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The Hemo-Quik

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The Hemo-Quik

- Designed for Project Stakeholder -

Dr. Matthew Mihelic, M.D.

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April 24, 2014

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Executive Summary

This report serves to introduce the Hemo-Quik, a streamlined device for quick, easy, and reliable fecal occult blood detection. Common methods to screen precursors of colorectal cancer and general health conditions in an emergency room setting rely on the stool guaiac test. The stool guaiac method involves digital stool sample collection smeared onto a guaiac resin card, with hydrogen peroxide developer applied to test for a presence of heme. The presence of heme, indicating blood presence in a stool sample, grants clinicians useful information for diagnostic, further testing, and treatment measures. However, this current method is cumbersome and therefore not administered as often as necessary. Project stakeholder, Dr. Matthew Mihelic, determined the needs of the system as follows: as sensitive and accurate as the current stool guaiac test, small size, contain a control, inexpensive, and low-level skill require to operate. Since the working prototype uses the same chemical reaction to test for a presence of heme, it is shown to be as sensitive and accurate as the current stool guaiac test.

Our design group spent the past two semesters planning and producing a revised test system, which will provide doctors with greater flexibility, enable wider range of device use in clinical settings, provide quick and accurate results, and come in one complete and self-descriptive package. The Hemo-Quik is intuitive and simple to use, permitting administration by nurses and medical technicians in a manner comparable to taking a rectal temperature measurement. This all-in-one sample collection and test device, which comes pre-lubricated and is completely disposable after a single use, eliminates cumbersomeness associated with the current stool guaiac method; no additional products, other than the standard of wearing gloves, are required for its use. The Hemo-Quik is small in size and able to fit comfortably inside the human rectum. The primary goal of not causing harm to the patient was determined using an anatomical model constructed to test the Hemo-Quik's dimensions. The working prototype uses the same control as the currently available Hemoccult SENSEA exam, which grants clinicians insight to both proper performance and results interpretation of the test. The working prototype, which was manufactured with 3D printing technologies, was not inexpensive. Our design group proposes a method by which the Hemo-Quik can be mass-produced in a cost-efficient manner should it become adopted by the medical community. This promotes economic viability in both in-patient and out-patient settings, where its use will allow for improved quality of care, decreased patient wait times, and reduced hospital readmission rates.

Background

The problem at stake concerns the detection of fecal occult blood, or unseen blood in the stool. One may safely lose about 0.5 milliliters of unseen blood in the stool, usually through the stomach lining, per day in the absence of disease or illness.

However, an average of two teaspoons of blood may be present in the stool without visual detection. Cancer, polyps, angiodysplasia, bleeding ulcers, and sickle cell anemia all contribute to occult blood in the feces; early detection will enable clinicians to investigate possibilities of disease earlier, therefore reducing disease mortality rates. The standard hemoccult test's administration in an emergency room setting is limited by time, ease of use, patients' preliminary dietary alterations, and the fast-paced nature of the emergency clinic itself. Our product aims to grant clinicians a hassle-free, reliable, disposable, and rapid results-generating mechanism to detect fecal occult blood. We hypothesize these characteristics will promote increased testing for fecal occult blood, and not limit the test to populations labelled as "at risk" for gastrointestinal bleeding, as is the current standard.

Current test mechanisms to detect fecal occult blood include the fecal immunochemical testing (FIT) and immunochemical fecal occult blood test (iFOBT), the stool guaiac test (gFOBT), fecal porphyrin quantification (HemoQuant), and fecal DNA tests (PreGen-Plus). The FIT method detects the presence of globin in stool samples, using an antibody combined with gold. Stool guaiac tests rely on a reaction between hydrogen peroxide and a particular guaiac-resin paper to determine a presence of heme in a stool sample (Baker et al). Both of these methods denote visual feedback via color change in the sample before and after a chemical reaction. Immunochemical fecal occult blood tests are more sensitive to blood presence than the guaiac test, but are restricted to bleeding only in the colon; the guaiac method detects bleeding in the stomach, small intestines, and colon. This test is therefore the most sensitive with multiple samples collected on multiple appointments (Jorgensen et al). The fecal DNA tests compares the DNA sequences found in stool samples to 23 different alterations indicative of abnormal, or cancerous, cells. Although this is the most accurate and sensitive screening mechanism thus far for colorectal cancer, fecal DNA tests are infrequently used in due to increased cost and two week waiting period before results are given back to doctors (Imperiale et al). In most clinical settings, the stool guaiac test is the standard hemoccult test.

Medical doctors have expressed a desire to see the current tests for fecal occult blood revised to offer lower skill-level operation and quicker feedback. The societal impact of an improved fecal occult blood test is early screening and accurate disease diagnostics; this will be achieved with higher test sensitivity to blood presence. A test with higher sensitivity will improve clinicians' ability to refer patients to further screening procedures and specialists. A pre-lubricated and disposable collection-test combination design will reduce cost, improve sanitation, and ease operation. A possible candidate solution is similar in appearance to a plastic tampon applicator. The tampon applicator has a unique propellant property that can prove useful for ejecting a swabbing device into the rectum for stool collection. This type of casing, when used to house the sample collection mechanism, can also be useful for sanitary extraction of the sample upon retraction of the applicator. The slender, compact design can be tailored

for comfortable access to the lower gastrointestinal tract. A new system for fecal occult blood detection, given by the proposed Hemo-Quik test device, will improve medical facilities' diagnostic capabilities, wait times, readmission rates, and overall flow of patient care processes.

Problem Definition

The Hemo-Quik is a complete device for fecal sample collection and fecal occult blood detection. The goals for our product, to compete with existing methods and serve our stakeholder, are: combined sample and test device, high sensitivity, small size, inclusion of a control, economic viability, and low-level skill to operate.

The revised must be at least as sensitive and accurate as the current stool guaiac test, since Dr. Mihelic is content with the parameters of the current stool guaiac test. The Hemo-Quik must contain some sort of automated design aspect for testing the sample acquired and revealing the results. The final product must be able to comfortably fit into a patient's rectum, and be small enough that any adult can feel confident in administering its insertion. One of the primary goals is to allow more personnel besides doctors to be able to perform the hemoccult test, which will enable the doctors more time for other pertinent tasks in busy clinical settings. The device should have a similar feel to rectal thermometer, and be small enough so that little risk exists for the device to hurt or harm its patients. The Hemo-Quik includes a control, which both allows the user to see that the device is working properly and to see what visible cue indicates a positive reading. Other current tests for fecal occult blood include a control, because it is an FDA regulated mandate. Our product must be inexpensive in order to compete with the current tests on the market. To meet this need, our product will be designed for disposability. When the Hemo-Quik enters mass production, it will be very inexpensive to manufacture and sell in large quantities, making it ideal in hospital/clinical settings. In comparison, the Hemo-Quik will be packaged and sold in a similar fashion to the average plastic tampon.

Current stool guaiac test methods require that doctors carry several separate items including a glove, KY jelly (for lubrication), guaiac test paper, and developer (hydrogen peroxide) in order to administer the hemoccult test. Not having one of these items readily at their disposal can cause a doctor to skip administration of the test, due to the cumbersomeness of locating or carrying around the aforementioned items. Having the Hemo-Quik be an all-inclusive unit to both collect and test a stool sample streamlines the process and allows for more frequent and routine checks for gastrointestinal bleeding. Having the device as one unit also reduces the skill level of operation; this device is simple and straightforward. The purpose of making the test easier to administer is to both save doctor's time, in the case that other hospital personnel could perform a hemoccult test, and reduce the likeliness of the test being neglected due to a complicated protocol. The Hemo-Quik facilitates a person with

“ordinary skill” in the medical field to make use of the product without prior experience; written description of the device will be included to enable any person in a medical profession to perform the device’s task. The operating skill required to use the Hemo-Quik is equivalent to using a rectal thermometer within a clinical setting.

The Hemo-Quik uses biocompatible materials, to reduce the chance of immune response and irritation when used. The objective is to have one small device that works universally on all types of patients (age, gender, sex, weight, etc.) without causing harm. Stool samples collected by the Hemo-Quik will be self-contained inside the device’s body cylinder, so as to prevent contamination and reduce mess. The device is designed for disposability, so it needs only be reliable for a single, quick and accurate reading. Upon reading the results, positive or negative, the product will be treated as a biohazard and disposed of appropriately with its original packaging. Using a pre-determined amount of developer solution in the liquid capsule along with a single-use lubrication packet also prevents material waste.

Literature searches and patent reviews provided information on current colorectal screening methods, but Dr. Matthew Mihelic, a doctor in family practice and associate professor at The University of Tennessee Graduate School of Medicine, is the primary driver for this project. The current method used to detect fecal occult in Dr. Mihelic’s practice is the stool guaiac test, which is the basis for this project’s standards. Dr. Mihelic has shared his own frustrations with the stool guaiac test, ways in which it can be improved upon, and the aforementioned needs of a revised system to ensure it is used properly and frequently in clinical settings such as his own.

Conceptual Development

After extensive literature review and comparison of current state-of-the-art technology, our team searched for creative solutions in designing a revised fecal occult blood test. Taking into consideration the standard test administered to determine whether a presence of fecal occult blood exists is the stool guaiac test, which is the most inexpensive and readily available in hospital settings. As a result, all considered concepts were purposeful attempts to improve upon said method. An initial need determined by our stakeholder, Dr. Mihelic, which became a primary function and requirement, is that our proposed system eliminate the cumbersomeness associated with current stool guaiac test methods. From speaking with Dr. Mihelic, the cumbersomeness associated with the stool guaiac test stems from digital sample collection, having to carry several items (gloves, lubricant, hydrogen peroxide, Hemoccult SENSE test cards) to administer one test, time required to perform the test, and limited personnel able to administer the test. Cumbersomeness of current stool guaiac test methods directly correlates to the exam being overlooked and not administered as often as it should, consequently resulting in ineffective cancer and disease screening, delayed diagnostics, and increased hospital readmission rates.

The primary need for the system to be simple and low-level skill to operate, to streamline the test procedure and reduce cumbersomeness, was determined at the beginning stages of design and guided all concepts considered by the design team. As a result, all considered concepts are all-in-one, disposable sample collection and test devices. This reduces the volume of products a doctor or nurse must carry to one single package, eliminating the excuse of not having one of the test materials on hand to administer a hemoccult test. Although none of the following original concepts were selected to produce a prototype, the design team was able to gain feedback from Dr. Mihelic on components and mechanisms of each, which guided the selection for a candidate solution.

Criteria for all designs considered is that they must be suitable rectal insertion, sample collection, and fecal occult blood detection. Consequently, all are shaped rather similarly. Anatomical restrictions mandate that the device be small in size and slender, similar to a pinky finger, in order to fit comfortably inside the rectum and not inflict harm to the patient. An existing idea, derived from common personal care items, was to shape the device similarly to a tampon. Tampon applicators, which resemble syringes, are composed of two major cylinders: a barrel containing the absorbent tampon and a plunger-like wand to propel the absorbent out of the barrel. Modern plastic tampon applicators are designed for quick and comfortable insertion of an absorbent material into a channel similar in size and shape to the rectum. The shaft of a plastic tampon houses an absorbent material, and has a chamfered edge to glide smoothly into the body and prevent the device from scratching its user. The applicator wand is used to propel the absorbent material out of its casing and into the body, where the absorbent material stays in place and the entire plastic applicator is removed and disposed of. For our design, it is desired that the absorbent material used for sample collection remain attached to the applicator wand and retract back inside the shaft of the device upon the device's removal from the rectum. Plastic tampons also often have prong-like structures on the chamfered end of the shaft, which splay outward when the absorbent material is pushed out of the device and into the body. Our device does not feature such structures, since the absorbent material is to be retracted back into its housing for occult blood testing. Inclusion of such prongs, or opening and closing mechanics, may result in pinching or scratching of the rectal lining.

Tampon's inclusion of a cord for removal from the body also guided our choice to consider concepts in which a drawstring extends beyond the cylindrical applicator wand. However, unlike the function of removal from the body that these cords serve for tampons, our device's cord would be used for activation of the chemical test process following sample collection. The current packaging for tampons, which are individually sealed and easy-to-open bags, also guided marketing decisions for our product. Hospitals will be able to purchase cases of individually sealed, complete hemoccult tests, similar to the way tampons are purchased in a drugstore.

Material selection for all concepts considered is based upon currently FDA approved materials, to ensure biocompatibility, safety, and reduced likelihood of any adverse reaction. The absorbent material used for the actual tampon portion of the existing device is often rayon, or a blend of rayon and cotton. The thin plastic used for the applicator portion of ordinary tampons is proven to exist in numerous colors and easily moldable into sleek shapes. Existing brands of translucent tampon applicators ensure that our device can be manufactured with a clear plastic, where results will be read via visible color change on the absorbent material by looking through the device itself. Material selection for the test component of the device must be inexpensive, since the overall device is to compete with the stool guaiac test in clinical settings. The guaiac acid reactant and hydrogen peroxide developer, used in the current stool guaiac test, provide acceptable and reliable sensitivity according to Dr. Mihelic and were therefore a promising design consideration.

Several original sketches were created by the design team to explore the possible landscape for a candidate solution. The first concept considered, shown in Figure 1, functions much like a click pen. The plunger mechanism used to propel the sample collecting absorbent material into the rectum, then retract it back into the barrel of the device, is spring-loaded like a click pen. Clicking the spring-loaded plunger initiates fecal sample collection, and clicking the plunger again retrieves the absorbent from the rectum. This design, like many considered, includes finger holds behind a large, round disc-shaped guard. The disc-shaped guard is a safety measure to prevent the device from becoming consumed by the rectum during operation, and the finger holds allow single-handed operation of the device. The opening and closing of the barrel cylinder to eject and then store the sample collecting material were considered ideal for sanitary containment of the sample, but later deemed dangerous. Having the tip of the device open and close introduces opportunity to pinch or scratch the patient, and preventing patient harm is of utmost importance. This sketch did not consider where the test chemical(s) would be housed, how the chemical(s) would be applied to the sample, or how the results would be analyzed.

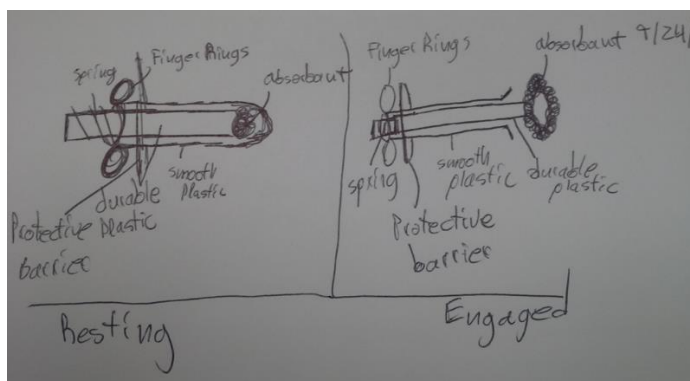


Figure 1: First considered design solution

The second original sketch, shown in Figure 2, operates very similarly to the current stool guaiac test with the inclusion of sample collection. This device, like the first concept, is spring-loaded and contains finger holds and a disc guard. The inner surface of the barrel where the absorbent material is housed is lined with guaiac paper, similar to that used in the Hemoccult SENSА cards. The outer body of the barrel cylinder is a porous material. The absorbent material expands when released into the rectum, then retracts back into the body of the device. It was considered that this expanding and compressing of the material may result in failure to collect a sample, snagging/tearing/breaking of the absorbent material on the end of the barrel upon retraction, and/or trace amounts of the absorbent being left behind in the patient's rectum. The porous outer portion of the barrel is designed such that once removed from the rectum, the entire device can be coated in hydrogen peroxide developed via a squeeze bottle. This would not meet the goal of an all-in-one, simpler device and could be very unsanitary. This also relies on the sample being adequately smeared on the inner guaiac paper upon retraction into the device.

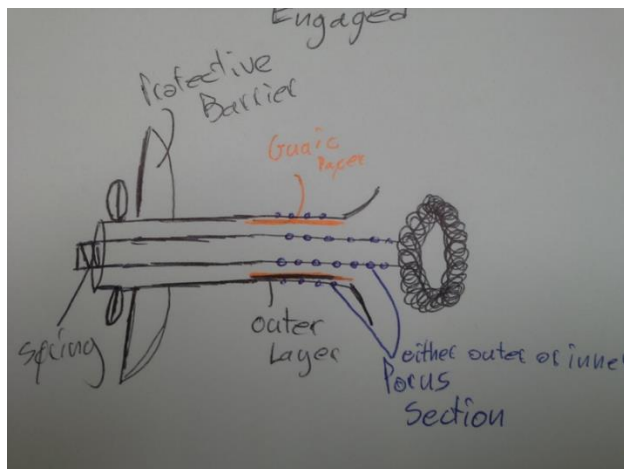


Figure 2: Second considered design solution

The third concept considered, shown in Figure 3, is a “bend and shake” device. This device also is spring-loaded, has a disc guard, and includes finger holds. Guaiac paper lines the inside of this device, similar to concept 2. In this design, a breakable capsule of hydrogen peroxide is stored in the body cylinder; after the sample is collected, a snap-on cap is applied to the end of the device, which is shaken to break the capsule and initiate the chemical reaction between the peroxide, guaiac acid, and potential heme present. Concerns arise regarding sanitation, both from the ability of the snap-on cap to seal the device completely and the shaking of the cylinder to produce the reaction. This could be messy to use, and it makes shipping and storage of the device difficult. Our design group does not want inadvertent activation to occur, ruining a number of devices in storage or shipment, due to the breakable hydrogen peroxide capsule within the device.

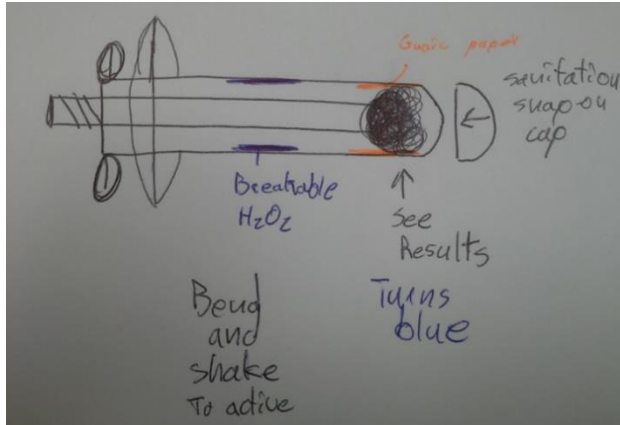


Figure 3: Third considered design solution

The fourth concept considered, shown in Figure 4, differs slightly in shape than the previous three. This concept does not include finger holds, but rather a round ring on the end of the smaller, plunger-like cylinder. The user of this device would rest their forefinger and middle finger against the disc guard during operation, and insert their thumb into the ring hole to operate the activation cylinder. The spring-loaded system clicks to lock into place and collect a sample, then unclics when depressed again to retract the sample back into the barrel. A guard inside the body cylinder ensures that the spring will click in and out of place, and will not eject the absorbent material too far into the rectum. A rigid rod beneath the absorbent material will keep it in place and prevent it from becoming unattached from the device during use.

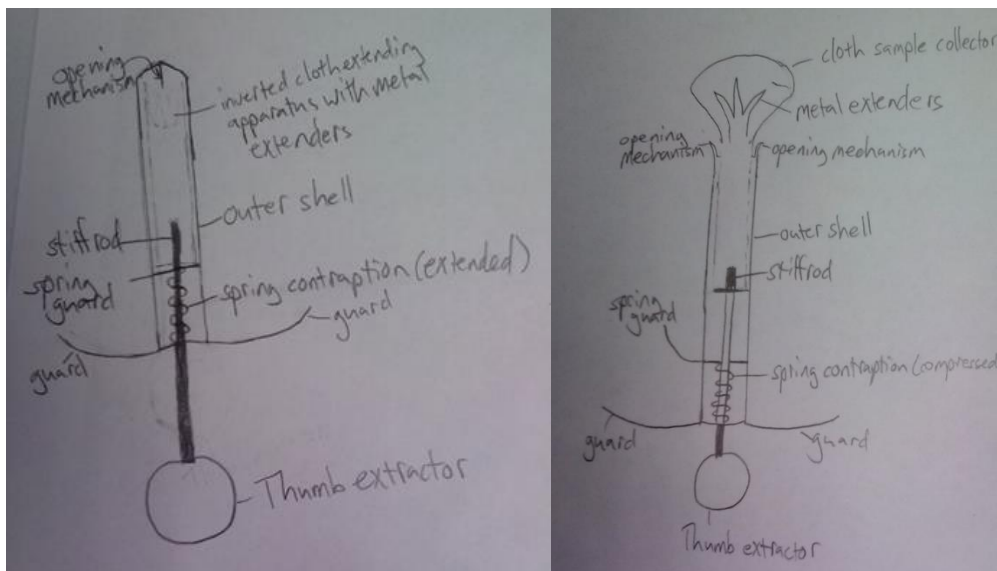


Figure 4: Fourth considered design solution

The fifth concept considered, shown in Figure 5, has a large disc guard to prevent rectal consumption of the device and a small push-button to release the sample collector. The push button is also spring loaded, with stoppers that prevent the spring

from ejecting the sample collector too far. The testing chemical is housed near the opening of the device, but this concept does not consider how it will be released onto the sample. As a result, it is unknown how unwanted spills or contamination of the devices internal components prior to use could be prevented.

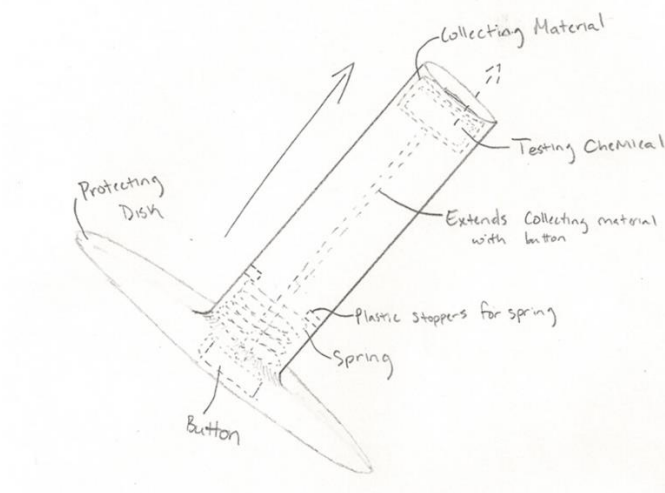


Figure 5: Fifth considered design solution

Although none of the original concept sketches created by the design team were selected for prototype development, the questions and concerns provoked by their shortcomings and strengths ultimately guided our design process in the right direction. Equipped with knowledge of currently available tampons and their applicators, the stool guaiac test, and our original concept designs, our design team was able to formulate the components of a successful and marketable system that meets stakeholder needs.

Product Description

The Hemo-Quik is a device to test for the presence of fecal occult blood. The product is composed of two interlocking cylindrical parts, termed the body cylinder and activation cylinder. The entire assembled device is approximately 10 centimeters in length. The body cylinder has an outer diameter of 1.6 centimeters, and its top edge is chamfered to a 1.4 centimeter outer diameter. The chamfered end is the front of the cylinder, which is open; this will be the end inserted into the patient's rectum. The chamfered edge insures patient safety by preventing potential pinching from the device's components. The back end of the body cylinder has a large round shield extending radially from the cylindrical tube, which prevents the device from being consumed by the patient's rectum during use. Two finger holds are attached to the back of this guard for the administrator's pointer and middle fingers. This allows the administrator to hold the device in one hand, insuring the device is easy to use. Inside

and extending beyond the guard end of the body cylinder the smaller activation cylinder. The activation cylinder has an absorbent collection material adhered to the top portion of it, which is housed inside the body cylinder. An activation string runs through the length of the activation cylinder from the base of the collection material to slightly beyond the back end of the activation cylinder. This activation cylinder is used to push the absorbent collection material from within its cylindrical casing (the body cylinder) and into the patient's rectum. This same activation cylinder is used to retract the collection material after a sample is taken. The device is removed from the patient's rectum, and the activation string extended beyond the activation cylinder is pulled to return the absorbent material back into the body cylinder. The activation cylinder is then "swirled" around the transfer the stool sample to the guaiac paper lining the inside of the body cylinder. The entire device can be placed back inside the clear bag in which it was originally packaged, to serve as a sheath and prevent the spread of fecal matter and/or bodily fluids. The test administrator can then grip the device by its sheath, and pull the activation string further to compress a liquid capsule containing hydrogen peroxide, resting at the base of the body cylinder, which initiates the fecal occult blood test.

The inside of the body cylinder is lined with gum guaiac impregnated paper including a control box. The base of the body cylinder, resting on its inner lip, is a liquid capsule containing hydrogen peroxide. The phenolic compound in the gum guaiac paper (alpha-guaiac acid) reacts very slowly with hydrogen peroxide; this reaction is catalyzed by the presence of heme, causing an immediate blue color change. A positive result, indicating the presence of fecal occult blood, will be determined by a visible color change viewed through the device. The Hemo-Quik device is made of thin-walled transparent plastic, allowing this visible indication of results. The absorbent collection material is located inside the body cylinder towards its opening. This material is pushed out of the body cylinder by the activation cylinder, where it collects a sample. When the activation cylinder is retracted, the collection material slides back inside the body cylinder. Swirling the activation cylinder in a small circle will help transfer the stool sample to the test paper lining the inside of the body cylinder. As stated before, a liquid capsule containing hydrogen peroxide is located in the base of the body cylinder. Pulling the activation string pulls the collection material back further, compressing the capsule until it bursts, applying hydrogen peroxide to the inner chamber. The entire device is distributed in an easy to open, transparent cellophane package containing both the Hemo-Quik and a sealed 5-gram packet of lubrication. Having the lubrication separate from the device and applied just prior to its use ensures that the entire device is not covered in lubrication; it was hypothesized by our design team that pre-lubrication of the Hemo-Quik could potentially interfere with the test's efficacy upon storage and shelf life. It was also determined that having the Hemo-Quik pre-lubricated could make its operation difficult and alter sensitivity, which is why a one-time use lubrication packet is enclosed.

The test administrator will open the sealed package, which is easy to tear along its top double-sealed seam, to reveal the Hemo-Quik device and lubrication packet. The Hemo-Quik comes vacuum sealed in a thin, transparent cellophane package which also serves as a sheath and means of disposal. He or she will tear open the lubrication packet, use it to lubricate the shaft of the body cylinder, and then discard the packet. The administrator will then place their index and middle fingers into the finger holds behind the disc guard. The device will be carefully inserted into the patient's rectum up to the rectal disc guard. Using either the thumb or other hand, the activation cylinder is pushed to insert the absorbent collection material into the patient's rectum. The administrator can then remove the entire device from the patient's rectum and retract the activation cylinder. Once the sample is retracted into the casing of the body cylinder, the administrator can place the device back into its cellophane package. Holding the device outside the cellophane package, the administrator will pull the activation string back firmly to break the hydrogen peroxide capsule. This action soaks the inside of the body cylinder, coating the sample on the guaiac paper. The test's results will be displayed within a minute by the presence or absence of a blue color change. The Hemo-Quik can then be disposed of inside its packaging. The entire test, from opening the package to disposal, can be administered within approximately 3 minutes.

This concept was selected because it shows great promise to meet or surpass all of the project needs and requirements. The inclusion of the guaiac resin test paper and hydrogen peroxide developer gives the device a sensitivity equal to that of the current stool guaiac test. This concept includes finger holds, allowing the user to firmly grasp the device, making it stable and easy to use. The rectal shield prevents possible mistakes by test administrators. The simple activation cylinder and string allow the user to operate the entire test without complicated instruction. The small size and cylindrical shape of this design protect the patient from potential harm. The working prototype, which was manufactured using rapid prototyping, was constructed from ABSi filament. Future product designs will be constructed from an inexpensive and transparent low density polyethylene, helping reduce the total cost of each unit. These future designs can be produced with injection molding, for just a few cents per unit after the initial mold is constructed. To reduce construction expenses further, the initial mold could be 3D printed rather than outsourced by an injection molding company. Each Hemo-Quik comes with a small quantity of lubrication in the package, which reduces waste in offices that misplace or discard of partially full lubricant bottles. Once the test is used, the sample is housed within the body cylinder and the body cylinder is contained within the cellophane packaging sheath, allowing the user to sanitarily dispose of the device in the proper waste receptacle.

The body cylinder and activation cylinder were manufactured separately, as two independent units, then assembled by hand to include the additional device components. Our group considered numerous companies for the rapid prototyping of

our candidate design solution, and decided to manufacture the first prototype at Oak Ridge National Laboratory's Manufacturing Demonstration Facility (MDF), which features a Stratasys Fortus 400mc 3D printer. This machine was used for the additive manufacturing of both the body and activation cylinders with ABSi material. Unfortunately, the desired clear material was unavailable for manufacturing initial prototypes. This process of fused deposition modeling (FDM) uses minimal material, since the design is built layer-by-layer in an additive fashion. The computer-aided design models used to manufacture the body and activation cylinders are given by Figures 6 and 7 respectively. The use of soluble support material will enable easy removal of the support material post-manufacturing of the thin-walled components. Both cylinders were subject to post-processing. Sandpaper (3M brand 336U aluminum oxide 120 grit) was used to smooth the surface of the tube-shaped portion of each cylinder, first applied in the same direction as the layers of filament and then applied perpendicular to the direction in which the layers were built. This was repeated until the tube-structures were smooth and free of ridges between the deposited layers. The collection material and attached activation string in the first prototype came from a currently available consumer product. Our group decided to use readily available tampons for this absorbent collection material. Tampax® brand "Pearl Lite" Tampons made by Proctor and Gamble were found to have the desired material properties, dimensions, and attached string characteristic of our proposed system. These are a cotton/rayon blend and have received FDA approval for biocompatibility with prolonged contact in a mucosal membrane. We simply removed the desired absorbent material of these products from their plastic applicators and attached them to our device's activation cylinder using contact adhesive, with the string running through the hollow center of the activation cylinder (Figure 8). These tampons can be purchased at numerous local retailers including supermarkets and convenience stores. Assembling the liquid capsules that contain 3ml of hydrogen peroxide developing solution was performed using a VacMaster VP112 portable chamber vacuum sealer (Figure 9) and a unique protocol developed by our design team.

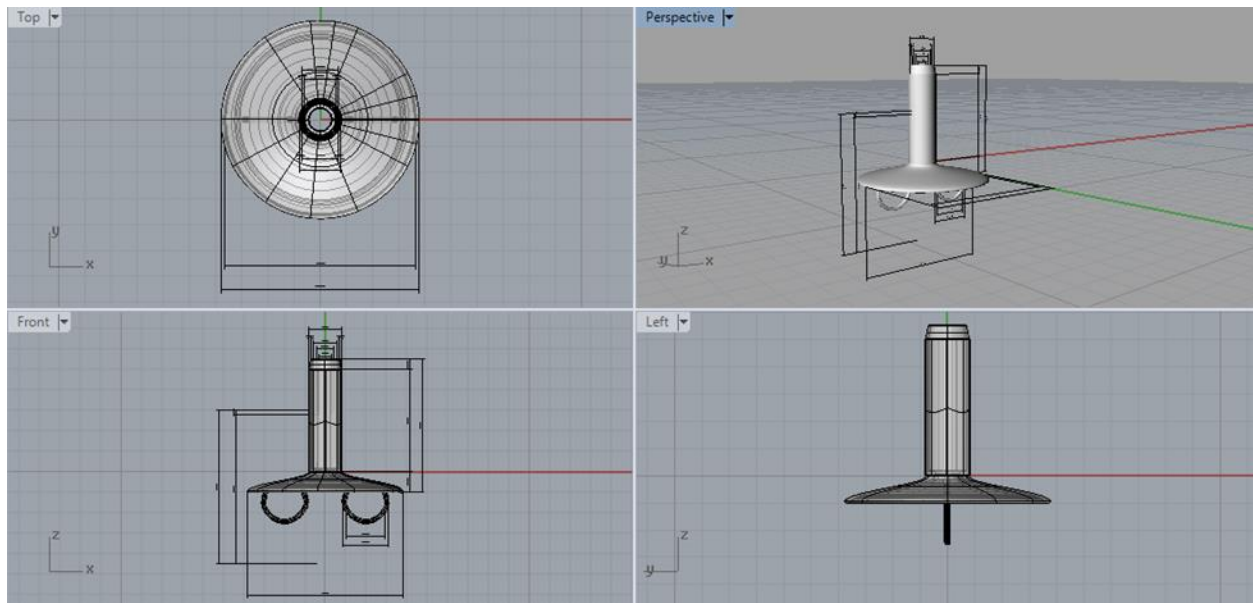


Figure 6: Body cylinder

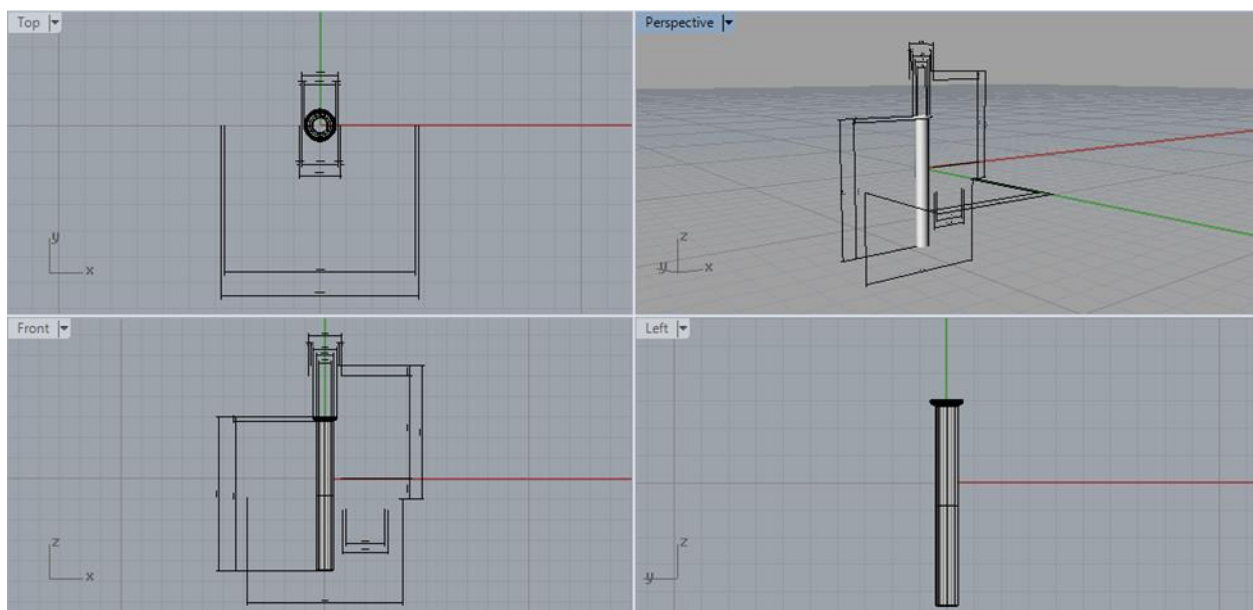


Figure 7: Activation cylinder



Figure 8: Activation cylinder with absorbent collection material and activation string



Figure 9: VacMaster VP112 portable chamber vacuum sealer

To assemble the Hemo-Quik, begin by cutting the test paper and its control from its collection card using a straight edge. Roll the test paper in a cylindrical shape, such that the control box has both circles exposed and oriented horizontally on the bottom of the rolled up cylinder. Insert this cylindrical paper roll into the body cylinder, control box side first, until the bottom of the paper is resting on the body cylinder's inner lip. Using a pin, assist the paper in "unrolling" until it fills the cavity of the body cylinder, completely and snugly lining the inside walls. The ridges inside the body cylinder, characteristic of its material and manufacturing method, hold the test paper securely in place above the inner lip (Figure 10). Roll the hydrogen peroxide capsule into a circle (like a donut) and insert it into the top of the body cylinder, such that the "hole" of the circle is in the center of the cylinder, and the perimeter of the gel capsule rests on the lip inside the body cylinder. Holding the activation cylinder at the junction between the splayed upper portion and the collection material, carefully slide the activation cylinder into the body cylinder, narrow end first. Be careful such that the activation string is still exposed below the body cylinder. The activation cylinder should slide into the body cylinder until the junction rests on the gel packet, and the collection material is completely contained within the body cylinder. The HemoQuik, now fully assembled (Figure 11), is ready to be packaged.



Figure 10: Gum guaiac test paper lining inside of body cylinder



Figure 11: Fully assembled Hemo-Quik

Once the device is assembled, it is placed inside a cellophane bag along with a 5 gram foil packet of Surgilube medical-grade lubricant (Figure 12). The bag containing the Hemo-Quik and lubricant is placed flat inside the chamber vacuum, with the opening of the bag facing the direction of the vacuum. The lid to the chamber vacuum is closed, such that the opening of the bag is in the open space overhanging the heat sealing edge. The vacuum will fill the bag with air, then remove all air (forming a vacuum seal) while sealing the top of the bag with a double-reinforced heat seal. The vacuum will the release and the lid will open, revealing an air-tight packaged Hemo-Quik. The double heat seal allows for an easy-open tear location along the top of the bag, for when the Hemo-Quik device is ready for use. This will keep the bag in tact when it is torn open, so that it can be used appropriately as a sheath when the device is removed from the patient after collecting a sample.



Figure 12: Packaging the Hemo-Quik

Our design team faced the greatest manufacturing difficulties with gel capsule construction and assembly. Initially, the plan was to house both hydrogen peroxide and alpha-guaiac acid in a dual-chamber liquid packet in the base of the body cylinder. Upon further analysis of the test dynamics, it was decided that this was not the best method for many reasons. This method required that upon pulling the activation string, both capsules would burst. This requires that each Hemo-Quik be constructed and packaged such that the dual-chamber gel capsule were in the exact same orientation in each device, and even then, it is unclear whether the varying pulling force among test administrators or shipping conditions would result in translation/rotation of the capsule preventing its ideal rupture. Another concern with this initial design, assuming that both chambers burst when the activation string is pulled, is the uncertainty that the sample collection material would be adequately coated with both chemicals. The reaction between hydrogen peroxide and alpha-guaiac acid is catalyzed by the presence of heme, so both chemicals would need to come in contact with the entire sample collection material in order to provide proper detection conditions. Our group decided to change the Hemo-Quik test parameters to better accommodate the reliability, accuracy, and ease of use previously defined as required system parameters. The new design changes are as follows: coating the inner surface of the body cylinder with a transparent test paper impregnated with gum guaiac and housing a single chamber hydrogen peroxide capsule in the base of body cylinder.

In assembling the newer liquid capsule design, our team ran into challenges creating small enough capsules that both fit inside the Hemo-Quik device and contained enough hydrogen peroxide to soak a collected stool sample. We used the Food Safety and Processing laboratory's commercial grade vacuum sealer to develop a methodology of constructing small liquid capsules; this protocol involved freezing the hydrogen peroxide before sealing it into the capsule, since the vacuum chamber did not handle liquids well. Our team decided to purchase a chamber vacuum sealer for home use, which increased our ability to practice producing capsules and testing them promptly inside the Hemo-Quik. This refined methodology also bypasses freezing the developer, allowing the hydrogen peroxide to be directly pipetted into each capsule prior to vacuum sealing. However, the small size still poses a challenge for our group. Construction of capsules of the size intended to fit in the base of the body cylinder is very difficult to do by hand, and even more challenging to make repeatable with the same level of precision each time. Automating this process would be the best option for future manufacturing of the Hemo-Quik on a mass production scale.

Design Evaluation

The initial Hemo-Quik prototype designed and manufactured by our design team to serve Dr. Matthew Mihelic's medical practice is compared the aforementioned needs in the Problem Definition section of this report. Many of the device's needs,

pertaining to those elicited from Dr. Mihelic, require qualitative, rather than quantitative, measurements. Evaluations of the Hemo-Quik are supported with both product testing and user satisfaction. The needs analyzed on the device are as follows: small size, easy to use, low-level skill to operate, high sensitivity to heme, contain a functioning chemical test mechanism, and low cost. Fulfilment of each need is scored on a scale of 1-10, by both the design team and stakeholder's satisfaction with the Hemo-Quik.

Small Size & Preventing Patient Harm (10/10)

The Hemo-Quik must be small enough to not harm or cause discomfort to the patient. The standard of digital sample collection employed in clinical setting necessitates that our design be similar in dimension to an adult pinky finger for this failure mode. The size of the Hemo-Quik was dimensioned using computer-aided design prior to manufacturing, then physically measured against these specifications using calipers. The measurements obtained were verified to match, between the prototype and the model, and be comparable in size to an adult pinky finger. The Hemo-Quik manufacturing process includes post-processing with fine-grit sandpaper and a dremel tool to smooth the surface of the body and activation cylinders. Post processing of the Hemo-Quik body cylinder ensures a smooth surface free of impurities that would likely contribute to patient harm or discomfort. Detection of surface impurities by visible and tactile inspection was deemed sufficient to completely smooth the device's surface.

Ease of operation (10/10)

The fluidity of component movement in the Hemo-Quik device is such that the activation cylinder glides efficiently in and out of the body cylinder, without any catching or snagging. This failure mode coincides directly with the question, does the Hemo-Quik device move freely and easily during operation? Post processing of the Hemo-Quik body and activation cylinders ensures smooth surfaces that prevent snagging and allows for fluid operation. Detection of fluid movements during the operation of the device was achieved by moving the activation cylinder up and down inside the body cylinder, mimicking its ejection and retraction.

Low-level skill to operate (9/10)

The Hemo-Quik is an all-inclusive stool sample collector and fecal occult blood detection test device. The device includes lubrication, a means of obtaining a stool sample, and a means of testing the stool sample for occult blood presence. This is directly associated with the question: does the proposed system eliminate the cumbersome characteristic of the current stool guaiac method? Performing a hemoccult test is as simple and streamlined as picking up a Hemo-Quik package, which is complete with all necessary components in an easy-to-interpret presentation. The simplicity of this package permits any reasonable adult in a medical profession to administer the exam. It will still be necessary to include instructions for the Hemo-Quik's intended procedure, which ensures proper function is achieved.

High sensitivity (8/10)

The Hemo-Quik is designed such that a gum guaiac resin paper surrounds the internal lining of the body cylinder. The paper rests on the lip at the base of the body cylinder and is further supported by the ridges of ABSi filament lining the inside of the body cylinder. This paper is used to transfer a stool sample onto from the collection material, which will later react with the hydrogen peroxide developer when the liquid capsule is burst. This failure mode coincides directly with the following questions: does the Hemo-Quik's chemical test mechanism provide comparable sensitivity to the current stool guaiac test? Since the Hemo-Quik features the same test reaction as the current stool guaiac test, the desired sensitivity is achieved. Results from sensitivity testing are given in the Appendix. Since future prototypes are to be constructed from low-density polyethylene by injection molding (reference the Recommendations and Future Work section of this report), it is unclear whether the material properties of the future Hemo-Quik devices will be sufficient to hold the guaiac test paper lining to the body cylinder without the addition of an adhesive. This new need for adhesive may alter the sensitivity achieved by the test paper when reacted with hydrogen peroxide developer.

Test process operates as intended (5/10)

The Hemo-Quik is designed such that a liquid capsule containing hydrogen peroxide can be burst due to compression between the flange on the activation cylinder and the lip at the bottom of the body cylinder. This failure mode coincides directly with the test process operating as intended, answering the questions: does the liquid capsule burst consistently with the compression between the flange of the activation cylinder and the extended lip at the bottom of the body cylinder? In testing of liquid capsules constructed by the design team, there was below a 40% success rate bursting the capsule of hydrogen peroxide with one depression of the activation cylinder. When the activation cylinder was pulled back repeatedly, the success rate of capsules bursting increased to nearly 60%. Since the Hemo-Quik's intended purpose is to screen for unseen blood in the feces, the chemical reaction between the developing solution, gum guaiac paper, and stool sample must occur. Without the ability to consistently break the capsule of hydrogen peroxide, this test reaction is not possible. We predict this failure rate can be improved by redesigning the activation cylinder's flange.

Low cost (5/10)

A key need indicated in early phases of design is for the Hemo-Quik be inexpensive in an effort to compete with the stool guaiac test. The first working prototype generated was not inexpensive and is not producible for the Hemo-Quik's intended disposability aspect. The working prototype's higher expense is due largely to the rapid prototyping method to manufacture the body and activation cylinders, and the purchase of a \$700 chamber vacuum sealer for liquid capsule assembly. These higher manufacturing expenses over the stool guaiac test are arguably outweighed by the economic viability

the Hemo-Quik provides, as explained in this report's Recommendations and Future Work section.

Recommendations and Future Work

The value of the Hemo-Quik is given by its economic viability in both in-patient and out-patient settings. For out-patient settings, we can expect to see improvement in the amount of time required to see a patient. Since any reasonable, competent medical technician or nurse can administer the Hemo-Quik, doctors' time will be saved and the patient can move through the office quicker. When a doctor does see a patient, the stool hemoccult test results will be available with their initial laboratory results; this improves both the quality and time of care provided. Decreased time per patient will also reduce wait times, particularly important in emergency clinics. The same benefits of improved quality and reduced time apply to in-patient settings. Ability of medical staff to administer the stool hemoccult will improve the likelihood the test is performed. This may decrease length of stay in the hospital, which saves money, and better inform physicians of a patient's general health conditions before seeing the patient.

It would be a great oversight to ignore ways in which the Hemo-Quik can be improved. The three areas of interest our group would like to pursue are the replacement of lubrication packets with lubricating wipes, automation of the liquid capsule production process, and use of injection molding with low density polyethylene to manufacture the body and activation cylinders.

Our design team would like to create a lubricating wipe to replace the foil packet of lubrication currently provided with the prototype. A wipe will provide greater simplicity and ease-of-use to the device, since the administrator's glove will not be partially coated in lubrication as it is with the Hemo-Quik's foil packet of Surgilube® or the current method of dispensing from a KY® Jelly bottle. The less mess associated with the hemoccult test, the less cumbersome it will seem, and the more often it will be administered. While lubrication wipes do not currently exist, we have contacted Surgilube with the intention to create one.

Mass production of the Hemo-Quik requires automation of the liquid capsule assembly process, to ensure the same precision and accuracy can be achieved in each device. Currently, the capsules of hydrogen peroxide developer are assembled individually by hand; this requires manually measuring out the capsule bag, dispensing a known amount of developer solution inside, and vacuum sealing it closed. While this process does create functional products, it is timely and tedious. In order to assure clinicians they are using a reliable, quality product, it must be certain that each packaged Hemo-Quik contains uniform concentrations of the developing solution. These capsules could also be produced in bulk with an automated process, which will be essential for large scale distribution.

Future renditions of the body and activation cylinders will be manufactured using injection molding in low-density polyethylene, rather than the 3D printing used for the working prototype. The prototype was constructed in a Stratasys Fortus 400mc, which has the capacity to produce products in a transparent, FDA-approved medical grade ABS-M30i material. While this production method is convenient, it is too expensive to create a disposable product with. In addition, the products must undergo post-processing to ensure the surfaces are smooth and free from surface impurities. A transition to injection molding will be expensive initially, but each unit price is significantly cheaper.

Continued effort to improve the manufacturing process and market the Hemo-Quik will require a significant amount in start-up funds. Creation of an initial mold for injection molding the body and activation cylinders will cost around \$40,000 (Quote by DeRoyal Industries OEM in Powell, TN), but the price per subsequent injection is a mere \$0.20. An automated assembly process for the hydrogen peroxide capsules will reduce human error, but will require increased infrastructure as well as personnel to do so. Fabrication of a lubricating wipe will be expensive to implement, but profitable when it is requested and purchased for applications other than the Hemo-Quik. These combined processes may require another year before the Hemo-Quik is ready for nationwide distribution.

Appendix: Sensitivity Testing Methods + Results

Methods:

1. Chocolate pudding (FoodClub® brand sugar-free instant pudding mix) was prepared according to package instructions, using water in place of the milk. The pudding was allowed to thicken in the refrigerator for 20 minutes to reach desired consistency.
2. Once thickened, $\frac{1}{2}$ cup measure of pudding was dispensed into each of four plastic cups and set aside. The cups were labelled as: 2ml, 4ml, 6ml, and 8ml.
3. Meanwhile, we thawed several individually-sealed (previously frozen) beef livers in a bowl of warm water for 30 minutes. Once thawed, the packages were opened and the beef livers with their accompanying juices were transferred to a large bowl.
4. A serological pipette was used to extract 2ml of blood from the bowl (Figure 13) and dispense it into the cup reading “2ml”. A stirrer was used thoroughly combine the blood with the pudding (Figure 14).
5. Three separate gum guaiac test cards were labeled as trial 1, trial 2, and trial 3. A cotton swap was used to obtain a sample of the blood-pudding mixture and smear it on both sample portions of the test card (Figure 15). Hydrogen peroxide developing solution was dripped onto the sample card to coat both the samples and the control box.
6. A visual inspection was used to indicate whether the sample changed color to match the “positive” reading of the control box, or remained unchanged to match the “negative” reading (Figure 16).
7. Steps 4-6 were repeated for the pudding mixtures with 4ml, 6ml, and 8ml of blood added (Figure 17). New sample cards were used each time and results were recorded for three trials of each concentration.

Results:

Our group chose these concentration amounts, since moderately sensitive stool guaiac tests can detect up to 10 ml per day of bleeding, but require at least 2 ml present in a stool sample to return a positive result. Using 2ml, 4ml, 6ml, and 8ml of blood each mixed with $\frac{1}{2}$ cup of chocolate pudding gives concentrations of 1.69%, 3.38%, 5.07%, and 6.76%, respectively, of blood per unit volume. Our results indicate that by visual inspection, our method detects as little as 1.69% blood per unit volume, but is better at detecting concentrations greater than 3.38%. A visible color change was evident for each trial with each blood-to-pudding ratio testing, yet the given color change was more prominent for concentration of 4ml and higher of blood.



Figure 13: Beef liver used to extract blood



Figure 14: Cups of pudding labelled according to the amount of blood added

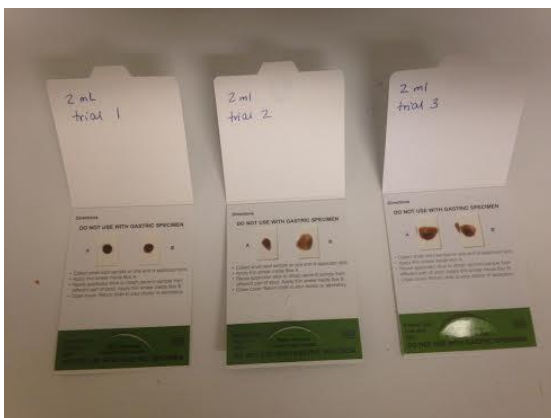


Figure 15: Sample preparation prior to developer application



Figure 16: Visible color change, indicating positive heme detection, following the 2ml test



Figure 17: More notable color change, indicating positive heme detection, following the 4ml test

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