specific, safe, and effective diagnostic test for pneumonia. The PneumoniaCheck, a new specimen collection device, was designed to selectively sample pathogen-containing aerosols generated from the lower lung during deep coughing and to minimize contaminating material from the oral cavity, according to the following Design Inputs:

1. *Samples only pathogens from lower lung:* The main objective was to selectively sample the pathogens in the lower airway, bypassing the upper airway.

Directly sampling the lungs should give a more accurate diagnosis for pneumonia, so physicians can more effectively treat the patient.

2. *Excludes oral contents:* Another important design objective was to exclude oral contents, including liquids and aerosols. Many people harbor the same bacteria that cause pneumonia in their upper airway and mouth, but the bacteria is harmless there [21]. Should the upper airway and mouth areas be sampled for pathogens, false-positives may occur, leading to the over-prescribing of antibiotics. The mouthpiece (Figure 10 [a]) is designed to help prevent contaminating oral contents from entering the device. It has a ridge as a physical barrier that tells patients how far to put the mouthpiece into their mouth. This helps the patient feel when he or she is using the PneumoniaCheck correctly.

3. *Non-invasive:* To avoid risks such as infection and to decrease possible discomfort for the patient, we wanted our device to be non-invasive. This would make our device competitive with diagnostic tests such as sputum sample cultures and urinary antigen tests.

4. *Collects pathogens on filter:* The PneumoniaCheck is designed to collect pathogens from the lower lungs on a filter (Figure 9) for laboratory determination by microbiology techniques such as culture, immunoassay or Polymerase Chain Reaction (PCR). The device consists of a mouthpiece, liquid trap, Venturi pressure chamber, a ball

valve, a bag reservoir (Westmed, #7-6206) and a collection section. It is shown in Figure 10 with parts labeled.

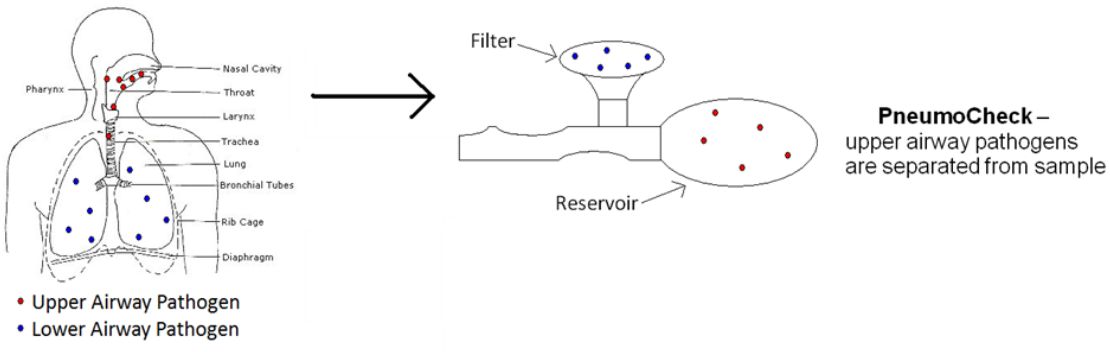


Figure 9. Pathogens collected in the PneumoniaCheck. The patient has contaminating bacteria in his upper airway (red), and a different pathogen causing his pneumonia in his lower airway (blue). He coughs into the PneuoniaCheck. Only bacteria from the lower airway end up on the filter.

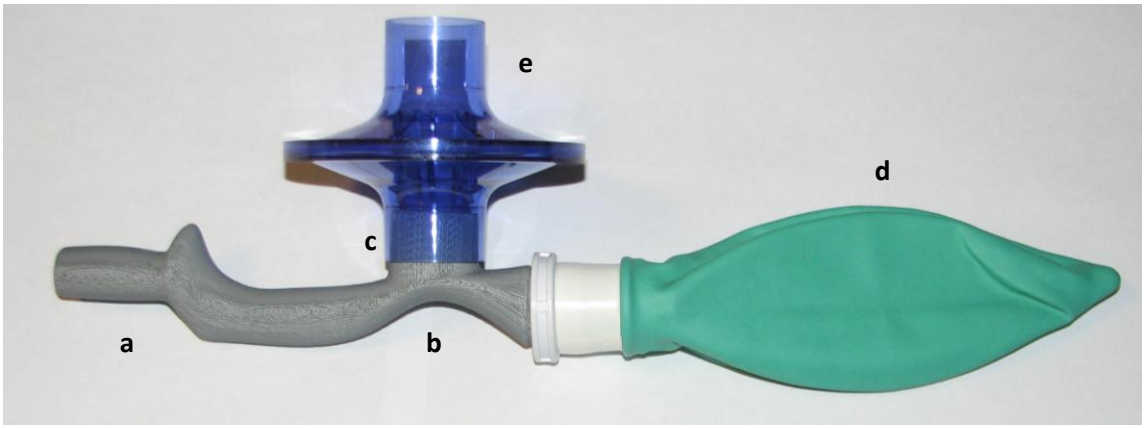


Figure 10. The PneumoniaCheck. The patient coughs into the extended mouthpiece of the device (a). As the air passes through the Venturi (b), the negative pressure in the main tube causes the ball valve (c) to close. Thus, the first flow of air fills the reservoir (d). Once the reservoir is full, the backpressure then forces the rest of the air to flow past the ball valve and through the filter (e).

5. *Excludes oral contents even during non-ideal conditions:* The expiratory flow rate of patients with pneumonia can drop to half that of a healthy person [22]. The PneumoniaCheck should function correctly even at a lower flow rate. Patients also may hold the device slightly incorrectly, and this should not affect the functionality of the device.

The liquid trap is located between the mouthpiece and the filter tube. The PneumoniaCheck is designed in such a way that any liquids that enter the device through the mouthpiece will hit a barrier and slide down into the liquid trap. The liquid trap doubles as the handle for the device.

A Venturi valve is located directly below the tube leading to the filter (Figure 10 [b]). The Venturi valve is designed to create a negative pressure in the filter tube, causing the ball valve (Figure 10 [c]) to close. This should close off the filter tube so the first flow of air, that from the upper respiratory tract, fills the reservoir (Figure 10 [d]).

Once the reservoir is full, the back pressure should force the ball valve to open, and the remaining flow of air, from the lower airway, will pass through the filter (Figure 10 [e]).

The patient will inhale deeply and put the mouthpiece in his mouth until his lips touch the ridge on the device. Then, he will deep cough into the PneumoniaCheck and exhale completely. Multiple coughs into the device per inhale are acceptable, but the patient must be sure not to inhale again until his mouth is removed from the mouthpiece, or pathogens on the filter may come loose and re-enter the patient's airway. After each cough, the patient will remove the device from his mouth and squeeze the air out of the

reservoir. For the same reasons the first flow of air does not pass through the ball valve, the air from the reservoir will exit the device through the mouthpiece only.

Unlike the BAL or other previously patented devices, the PneumoniaCheck is simple, easy to use, and successfully separates the upper and lower airway air without complicated valves, sensors, or active user control.

The purpose of this thesis is to show whether or not the PneumoniaCheck functions as it is supposed to. Nine verification tests were performed to test if the device selectively samples the lower lung while excluding oral contents, and whether or not the filter collects aerosols. This thesis also evaluates different manufacturing methods for the PneumoniaCheck, which will lead to a manufacturing method recommendation.

CHAPTER 2: METHODS FOR VERIFICATION TESTING

The PneumoniaCheck is designed to 1) sample and collect lower lung aerosols during deep coughing; 2) selectively exclude upper airway gas from the collection chamber; and 3) exclude oral contents, both watery liquids and viscous sputum solids. The proper use of the device requires the patient to deep cough into the device and continue exhaling residual air in the lungs. Coughing and sneezing have been shown to aerosolize lower lung pathogens, whereas exhalation alone produces very few lower lung particles [12].

The US Food and Drug Administration (FDA) defines verification as "confirmation by examination and provision of objective evidence that specified requirements have been fulfilled" [23]. The FDA requires verification that the design output meets the design input (Figure 11). Several verification tests were created to demonstrate each of these design inputs (Table 1). Four lower airway aerosol separation tests are described first, then four oral exclusion tests, and then a filter collection test.

There were five participants total. Two of the participants were male, and three were female. They were all graduate students at the Georgia Institute of Technology between the ages of 21 and 30. The majority of the verification tests were done by one participant. The Georgia Institute of Technology Institution Review Board approved the tests on human subjects as IRB Protocol H08353.

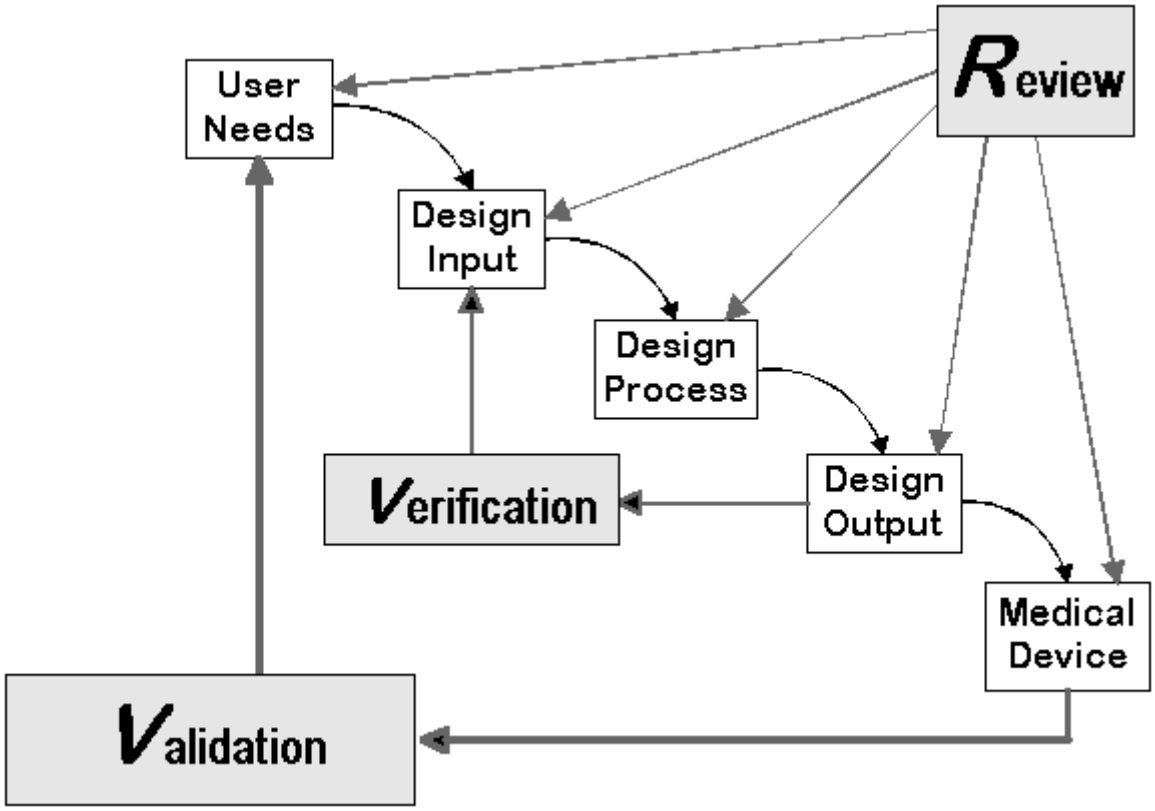


Figure 11. Application of design controls to design process. The FDA requires verification showing that the design outputs meet the design inputs. (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070627, 03/10)

Table 1. Design Inputs and their corresponding Verification Tests

Design Input	Verification Test
1. Samples only pathogens from lower lung	2.1 Oxygen Separation Test 2.2 Lower Airway EtOH Separation Test 2.4 Venturi Test
2. Excludes oral contents	2.5 Mouthpiece Test 2.7 Phlegm Exclusion Test 2.8 Trap Test
3. Non-invasive	
4. Collects pathogens on filter	2.9 Filter Collection Test
5. Excludes oral contents even during non-ideal conditions	2.3 Minimum Flow Test 2.6 Angle of Mouthpiece Test

2.1 Oxygen Separation Test

Oxygen absorption by blood occurs only in the lower airway (alveoli), and not in the upper airway (mouth, trachea). Air from the lower lung should have an oxygen content about 16%, as compared with room air of about 21% [24]. Participants cough into the PneumoniaCheck, exhaling all residual air in the lungs. The oxygen content from the upper airway air in the reservoir is tested and compared with the oxygen content of the lower airway air collected in a large collection bag connected to the filter tube. The percentage of oxygen in each sample is measured with an oxygen meter (Teledyne Analytical Instruments, Model # GB 300). The experiment is repeated ten times with statistical significance defined at the $p<0.05$ level.

A second test variation is performed to assess the function of the ball valve. The Oxygen Separation Test is performed without the ball valve to quantify the effect of the ball valve on the separation of lower airway samples from upper airway oxygen content.

2.2 Lower Airway EtOH Separation Test

A second test independently establishes the direct ability of the device to sample molecules produced only in the lower lung. Ingested ethanol appears 20 minutes later in the blood stream and becomes volatile in the alveolar space, not in the upper airway. For high blood alcohol levels, lower airway samples should reflect this high level, whereas oral levels should be low since there is no blood-gas exchange in the mouth. The lower aerosol alcohol content can then be compared with upper airway aerosol content to demonstrate the specific sampling of lower lung aerosols.

A pair of 0.02% breath alcohol testers (Advanced Safety Devices) are connected to the PneumoniaCheck as shown in Figure 12. The participant is asked to drink 50 proof alcohol, 60 ml for females and 80 ml for males. The participant is then asked to rinse the mouth with water, but is not allowed to swallow the water. After 20 minutes, the participant drinks an 8oz glass of water and then deep coughs and exhales all residual air into the PneumoniaCheck. The Testers are removed from the device and the color changing crystals are allowed to develop for 2 minutes. The paired breath alcohol testers are photographed. The colors of the testers in the photograph are analyzed with Gimp photo editing software (http://www.gimp.org/), and the quantitative saturation and blue levels are measured.

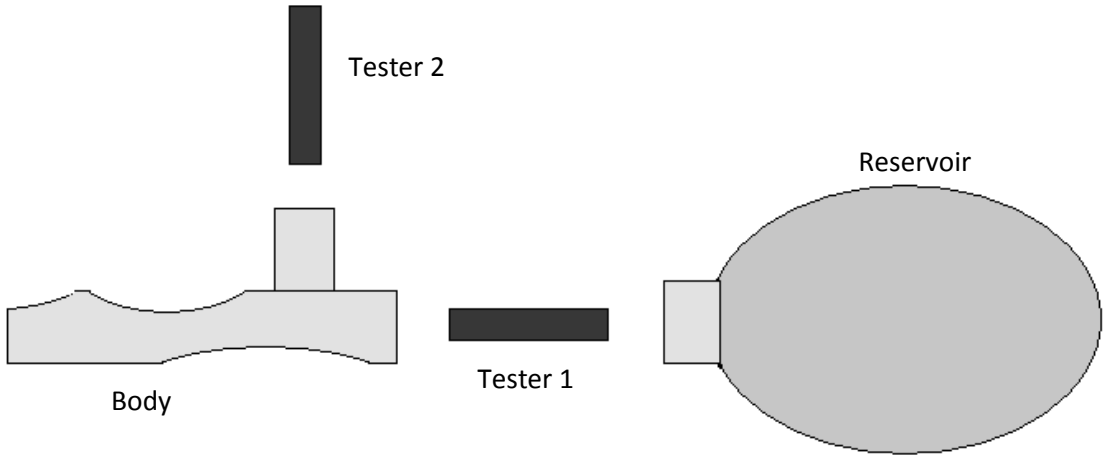


Figure 12. Placement of blood alcohol testers of EtOH testing. Tester 1 samples the upper airway gas and Tester 2 samples the lower airway gas reflecting volatiles released by the blood in the alveolar space.

As a control, a second reservoir is used to restrict the volume of lower airway aerosols through Tester 2. The participant coughs and exhales residual air into the PneumoniaCheck. After 2 minutes, the breath alcohol tester with restricted volume is photographed and analyzed with Gimp software.

2.3 Minimum Flow Test

The device may be affected by varying flow rates and coughing pressures with disease. The device should function at low flow rates seen in restrictive airway disease. There is a minimum volumetric flow rate, Q, below which the exhalation will not produce enough pressure to fill the reservoir completely. For normal pulmonary function, forced expiration yields a flow rate of greater than 1.0 liters/second (l s^{-1}). However with pathologic restrictive disease, forced expiratory flow rates may fall to 0.5 l s^{-1} [22]. The reservoir should then inflate with flow rates less than 0.5 l s^{-1}.

The minimum flow rate is measured for bag reservoir filling. Participants deep cough into a known reservoir volume. Exhalation flow rate is measured by the amount of time it takes to fill the reservoir (Q = volume/time). Participants deep cough into the PneumoniaCheck with the same flow rate, and the reservoir inflation is measured with decreasing flow rates until the bag no longer inflates.

2.4 Venturi Test

The PneumoniaCheck is designed with a Venturi to ensure that the first flow of upper airway aerosols enters the reservoir and not the filter. A test was devised to demonstrate the proper functioning of the Venturi in creating a negative pressure in the collection chamber leading to the filter. The ball valve and green reservoir are removed, and the filter is replaced with a thin plastic bag filled with 50 ml of air. Deep coughing into the device should cause the thin bag to deflate. Participants deep cough into the device with the 50 ml plastic bag attached, and the direction of flow through the Venturi is quantified by the time required to deflate the bag.

2.5 Mouthpiece Test

The extended mouthpiece is designed to keep oral liquids out of the device better than a mouthpiece that is placed in front of the teeth. The average person has a daily salivary output of 1500 ml, including both major and minor salivary glands [25]. An average saliva production of less than 5 ml should occur in the 5 minutes of normal sampling. According to Lagerlof and Dawes, the average volume of saliva in the mouth before swallowing is 1.19 ml for men and 0.96 ml for women [26]. Thus, the range of salivary output during the use of the PneumoniaCheck is 1-5 ml. Therefore, the mouthpiece should successfully keep 5 ml of water from the mouth out of the device.

The device is tested in the correct position and compared with an incorrect position with the lips at the edge of the opening of the mouthpiece. After placing a set volume of water in his or her mouth, the participant deep coughs into the device, exhaling all residual air, and the amount of liquid that enters the device is measured and recorded. Initial oral volumes of 5, 7.5, 10, and 15 ml of water are used. The experiment is repeated for a total of three measurements for each initial volume of water.

2.6 Angle of Mouthpiece Test

A potential risk of use of the device is that the patient will hold the device at an incorrect angle. This test measures the amount of water entering the device when it is held at 45 degree angles from the perpendicular to the plane of the face (Figure 13). The participant holds 5 ml of water in the mouth. With the mouthpiece positioned correctly, the PneumoniaCheck is held at an incorrect angle. The amount of water that enters the device is measured and recorded. These steps are repeated with 7.5, 10, and 15 ml of water. Then, for each volume of water that started in the participant's mouth, the steps are repeated at different angles. The device should exclude oral contents even with mal-positioning of the mouthpiece.

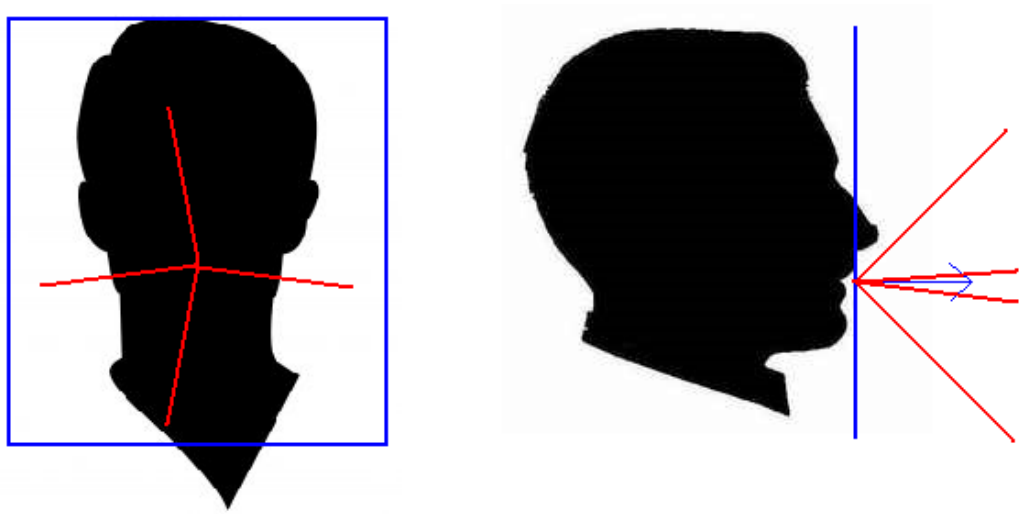


Figure 13. Placement of the PneumoniaCheck during the Angle of Mouthpiece Test. The blue represents the plane of the face, and the red shows the angles at which the PneumoniaCheck was held during the test.

2.7 Phlegm Exclusion Test

The PneumoniaCheck should prevent upper airway sputum/phlegm to reach the filter.

A 2.5 ml volume of viscous solid jelly is used as a surrogate for phlegm in the oral cavity. The participant places the volume of jelly in his or her mouth and deep coughs into the device, exhaling all residual air, with proper and improper mouthpiece placement. The amount of jelly on the filter of the PneumoniaCheck is measured and recorded. This amount is compared to the control of expectorating the jelly sample directly into a sputum cup.

2.8 Trap Test

As a second guard against liquid contamination, a trap is incorporated into the device. Should any oral saliva actually enter the mouthpiece and into the device, some of that material should be trapped in the device and not in the collection chamber. As noted

above, the volume of saliva in the mouth before swallowing is 1.19 ml for men and 0.96 ml for women [26]. A volume of water is placed in the participant's mouth, and he or she deep coughs into the PneumoniaCheck, forcing all the water from the mouth into the device. The volume of material contained in the trap is measured after successively larger oral volumes of 1, 2, 3, and 4 ml of water. The experiment is repeated three times for each initial oral volume.

2.9 Filter Collection Test

The PneumoniaCheck is designed to be used with VBMax filters from A-M Systems, Inc. A Bacterial Filtration Efficiency Test and a Viral Filtration Efficiency Test are performed on the filter by the supplier. Both test procedures were adapted from ASTM F2101. The bacterial filtration efficiency test uses the challenge organism *Staphylococcus aureus* (procedure number STP0009 Rev 02). The viral filtration efficiency test uses bacteriophage φX174 as the challenge organism (procedure number STP0010 Rev 03). (Test information available upon request from A-M Systems, Inc., Carlsborg, WA.)

CHAPTER 3: RESULTS OF VERIFICATION TESTING

3.1 Oxygen Separation Test

The results of the Separation Test of the oxygen values in the collection chamber versus the reservoir bag are graphed in Figure 14. The average percentage of oxygen in lower airway sample through the filter was 15.9%, whereas the average upper airway sample (green reservoir) was 18.4%. The average percentage of the room air oxygen was found to be 20.9%. The lower airway sample was statistically lower than the upper airway sample or the room air with a p-value of <0.0001, n=10. From this data, we conclude that the device selectively samples the lower airway aerosol content that is separate from the higher oxygen content present in the upper airway gas.

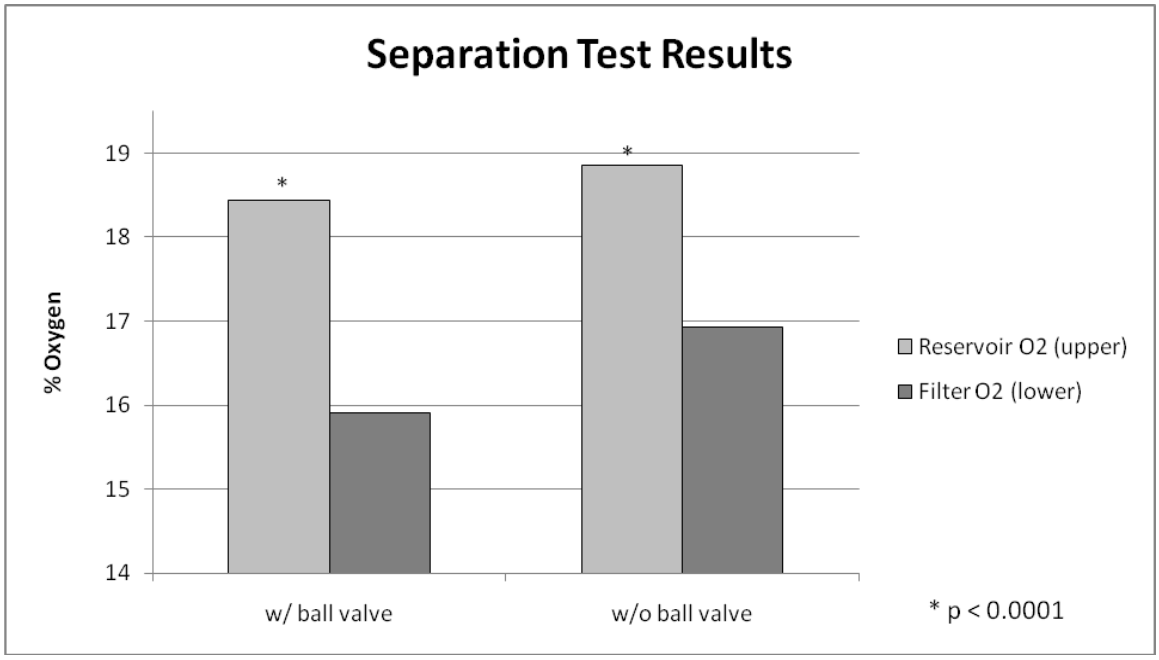


Figure 14. Separation Test results. Graph depicting differences in oxygen content in samples from the upper and lower compartments. The device is tested with and without

the ball valve for gas separation. The differences in oxygen content between the reservoir and collection chamber were statistically different to the $p<0.0001$ level, both with and without the ball. The difference in oxygen content in the lower airway chamber with and without the ball was also significant to the $p<0.0001$ level.

The experiment was then repeated without the ball valve in place. The average percentage of oxygen in the lower airway sample was 16.9% compared to the upper airway sample of 18.9% ($p<0.0001$). The percentages of oxygen in the bag attached to the filter tube with and without the ball valve were compared. The average percentage of oxygen in the lower airway sample with the ball valve was 15.9% and without the ball valve was 16.9% ($p<0.0001$). Thus, the valve has a quantitative effect on the amount of separation, but is not mandatory for separation.

3.2 Lower Airway EtOH Separation Test

EtOH from the blood will volatilize substantially from alveolar exchange only in the lower lungs. The lower and upper airway samples were tested for alcohol content. The color values (saturation and blue) of the lower airway breath alcohol testers versus the upper airway breath alcohol testers were analyzed and compared (Figure 15). In all cases, the lower airway samples changed in color, whereas the upper airway samples did not. The differences resulted in p-values as follows: saturation – $p = 0.0015$; and blue – $p = 0.0019$. As a control, the reservoir volume was separately tested to assure that this volume was enough to covert the colorimetric crystals (Figure 16). Since these two color values of the alcohol crystals were significantly different, we conclude that the PneumoniaCheck successfully samples the volatiles generated in the lower airway separately from the upper airway.

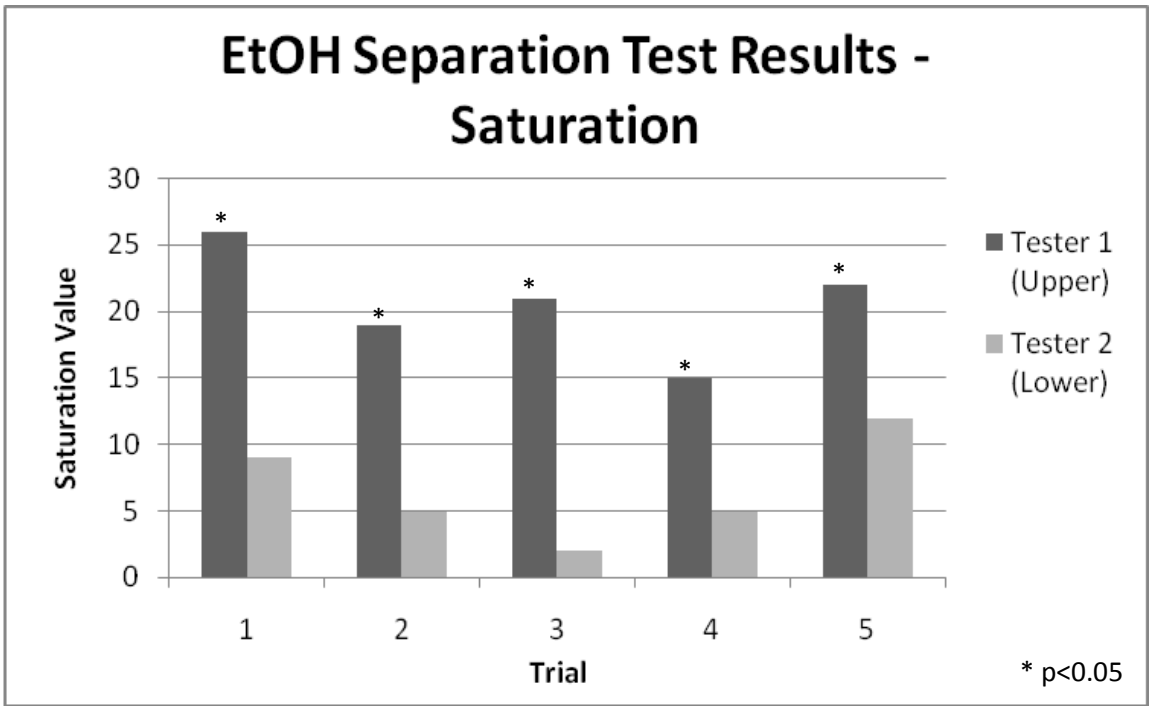


Figure 15. EtOH Separation Test results – Saturation. The saturation values for each tester per trial. A low saturation value indicates the presence of ethanol.

Figure 16. Measured volume results from the blood alcohol experiment. The tester on top is unused. The middle tester is the measured volume tester (MV), and the tester on the bottom (F) is a tester that was triggered when it was attached to the filter tube. The crystals in the control tester are very yellow, and the crystals in the MV and F testers are white.

3.3 Minimum Flow Test

The results of the Minimum Flow Test are shown in Figure 17, which plots the volume of the reservoir that was filled with exhalation for different volumetric flow rates. As the flow rate increases, the volume of the reservoir that is filled increases until it plateaus at 150 ml. The lowest volumetric flow rate that will completely fill the reservoir is approximately 0.1 l s^{-1}. This is well within the required 0.5 l s^{-1} flow rate for proper functioning of the device.

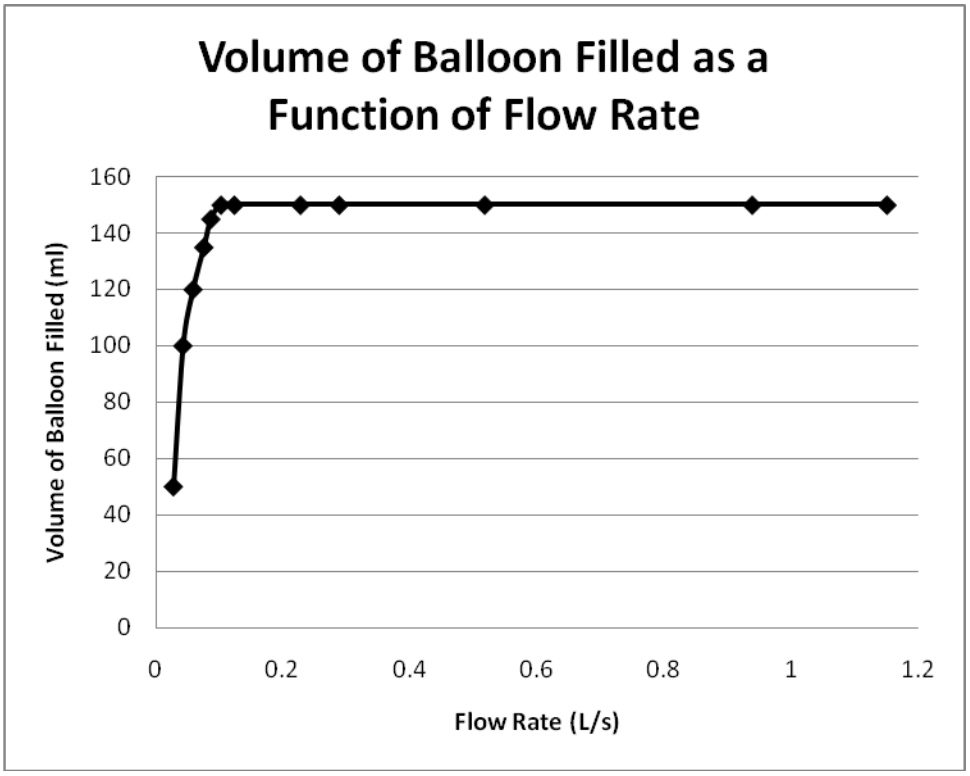


Figure 17. Minimum Flow Test results. Graph depicting the volume of reservoir filled at different exhaling flow rates. The reservoir fills completely at a minimum flow rate of approximately 0.1 l s^{-1}.

3.4 Venturi Test

With every deep cough and exhalation, the 50 ml bag attached to the filter tube fully deflated over an average of 1.25 +/-0.25 s. Table 2 shows the results of the Venturi test illustrating deflation of the filter bag. Thus, the Venturi creates a negative pressure in the filter tube. The results demonstrate that the device prevents the initial upper airway gas from passing through the collection chamber during deep coughing.

Table 2. Venturi Test results

n	Time (s) *
1	1.47
2	0.93
3	1.6
4	1.07
5	1.2
AVERAGE:	**1.25 +/- 0.25**

*Time to deflate bag over filter while blowing through device.

3.5 Mouthpiece Test

When the mouthpiece was correctly positioned, no water entered the device, even when the amount of water starting in the mouth increased to 15 ml as is illustrated in Figure 18. With incorrect positioning of mouthpiece in front of the teeth, much of the water from the mouth entered the device. Thus the designed mouthpiece effectively prevents volumes up to 15 ml of oral liquids from entering the device, well over the 5 ml design specification.

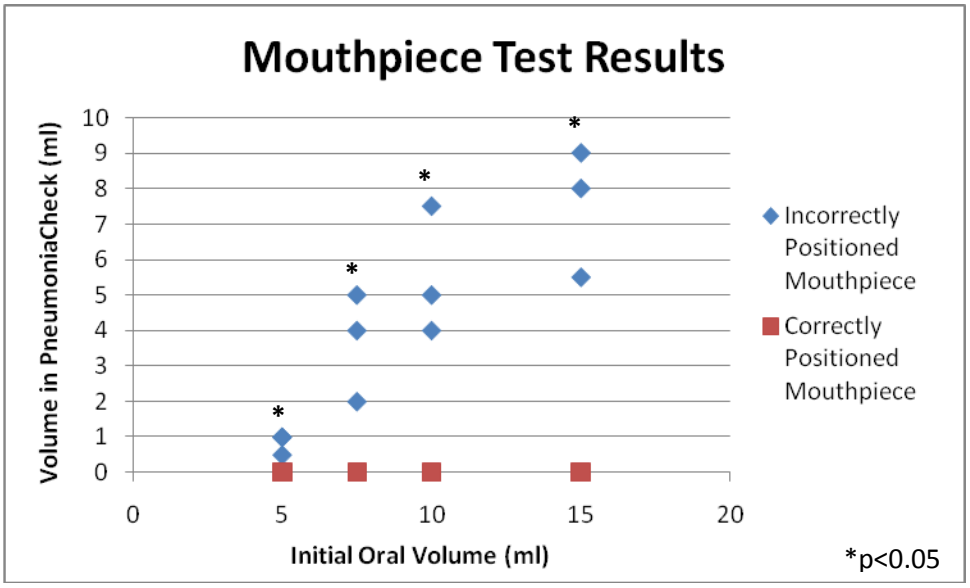


Figure 18. Mouthpiece Test results. Graph showing the volume of water entering the PneumoniaCheck for a correctly and incorrectly positioned mouthpiece at different initial oral volumes. The mouthpiece positioned correctly successfully keeps out 15 ml of mouth liquids.

3.6 Angle of Mouthpiece Test

The Angle of Mouthpiece Test evaluates user error in placement of the device. When the device is placed 45 degrees from the perpendicular to the plane of the face in any direction, no liquid enters the device, as long as the mouthpiece is positioned correctly with the lips at the ridge on the mouthpiece and the opening behind the teeth.

3.7 Phlegm Exclusion Test

The results of the Phlegm Exclusion Test are shown in Table 3. For all trials except one, no jelly ended up on the filter of the PneumoniaCheck; when jelly did end up on the filter, it was a very small amount (less than 1% of the starting amount). For all trials, all 2.5 ml of the jelly from the participant's mouth ended up in the sputum cup

($p<0.0001$, unpaired t-test). Thus, the device is shown to effectively exclude up to 2.5 ml of phlegm-like material from the sample collection.

Table 3. Phlegm Exclusion Test results.

Trial	Volume in Sputum Cup (ml)	Volume on PneumoniaCheck Filter (ml)
1	2.5	0
2	2.5	0
3	2.5	0
4	2.5	0
5	2.5	0.01

3.8 Trap Test

With a starting oral volume of 1 ml of liquid, 0.5 ml of liquid ended up in the liquid trap after the deep cough. The results of the Trap Test are shown in Table 4. The liquid trap effectively captures 0.5 to 0.8 ml of oral liquids from reaching the outlets of the device during deep coughing.

Table 4. Trap Test results showing that the design traps some oral contents.

Initial Oral Volume (ml)	Volume of Water in Liquid Trap (ml)			
	Trial 1	**Trial 2**	**Trial 3**	**Average**
1	0.5	0.5	0.5	**0.5**
2	0.5	0.75	0.5	**0.58**
3	0.5	0.5	0.75	**0.58**
4	1	0.5	0.5	**0.67**

3.9 Filter Collection Test

The VBMax filter was tested for capture of a mean particle size of 3.1 µm and reported as a Bacteria Filtration Efficiency. The average BFE was found to be 99.99977%. For the Viral Filtration Efficiency, the average filtration efficiency was calculated as 99.9975% with a mean particle size of 2.8 µm. With a filtration efficiency of greater than 99.99% for both bacteria and viruses, the A-M Systems, Inc. VBMax filter works well to capture bacterial and viral pathogens in aerosols. Further, PCR analysis can detect and identify bacterial DNA collected from human subjects on the filter samples from PneumoniaCheck [27-28].

A summary of the results can be found in Table 5.

Table 5. Overall results of the Verification Tests

Design Input	Verification Test	Pass?
1. Samples only pathogens from lower lung	2.1 Oxygen Separation Test 2.2 Lower Airway EtOH Separation Test 2.4 Venturi Test	Yes Yes Yes
2. Excludes oral contents	2.5 Mouthpiece Test 2.7 Phlegm Exclusion Test 2.8 Trap Test	Yes Yes Yes
3. Non-invasive		Yes
4. Collects pathogens on filter	2.9 Filter Collection Test	Yes
5. Excludes oral contents even during non-ideal conditions	2.3 Minimum Flow Test 2.6 Angle of Mouthpiece Test	Yes Yes

CHAPTER 4: MANUFACTURING CONSIDERATIONS

Several different manufacturing options were considered for manufacturing the PneumoniaCheck. Rapid prototyping, vacuum molding, and injection molding were the top three choices.

4.1 Rapid Prototyping

Rapid prototyping uses additive manufacturing technologies to build a 3D part layer by layer. Some examples of rapid prototyping include stereolithography (SL) and 3D printing. Stereolithography uses photo-curable resin and a laser. The laser cures the resin a thin layer at a time, until the part is built. 3D printing involves laying material down layer by layer. This can be accomplished by laying an adhesive down in the shape of the layer and then allowing a fine powder to stick to it or by depositing a thin layer of polymer to form the shape of the layer.

Advantages of rapid prototyping are that there are no tooling costs and there is very little lead time. Disadvantages of rapid prototyping are that it usually is not a good option for large numbers of parts, and that, for large orders, it is typically more expensive than other manufacturing options.

Since we are looking to manufacture the PneumoniaCheck in numbers in the thousands, rapid prototyping is not a good option. However, we have used rapid prototyping, both SL and 3D printing, to make 3D models of the different PneumoniaCheck designs along the way.

4.2 Vacuum Molding

Vacuum molding is a process that involves heating a sheet of plastic, draping it over a mold, and then using a vacuum to form the plastic to the mold (Figure 19). The molded plastic is then cooled and removed from the machine. As a final step, the excess plastic is trimmed away.

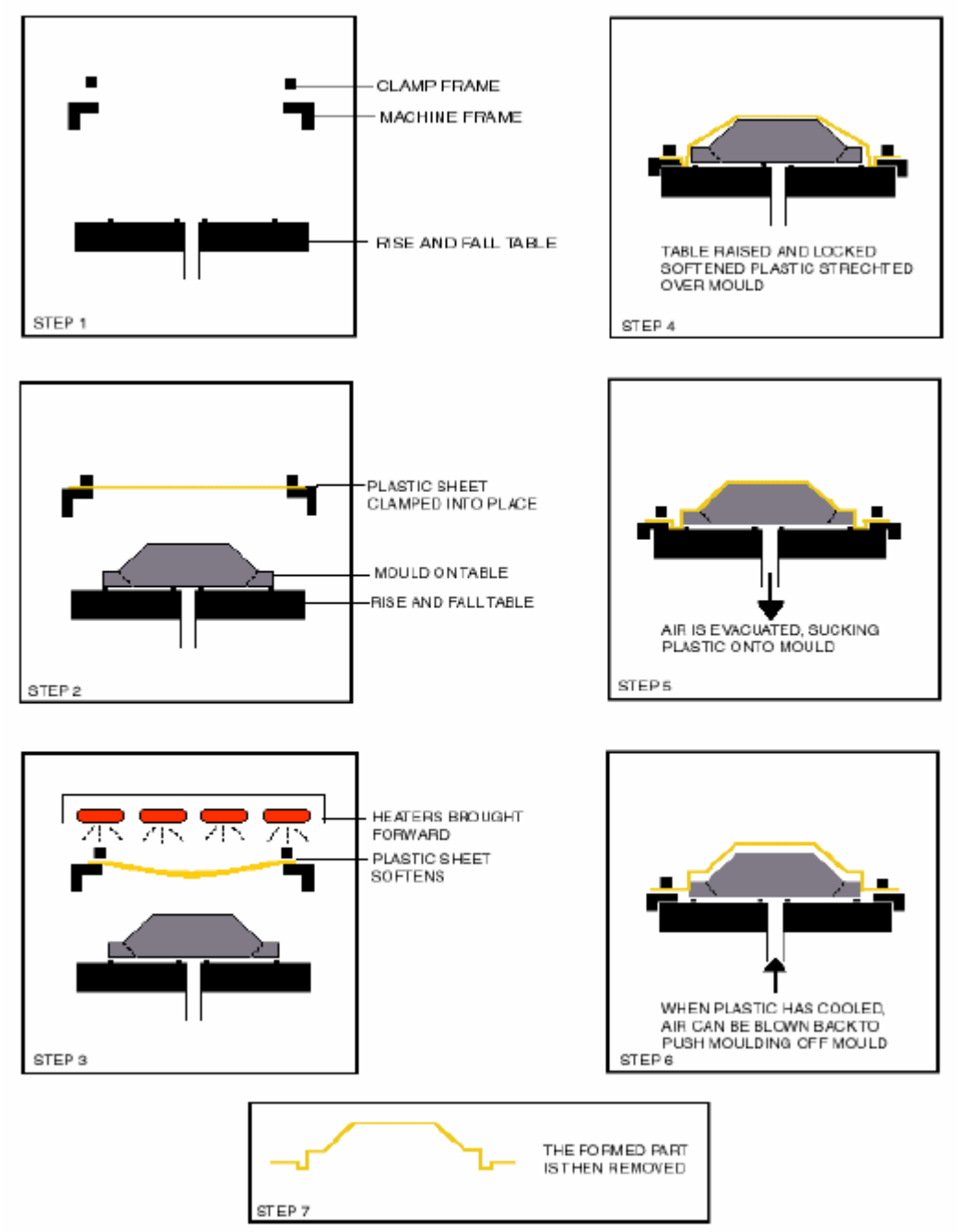


Figure 19. The steps of vacuum molding. Step 1 shows the parts of the machine, including the clamp, the frame, and the table. In Step 2, the sheet of plastic is clamped to the frame. The heating element is brought close enough to the plastic sheet to soften it in Step 3. Step 4 shows the frame and the heated plastic being draped over the mold. In Step 5, a vacuum is enabled, forcing the plastic sheet to form around the mold. Then, in Step 6, air is blown under the mold to push the plastic form off of the mold. Step 7 shows the final plastic part.
(http://isites.harvard.edu/fs/docs/icb.topic604638.files/FormechVacuumGuide.pdf, 02/10)

Advantages of vacuum molding include low cost tooling and short lead times [29]. Molds can be made from lower cost materials, since the relatively low pressure of the vacuum doesn't require the mold strength that other manufacturing processes do. A reduction in mold fabrication time causes the shorter lead times. Vacuum molding can also economically support larger molds that would be too expensive otherwise. On the other hand, the excess material that is trimmed away after the vacuum molding process is useless and is wasted.

The PneumoniaCheck could be vacuum molded in halves. Once each half was molded, they could be assembled with glue, chemicals to fuse the two halves together, or with heat. However, a lip of plastic would be required for the seam to connect the two halves. If the lip of plastic is positioned on the outside of the device mouthpiece, it could be uncomfortable for patients, and might cut their lips and mouth. If the device were cut in half along a vertical plane, the seam would also not allow the filter to fit correctly on the filter tube. The molds could be designed in such a way that, once assembled, the lip would be on the inside of the device, but this would disrupt the flow of the air through the device.

4.3 Injection molding

Injection molding is a process involving melting plastic and forcing it into a mold. There are five steps to injection molding [30]:

1. Mold filling: Melted plastic flows into the closed mold through the sprue, the runners, the gates, and then into the cavity.
2. Packing: The melted plastic is compressed with high pressure to ensure that the mold is filled completely.

3. Holding: The melted plastic remains in the mold under high pressure to compensate for shrinkage as the part cools slightly due to the cool mold. The pressure is maintained until the gate solidifies.
4. Cooling: The part cools off inside the mold.
5. Part Ejection: Once the mold opens, the part is ejected from the mold (usually from the core side of the mold) using ejector pins or a similar mechanical ejector.

There are some generally accepted design guidelines for injection molding [31]. First, the part must be designed with uniform wall thickness. If wall thickness is not uniform, sinks may occur in thicker areas due to uneven cooling. Second, the material and wall thickness should be chosen to minimize cost. Parts designed to be made from a more expensive material that has greater strength or stiffness can have thinner walls, which will reduce material cost and cycle time, thus offsetting the material cost increase. Third, projections from the main wall should have a thickness of between one-half and one-third the main wall thickness. This should eliminate any cooling problems due to thickness where the projection and the main wall meet. Next, projections should be aligned perpendicular to the parting plane, if possible. This will eliminate the need for complicated mechanisms in the mold. And finally, screw threads should be designed so they lie in the molding plane, if possible.

The walls of the PneumoniaCheck are thicker around the Venturi and the filter tube. In order to avoid sinks, the device will need to be redesigned. To keep the body shape the same, projections in compliance with the third guideline could be added to replace the thick section of the device around the Venturi.

The PneumoniaCheck could be cut in half and injection molded in parts and then assembled. The PneumoniaCheck could be cut in half in the vertical plane (Figure 20) and injection molded. A simple two-part mold would work for this design. A two-cavity family mold would be efficient; the left and right sides of the device could be molded at the same time. The device could also be cut with horizontal planes. A single horizontal plane would not work, because there would be undercuts (Figure 21). The cavity and core plates of the mold can align along several different planes, so we can cut the PneumoniaCheck with a variety of horizontal planes (Figures 22 and 23). Cutting the device along these planes eliminates undercuts, but the mold would be more complicated: a core would be required to mold the filter tube.

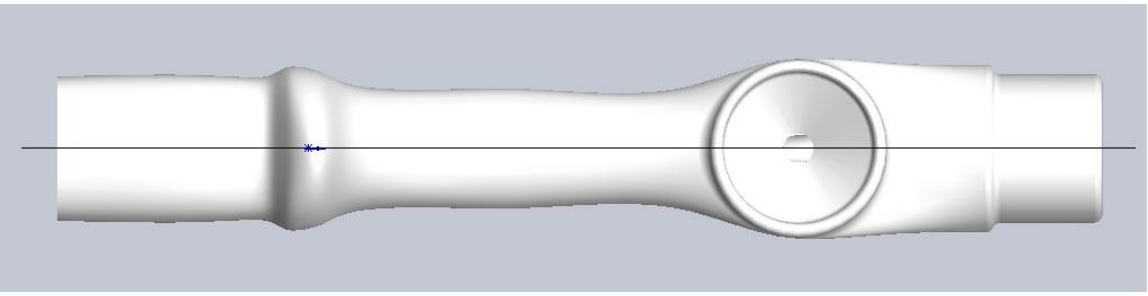


Figure 20. The PneumoniaCheck cut in half along the vertical plane. This is one way to cut the device in half to make injection molding a possibility.

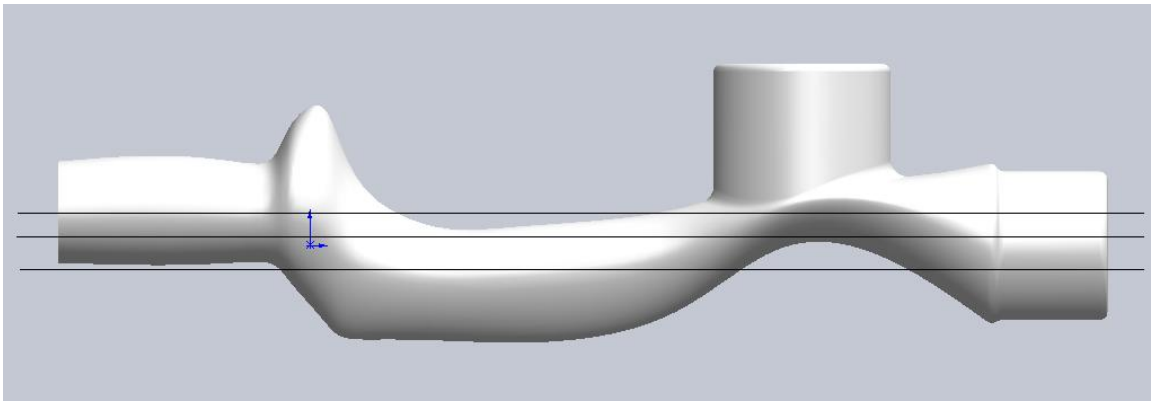


Figure 21. The PneumoniaCheck cut in half along a single horizontal plane. The PneumoniaCheck cannot be cut in half along a single horizontal plane and be injection molded. No matter where the plane cuts along the device, there will always be undercuts.

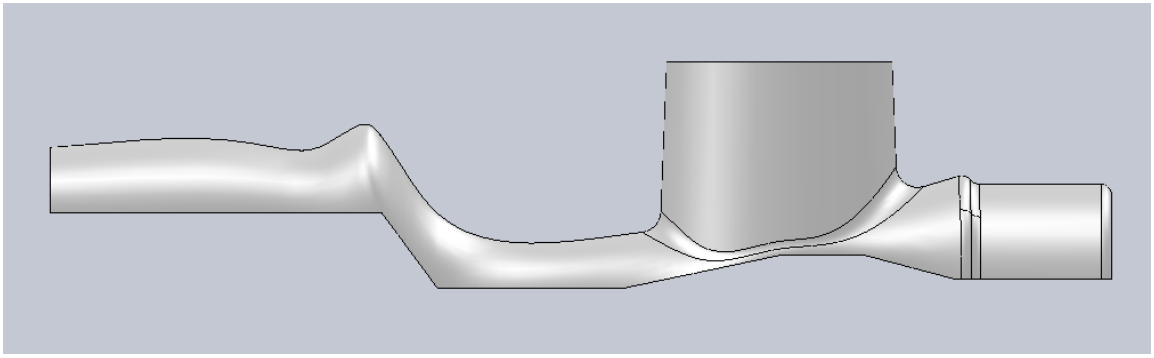


Figure 22. The top half of the PneumoniaCheck cut in half along multiple planes. The PneumoniaCheck can be cut into a top and bottom half along multiple planes in order to avoid undercuts. This is the top half of the device.

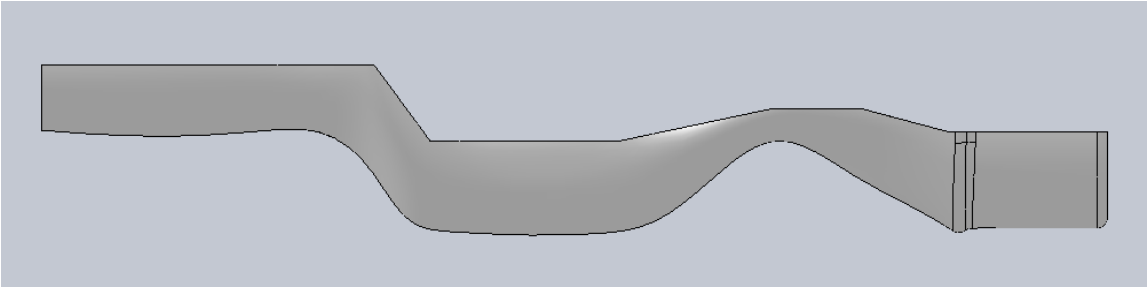


Figure 23. The bottom half of the PneumoniaCheck cut in half along multiple planes. The bottom half of the PneumoniaCheck when it is cut along multiple planes.

For injection molding, the PneumoniaCheck needs to be made in halves and then assembled. There are a few simple assembly techniques that are common for injection molded parts [31]. Press fitting and the use of rivets are also common in metals. Ultrasonic welding, the joining of two parts using high-frequency vibrations to create intermolecular frictional heat at the joining faces, is a method unique to plastics. Another assembly option is through the use of snap fit elements. Ultrasonic welding is generally an inexpensive addition to the manufacturing process, and would require fewer design changes and maintain the aesthetics of the device.

FDA has previously cleared certain plastics that the PneumoniaCheck could be made out of, including acrylonitrile butadiene styrene (ABS), polypropylene, and high-density polyethylene (HDPE). ABS is tough, rigid, and strong. ABS also has good surface appearance and is cost-effective. Polypropylene is tough and lightweight. HDPE is tough and lightweight and has high impact resistance. Low-density polyethylene (LDPE) has similar properties as HDPE, but it is more flexible. A more rigid material would be better for the PneumoniaCheck so that it feels more structured in patients'

hands. Any of these FDA-cleared plastics may be appropriate for the PneumoniaCheck [32].

Several manufacturers were contacted about injection molding both low- and high-volume runs of the device. The device design was cut in half along the vertical plane and along multiple horizontal planes and sent to them.

Manufacturer A recommended adding screw bosses to the device halves instead of using sonic welding. Manufacturer A also recommended the left/right design (split by the vertical plane), because they would not be able to sonically weld the top/bottom design (split by the horizontal planes).

Manufacturer B sent drawings for design change recommendations for the PneumoniaCheck. First, they suggested a draft of 0.5 degrees be added to the flat end of the mouthpiece (Figure 24). If draft is not added, issues such as drag marks or distortion may occur. It was also suggested that, in the case that we decide to add texture the device, draft be added to the flat sides of the device (perpendicular to the splitting plane). Manufacturer B recommended no less than 3-5 degrees of draft for these edges.

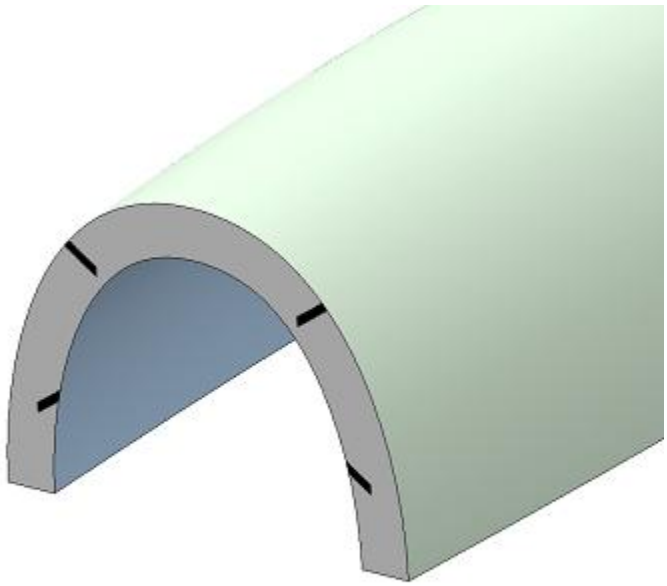


Figure 24. Surfaces of the PneumoniaCheck requiring draft. Manufacturer B suggested that we add draft to the surface with black dashes on it, in order to eliminate drag marks and distortion.

The wall thickness of the PneumoniaCheck is not uniform in some places, so Manufacturer B analyzed the device and recommended that the design be altered so that the wall thickness would be uniform to avoid possible sinks (Figure 25). They recommend that the wall thickness be between 0.045 - 0.140 inches for ABS, 0.030 - 0.200 for HDPE, and 0.025 - 0.150 for polypropylene. This could be accomplished with ribs on the outside of the device, by making the outside of the device have the same shape as the inside of the device, or by hollowing out the thicker portions of the device. By putting ribs on the funnel portion of the filter tube (so the ball valve still closes easily) and the areas of the device surrounding the Venturi, the PneumoniaCheck retains its interesting shape and is still easily injection moldable.

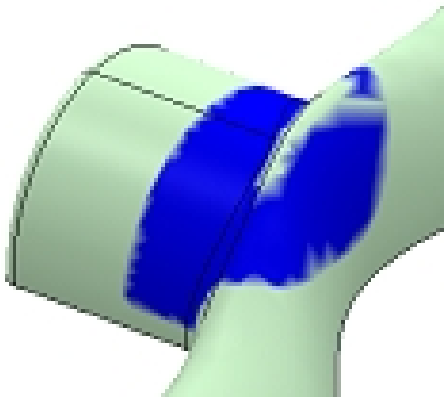


Figure 25. Thick-walled sections of the PneumoniaCheck. Manufacturer B suggested we make the portions of the PneumoniaCheck in blue thinner, so there will be uniform wall thickness throughout the device. This will help eliminate sinks.

Manufacturers C and D did not give us any design advice for the PneumoniaCheck to make it better for injection molding. They both said that they would be happy to discuss design suggestions once a contract was signed.

All four of the manufacturers gave us quotes for the PneumoniaCheck for both low- and high-volume runs. Table 6 summarizes the quotes for the device cut along the horizontal plane, into right and left pieces. The table uses units that are relative cost values, based on the lowest total cost per part of 1 unit. A graph of relative per part costs (including tooling) for low-volume runs is shown in Figure 26. Figure 27 shows comparative per part costs for high-volume runs. For low-volume runs (100-1,000 parts), Manufacturer D is the most economical choice. However, for higher-volume runs (10,000-100,000 parts), Manufacturer A costs less per part. Therefore, my recommendation is Manufacturer D for low-volume runs, and Manufacturer A for high-volume runs.

Table 6. Cost summary for four different manufacturers. Units are relative values based on the lowest Total Cost Per Part of 1 unit.

Company	Mold Cost	Cost per Part	Total Cost Per Part	Number of Parts
A	5,000	4	**50**	100
	5,000	0.6	**1**	10,000
B	7,000	7	**10**	1,000
	7,000	5	**5**	10,000
	7,000	4	**4**	100,000
C	40,000	5	**40**	1,000
	40,000	4	**7**	10,000
	40,000	2	**2**	200,000
	40,000	2	**2**	500,000
	40,000	2	**2**	1,000,000
D	60,000	2	**3**	1,000
	60,000	1	**2**	10,000
	60,000	1	**2**	20,000
	60,000	1	**2**	50,000
	60,000	1	**2**	100,000

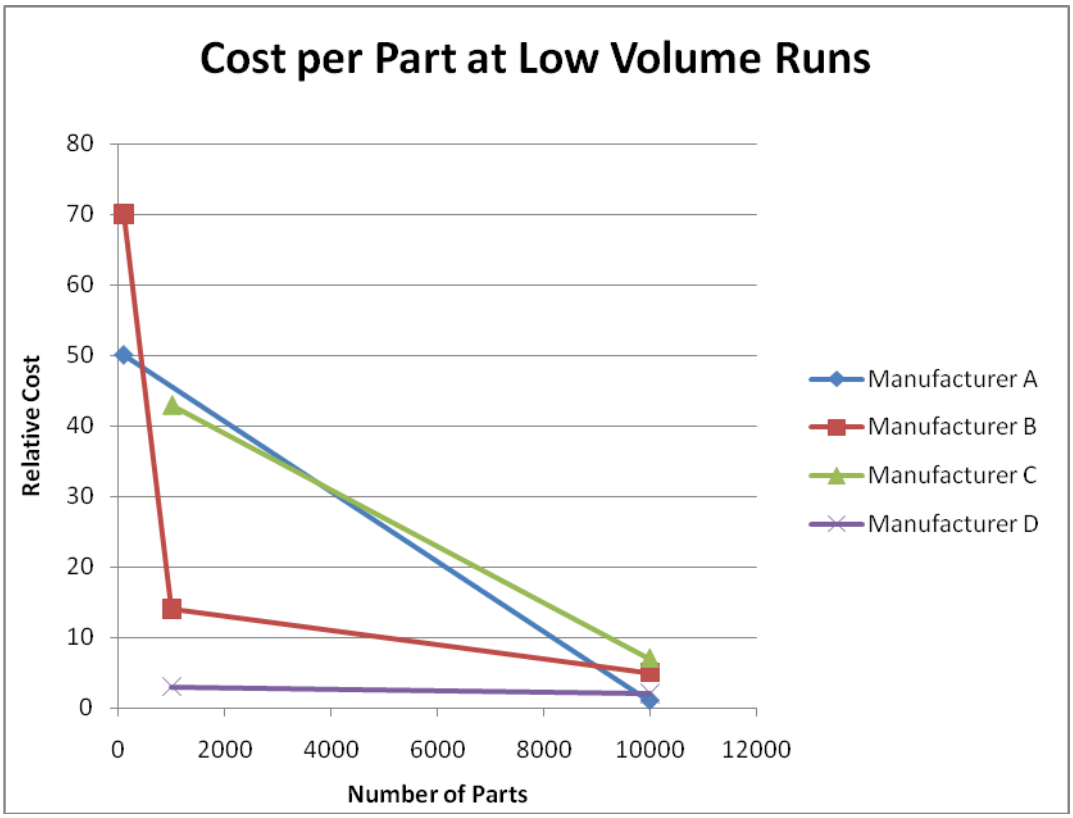


Figure 26. Relative cost per part at low-volume runs. Manufacturer D has the lowest prices for very low-volume runs (100-1,000 parts). However, at 10,000 parts, Manufacturer A has the lowest prices.

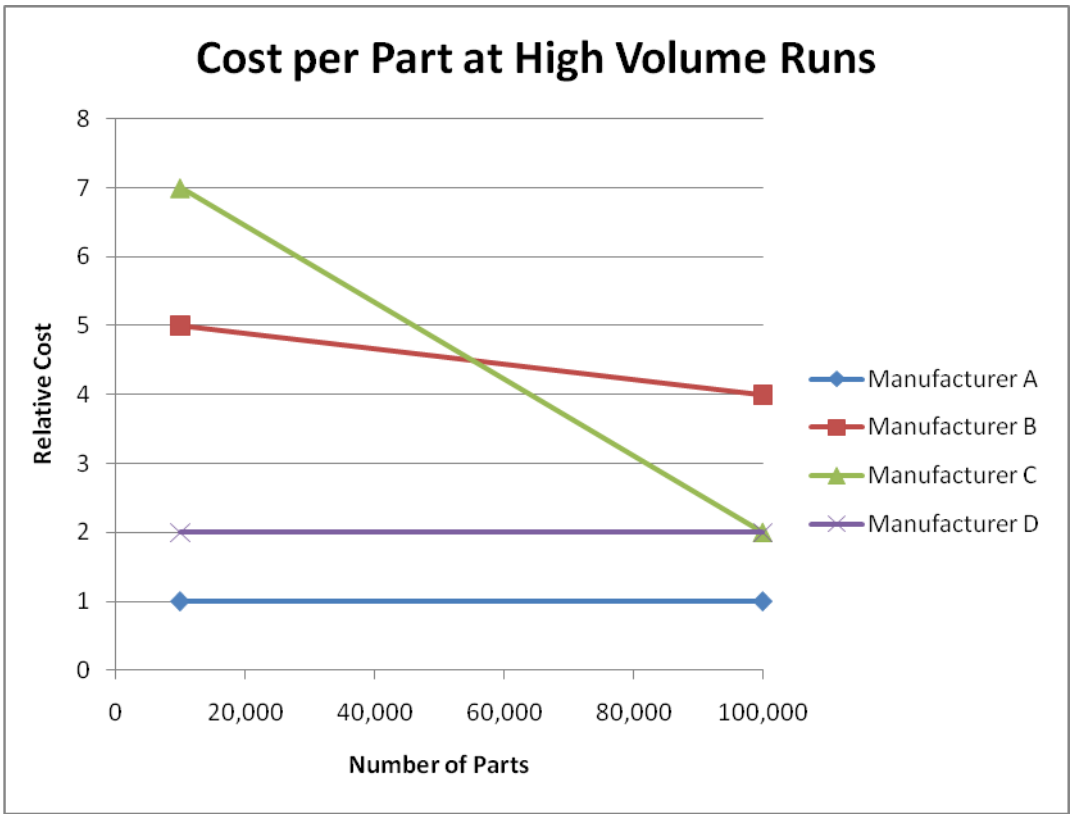


Figure 27. Relative cost per part at high-volume runs. Manufacturer A remains the most economical manufacturer between 10,000 and 100,000 parts.

CHAPTER 5: DISCUSSION

There is no sensitive, specific, non-invasive diagnostic test for pneumonia. Sputum cultures contain oral contaminants, and are often false-positives. In addition, many patients cannot give a good sputum sample. Pneumonia-causing pathogens often do not show up in blood or urine, so blood cultures and urine antigen tests may show up as false-negatives. The thoracentesis and the bronchoalveolar lavage are more invasive procedures, and therefore have a higher risk for the patient.

The PneumoniaCheck was designed to separate the upper and lower airway air and selectively sample aerosols from the lower airway. The patient simply places the mouthpiece into their mouth, coughs into the device, and exhales all residual air into the device. This action can be repeated as many times as necessary to get a sufficient sample onto the filter

The PneumoniaCheck is non-invasive, so it has a lower inherent risk and training than bronchial lavage, pleural tap, or venapuncture for blood culture. The only anticipated discomforts caused by using the PneumoniaCheck are those associated with repeated coughing. The ease-of-use permits sampling of lower airway disease for epidemiological surveillance.

The PneumoniaCheck passed nine verification tests to show that the design inputs are met. These tests demonstrated the device's ability to collect lower airway aerosols separate from upper airway aerosols, successful exclusion of oral contents, and capture of pathogens in the filter. Further, the PneumoniaCheck properly samples the lower airway

air, even at a very low volumetric flow rate from patients with severe restrictive lung disease or with mal-positioning from incorrect patient placement.

The majority of the oral exclusion tests were done by one person, and that person knew the purpose of the PneumoniaCheck and how it should work. This presents the possibility of a bias. Since this thesis, additional testing was performed on other students and gave substantially the same results: oral liquids and solids are virtually completely excluded from the PneumoniaCheck.

The PneumoniaCheck has the potential to change the way pneumonia is diagnosed and treated. If the device effectively captures enough aerosols from the lower lungs during deep cough, the PneumoniaCheck will provide a more definitive identification of the pathogen producing the pneumonia than any other non-invasive diagnostic test. Further, the PneumoniaCheck collects fewer oral contaminants than the sputum culture. The use of PCR analysis of lower airway aerosol samples may be more definitive without the large background noise of oral cells, bacteria, and viruses. The physicians will then know which pathogen is causing the disease and can treat the patient accordingly. This will reduce the prescribing of unnecessary antibiotics, which will help discourage the development of bacterial resistance. Treatments will be better tailored for each patient, so patients will have a better chance of recovery.

There are, however, some limitations of the device. First of all, it is still unknown whether or not the device successfully collects pathogens from the lower airway. In the verification tests discussed in this thesis, the gas from the lower airway has been shown to pass through the filter. However, the pathogens from the lungs were not demonstrated. Pathogens might be too heavy and have too much forward momentum to make the 90

degree vertical turn to travel up the filter tube and get caught on the filter. Perhaps the most important function of the PneumoniaCheck is to keep oral liquids out of the collected sample. Since the mouthpiece keeps nearly all oral contents out of the device, it may not be necessary to exclude the small amount of upper airway aerosols from the filter, as upper airway aerosols may account for only approximately 5-7% of the aerosols on the filter.

It has also not been shown whether or not bacterial pathogens from the lungs caught on the filter can be detected with sufficient sensitivity. The verification tests showed that 99.99% of pathogens will be caught on the filter, but it has yet to be shown whether or not pneumonia-causing pathogens form the lower lung can be collected in sufficient quantity and identified from the filter. Additionally, pathogens may be collected on the body of the device, the reservoir, or the ball valve instead of solely on the filter.

Some Georgia Tech students that participated in the verification testing complained of lightheadedness after coughing into the device repeatedly. Since all participants were healthy, this is a concern for pneumonia patients who may be using the device. It may take multiple coughs to get enough pathogen on the filter to be detected, and, for people who are already very ill, lightheadedness may be a drawback of the device.

Another drawback of the device is the amount of time that may be required to test for pathogens on the filter. If hospitals do not have PCR or immunoassay equipment, the filter will need to be sent to a lab for testing. This process could take days, and when a patient is hospitalized for pneumonia, treating them quickly is vital. The physicians may

still prescribe broad-spectrum antibiotics to pneumonia patients before test results from the PneumoniaCheck are received. Thus, the timing of selecting an appropriate narrow spectrum antibiotic may be delayed past the first day.

There are several ways the PneumoniaCheck could be redesigned. The current filter is relatively large, and it may be possible to make the filter smaller. This would not only make the device less bulky, but the pathogens would be concentrated in a smaller area, so extracting the pathogens off the filter may be more successful than with a large filter. Making the filter smaller is possible only if the resistance is still low enough to be comfortable for use by pneumonia patients. If the filter is smaller, the body of the device can be made smaller by shortening the liquid trap.

Another way the design of the PneumoniaCheck could be changed is by making a housing for the filter. It could be made to fit any sized filter that successfully captures bacteria and viruses, instead of only fitting the VBMax filter. The housing could be designed so that the filter does not cover the entire filter tube opening, which would allow any filter to be used, even if its resistance is very high. In that case, the aerosolized liquid pathogens expelled in the patient's cough would hit the filter, and the lighter gas would pass through the opening around the filter.

The PneumoniaCheck could be redesigned with a second filter in front of the reservoir to collect a mouth sample. With a filter sampling pathogens in the upper airway, physicians could test both filters for pathogens and compare the results.

There are human factors that could be taken into consideration for a redesign as well. First of all, it is slightly awkward to cough into the mouthpiece. It would be more natural to cough into a mask-like mouthpiece, since people naturally cover their mouths

in a mask-like fashion with their hands when they cough. However, the mouthpiece is vital for excluding oral liquids from the collected sample. Second, the device is back-heavy. The piece of plastic that attaches the reservoir to the body of the PneumoniaCheck is heavy, and the device might be slightly more comfortable to hold if the weight was more evenly distributed. It also may not be instinctive to hold the PneumoniaCheck with the filter pointing up, so it might be beneficial to have lettering or arrows that indicate that the filter should be pointing up during use.

In the future, the PneumoniaCheck may be made in multiple sizes, for children (ages 3 and over) and adults. Since there is approximately one milliliter of upper airway space per pound of person, the reservoir volume would change for different sized patients. A smaller mouthpiece would need to be made for small children. Different sized people should be able to use the device with the same results, as long as the reservoir volume is changed accordingly, with smaller volume reservoirs for smaller people. Children and infants who cannot cough on demand may need to use a modified PneumoniaCheck. Alternative uses of the device may be to obtain a more accurate sampling of blood alcohol levels not contaminated by oral mouthwash, surveillance of toxic volatiles in the lung, including screening for bioterrorism purposes, or detecting malignant cells from the lung.

CHAPTER 6: CONCLUSIONS

6.1 Verification

The PneumoniaCheck passed nine verification tests demonstrating the ability to collect lower airway aerosols separate from upper airway aerosols, successful exclusion of oral contents, and capture of pathogens in the filter. Further, the PneumoniaCheck properly samples the lower airway aerosols during deep cough, even at a very low volumetric flow rate from patients with severe restrictive lung disease or with mal-positioning from incorrect patient placement.

6.2 Manufacturing

Rapid prototyping is not a good choice for manufacturing the PneumoniaCheck in large quantities because it is very expensive. Vacuum molding is inexpensive and efficient. To be vacuum molded, the device would need to be cut in half, but it would require a lip to attach the halves of the device together. If the lip is on the outside of the device, it may cause discomfort for the patient, and if the lip is on the inside of the device, it may cause disruption of the airflow through the device. Injection molding is the recommended manufacturing option for the PneumoniaCheck, since it is inexpensive, fast, and would retain the device design and aesthetics. The device should be cut in half symmetrically along the vertical plane, molded, and then the two halves can then be sonically welded together.

In conclusion, the PneumoniaCheck functions properly, as shown by the verification tests, and can be modified for injection molding for medium- to high-volume runs. The device may be utilized for the selective sampling and collection of lower airway pathogenic material in patients with pneumonia. Proper identification and treatment of lower airway respiratory infections may save up to 400,000 lives annually.

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