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A SYSTEMATIC APPROACH TO BLOOD SHORTAGES IN LMICs: DESIGN OF A DEVICE FOR WHOLE BLOOD AUTO TRANSFUSION

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In partial fulfilment of the requirements for the award of Bachelors of Science in Biomedical Engineering.

Declaration

We team ugHealth, hereby declare that all the information in this technical report reflects all the activities that we have been carrying out concerning biomedical engineering design and it is our original report. This report has been written and organized by the team to the best of our knowledge and skills not as a duplicate or copied from anywhere and has never been produced as a whole by anyone for an award in any institution or university.



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Executive Summary

This report follows the activities of team ugHealth in an effort to fulfil the requirements of the design course series for the period of 7th September, 2018 to 20th December, 2020.

The report is structured in four sections, section one expounding on the needs finding exercise, problem statement, the synthesis of the proposed solution to solve the identified problem, and its justification. Section Two comprises of the prototype design, section 3 – testing protocols and section four – redesign and the design, development & business plans.

On Tuesday 11th September 2018, we carried out a needs finding field work exercise in two hospital environments that is CoRSU and Pan dental hospital. From the two environments, we interacted with different medical specialists and staff, and noticed some problems. The needs assessment exercise offered a vivid perspective of the problems faced in the Ugandan health care system. However, we were required to identify a single problem; the team used an elimination matrix to choose a principal challenge.

From the needs assessment exercise, UgHealth found that a lot of blood is lost during surgical operations by the patients, and there is a shortage of blood for transfusion especially for rare blood types. We had an interview with Dr. Antonio Loro an orthopaedic surgeon; he informed us about the deficit in the supply of donor blood at the blood bank and the high costs associated with current blood recycling methodologies in particular the cell saver machine. The hospital (CoRSU) carries out about 420 surgeries weekly and in over three quarters of these surgeries, the patients suffer haemorrhages. The hospital currently resorts to the expensive and un reliable method of blood bag transfusions which in recent research findings are not the best for trauma patients. An innovation for blood recycling and transfusion is of the essence. After profound desk based investigative research into this problem, we discovered shocking revelations like: “surgery deaths in Africa are twice the global average.” Furthermore, we found out that haemorrhages are the leading cause of death in the surgery setting of Africa and this in turn is accelerated by lack of blood donations and galore direct/indirect costs incurred by different stakeholders including patients.

The revelations from the needs finding exercise convinced us that it was important to solve the problem at hand. We carried out research pertaining the current solutions and their limitations in order to shape our solution. Our goal in this course series was to design of a device to carry out autologous blood transfusion. We believe that our solution - **haemoSAVE** will be a major driver in achieving universal health care as regards the surgery setting of Africa and other developing economies, it will further save stakeholders great amounts of money which can be directed to other problems in the health sector.

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Section One

1 Needs Finding Exercise

On Tuesday 11th September 2018, team UgHealth carried out a needs finding field work exercise in two hospital environments i.e. is CoRSU and Pan dental hospital. Below are some of the challenges that we identified after interaction with the different medical specialists and staff we interviewed:

- A. CoRSU doesn't have equipment for an emergency and causality section since the equipment is too expensive. Therefore, it is purely a referral hospital.
- B. The efficiency of suction machines quickly diminishes, surgeons face challenges during operating theatre.
- C. Power cuts interrupt operating procedures, spoil equipment and put patients on life support machines on higher risk of death.
- D. A lot of blood is lost during surgical operations by the patients, and there is a shortage of blood especially for rare blood types. An innovation for blood recycling is of the essence.
- E. Operating Rooms are congested by disorganised equipment and consumables
- F. Operating room doors (currently double swing) have to be touched to be opened, do not close properly and when opened bring in a lot of infections
- G. Poor infection control when operating rooms are not in use
- H. Club foot cases are reported late when available correction equipment cannot work.
- I. Many cases of injections gone wrong are reported at the hospital, innovation is required to improve precision of administering injectable drugs
- J. Some equipment that is to be re-used in different surgical operations cannot be sterilised
- K. The stand for administering saline solution on the arthroscopy machine has limited movement
- L. Lack of medical air to suppress complications of consumption of high oxygen concentration anaesthesia
- M. Delayed detection of complications during pregnancies especially due to family planning methods
- N. Miscarriages and abortions due to fear of complications from the current family planning methods
- O. There are no through knee amputation and hip joint replacements sized for infants on the market
- P. There is no way of recycling polypropylene and POP powder; materials used during fabrication of external limb replacements
- Q. Patients complain about the weight, strength and durability of prosthetics
- R. Dust raised by machines during fabrication of prosthetics causes respiratory diseases to the laboratory technicians
- S. Inefficient furnace used to prepare dentures
- T. Patients especially infants afraid of anaesthetic injections before dental procedures.

1.1 Assessment of results with needs finding matrix

The table below is a needs finding matrix with each problem identified by its letter as shown above.

	Needs finding matrix									
Problem	A	B	C	D	E	F	G	H	I	J
Frequency of occurrence	7	8	5	8	8	8	7	7	5	8
Impact of problem	7	8	7	8	5	8	7	7	7	4
Cost incurred to manage problem	0	8	3	8	0	2	5	7	8	5
TOTAL /30	14	24	15	24	13	18	19	21	20	17

Figure 1 Needs Assessment Problem Selection Matrix for problems A-J

	rix									
Problem	K	L	M	N	O	P	Q	R	S	T
Frequency of occurrence	8	9	7	7	7	10	7	9	7	8
Impact of problem	5	6	7	7	5	5	5	7	6	8
Cost incurred to manage problem	0	4	7	7	7	5	7	7	8	6
TOTAL /30	13	19	21	21	19	20	19	23	21	22

Figure 2 Needs Assessment Problem Selection Matrix for problems K-T

After consultation from our lecturers, we decided to move on with the problem D; A lot of blood is lost during surgical operations by the patients, and there is a shortage of blood especially for rare blood types. An innovation for blood recycling is of the essence.

2 Problem Statement

Surgery deaths due in Africa are twice the global average! It is therefore important to first understand the underlying phenomena and obtain a solution to the underlying causes of the scourge.

2.1 Problem Definition

Haemorrhage also known as bleeding, is the number one killer in surgery and the major cause of cardiac arrest in the operating room(Irita, 2011). Massive haemorrhage can be defined as; blood loss exceeding circulating blood volume within a 24-hour period, blood loss of 50% of circulating blood volume within a 3-hour period, blood loss exceeding 150 ml/min, or blood loss that necessitates plasma and platelet transfusion. Even though there is no universal definition(Jones, 2017), critical haemorrhage can occur even though the haemorrhage does not meet the above criteria(Irita, 2011). Surgery mortality rate increases with increasing blood loss and with decreasing minimum intraoperative haemoglobin level (Irita, 2011). When a patient loses 10-30% of their blood volume; they start feeling light headed, experience shortness of breath, palpitations among other things. After appreciable blood loss (>1000 mL), the injured person enters a state of hypovolemic shock, which requires the administration of replacement fluids as part of life-saving medical treatment(Jones, 2017).

2.2 Impact of Problem

Patients receiving surgery in Africa are younger than the global average, with a lower risk profile and complication rates and yet are as twice as likely to die (Eichert, Isgro, Kiessling, & Saggau, 2017). 20% of deaths in these surgeries are due to loss of blood. Countries with developing economies especially in Africa have not considered surgical care to be a public health priority (World Health Organization, 2016) and thus access to enough safe blood is almost impossible and not to mention,

costly. Blood transfusion is carried out to counteract blood loss. Blood transfusions are used to; treat a number of medical conditions such as anaemia and malaria among others, replace large blood loss during surgery and for emergency treatment. If the blood lost is of a patient with blood group A or AB which are significantly less prevalent in sub Saharan countries like Uganda, death is inevitable. In sub Saharan Africa, only hospitals with a bed capacity of at least 100 beds have blood banks (World Health Organization, 2016). In Uganda, only 10% of the health centre IVs can provide blood transfusion services (Medium, Macroeconomic, Development, Revenue, & Framework, 2017). Uganda Blood Transfusion Services spends about UGX 13 billion annually on blood transfusion despite a funding gap of UGX 8.4 billion (UBTS, 2018) and a budget cut of UGX 513 million in the FY2018/19; they are therefore unable to adequately collect, store and supply blood units.

Below we discuss some of the surgical procedures and other instances; both in and out of hospitals where haemorrhages are prevalent:

Post-Partum Haemorrhage (PPH) is the most common cause of maternal death. In Africa, PPH has been defined as an estimated blood loss of above 500ml during vaginal delivery and above 1500ml during Caesarean section (Edhi, Aslam, Naqvi, & Hashmi, 2013) and this severe bleeding can kill a healthy woman within two hours, if unattended. PPH in the surgery setting is the biggest maternal haemorrhage handled globally, and 14 million women suffer from this every year where about 99 % of the deaths occur in low and middle income countries and 97% of these women were hospitalized at the time of their deaths (Background & Bp, 2015). Of the 20 countries with the highest maternal death rates worldwide, 19 are in sub-Saharan Africa with the risk of maternal death being 16 per 1000 births. Many of these deaths could be prevented through access to safe blood (World Health Organization, 2016). Furthermore, as a consequence to unattended critical Haemorrhage, it might develop into cardiac arrest(or permanent disability of the central nervous system (Irita, 2011). In the developing economies like Uganda, efforts should focus on alternative means of providing safe blood in cases of haemorrhage, with particular focus on donation of warm whole blood, and autologous blood transfusion.

As regards orthopaedic surgeries, a lot of blood is lost particularly in the total joint arthroplasty procedure (Ji et al., 2017). At CoRSU, over 45 surgeries of orthopaedic surgeries are done daily; 90% of the patients suffer effects of blood haemorrhages and the vast expenses that come there with. The hospital is unable to provide free or price subsidised blood as it has a tight budget, even when funds are available, there is a lack of rare blood types most of the time.

Furthermore, operative mortality with elective surgery decreases in older Adults. 70% of deaths in surgery for older patients is due to haemorrhage; more than two thirds of these deaths are associated with shortage of blood packs for transfusion (Junction, Francisco, Francisco, & Junction, 2001). The operative mortality of older patients is significantly reduced greatly if methodologies are employed to ready blood for transfusion; in occurrence of haemorrhages life for this sect of patients solely depends on their quick regain of haemostasis since their body systems are much weaker(John B & Donald H, 2019).

Injuries account for 63 million of the disability-adjusted life year (DALYs) which are a measure of overall disease burden, expressed as the number of years lost due to ill-health, disability or early death. These injuries constitute 38 percent of the world's estimated surgical DALYs, 79 percent of death from these injuries is due severe blood loss (Ji et al., 2017). The occurrence of injuries highlights the need of blood for transfusion in pre-hospital situations and in the emergency department. After carrying out various informal interviews with ambulance drivers from Mulago hospital – Uganda and CoRSU hospital, we found that ambulance first aid kit lacks an “in ambulance blood transfusion kit”; that is neither for blood bag transfusion nor autologous blood transfusion.

2.3 Effects of the Problem

Blood haemorrhages have a number of physiological effects on the human body that surround the importance of blood in the human body like; delivery of nutrients and O₂ to different tissues and cells, transportation of waste products produced by metabolism to liver and kidneys, and the delivery of CO₂ to the lungs. Therefore, loss of blood immediately decreases the blood composition hence compromising numerous haemostasis processes and interferes with the cardiac output of the heart.

The aqueous phase of body composition — the total body water and its solutes — includes as its prime component the great working mass of body cells, participating in energy exchange and substrate oxidation for work performance. The body-cell mass is surrounded, infiltrated and bathed by a second watery component, slightly smaller in volume, and concerned with the bulk movement of oxygen, carbon dioxide, metabolites and regulators, via the circulation: the extracellular fluid. Whatever other differences exist between these two reservoirs of body water, none is clearer cut than the fact that within cell water the predominant cation is potassium at an approximate concentration of 150 milliequivalent. per litre, while in the water of the extracellular phase, potassium is present in very small quantities and the predominant cation is sodium, at an approximate concentration of 150 milliequivalent. per litre. Despite this distinction in the distribution of these two similar alkaline cations on the two sides of the cell membrane, total solute concentration is identical in both phases; there is no resting gradient for water distribution despite the large amount of energy expended to maintain this cationic distinction. In the steady state, partition within body water, as between cells and extracellular fluid, depends upon genetic determinants of body build, energy requirements and sex-linked regulators.

A haemorrhage distorts this steady state of body composition: a circulating segment of body composition is suddenly removed. Autoregulation of body composition is challenged so that its activities become more clearly evident. A multifaceted response ensues, whose understanding is essential to treatment.

Stage	Blood Loss	Vasoconstriction	Pulse Rate	Pulse Pressure/Strength	BP	Resp. Rate	Resp. Volume
1	<15%	↑	↑	→	→	→	→
2	15-25%	↑↑	↑↑	↓	→	↑	↑
3	25-35%	↑↑↑	↑↑↑	↓↓	↓	↑↑	↓
4	>35%	↓↓		↓↓↓	↓↓↓	↓	↓↓

Figure 3 Immediate Physiological Effects of blood Haemorrhage

2.4 Current Solutions

The general lack of blood for transfusion in developing countries has been well established by public health researchers and documented in academic literature as emphasised earlier in this document. Below are some of the methodologies used to combat blood loss:

2.4.1 Allogeneic blood transfusion

There are several options of blood transfusion depending on time and health factors. Some people prefer to receive blood from people they know, these are called designated donors. This blood has been found to be no safer than the community donor blood (Blood, Transfusion, & Surgery, WHO.). The replacement of blood losses by conventional allogeneic blood transfusion has for many years been the mainstay of management of major surgery and trauma.

However, there are two crucial issues related to allogenic blood transfusion in Africa, and these are blood shortages and unsafe blood, which both too frequently lead to severe problems, such as immunoreaction and infection (World Health Organization, 2016; Ji et al., 2017). Unsafe blood transfusions contribute to the enormous burden of HIV infections in sub-Saharan Africa and still continue to add to this burden with an estimated 3.2 million new infections of HIV in sub-Saharan Africa annually with 52,000 in Uganda alone (Medium et al., 2017). The risk of HIV infection through

unsafe blood and blood products is exceptionally high (95–100%) compared to other common routes of HIV exposure (Jacobsson, WHO.).

The safety and availability of blood transfusion is particularly under threat among refugee populations and in emergency situations where health systems have collapsed or have been weakened as a result of armed conflict, displacement of populations, natural disasters and other complex emergencies. In these extreme circumstances, making safe blood available to all patients needing transfusion is currently impossible (World Health Organization, 2016). Blood donation rates in Africa are generally very low, less than 1% of the population as per the WHO Fact sheet 2017. In its most recent global survey on blood safety and availability, WHO collected data from 40 of the 48 countries in sub-Saharan Africa. This data indicates that 35 (87.5%) of these countries collect less than half of the blood needed to meet the transfusion requirements of their populations. During a need finding by team *UgHealth* interview with head surgeon Dr. Antonio Loro at CORSU in Uganda 2018, it was found that hospitals spend so much to acquire blood packs for transfusion and their storage; but even in this, there is shortage of blood and a lack of rare blood types.

Because of heightened fears of virus infection transmitted through transfusion, as well as the better understanding of the risks and benefits of blood transfusion, there is an increasing demand for alternatives to allogeneic donor blood. Blood is often transfused unnecessarily, in African countries despite a severely inadequate supply of blood. This needlessly exposes patients to the risk of HIV, hepatitis and other serious side-effects. This poor-quality clinical care also reduces the availability of blood for patients for whom transfusion is essential and is a waste of scarce resources (World Health Organization, 2016). Application of autologous transfusion in such an environment would eliminate un-necessary transfusion since the system dictates that you get the blood that you lose. Access to safe blood could help to prevent up to one quarter of maternal deaths each year and blood transfusion has been identified as one of the eight life-saving functions that should be available in a first referral level healthcare facility providing comprehensive emergency obstetric and new-born care (UBTS, 2018).

2.4.2 Autologous blood transfusion

Autologous transfusion is where adults and some children use their own blood for a transfusion. Autologous blood transfusion is the collection of blood from a single patient and re-transfusion back to the same patient when required. This is in contrast to allogenic blood transfusion where blood from unrelated/ anonymous donors is transfused to the recipient. It is widely used in orthopaedic surgery, such as scoliosis surgery, hip and knee replacements. This technique is less popular now because it is very costly though it is highly efficient. (Blood et al., WHO.) However, it should be noted that rapid transfusion devices are useful to treat critical haemorrhage, although several precautions are required. (Irita, 2011). The current methodologies of autologous blood transfusion are not used widely especially in developing economies like Uganda because they are expensive; the device purchase, use and maintenance costs are high.

There are three main types of autologous blood transfusions performed in the clinical setting. Preoperative autologous donation (PAD) is used for planned surgeries with large expected blood losses. Blood is collected from the patient several weeks before the surgery and transfused after haemorrhage has stopped during the surgery. This method is very effective in reducing the need for allogenic blood and eliminates the risks of haemolytic, febrile or allergic reactions. Time is an important factor in performing PAD, as sufficient time must be allowed for the patient to replace some of the lost blood prior to surgery. PAD is normally more expensive than allogenic transfusions due to the added costs of increased administrative management of the blood units (Bilgili et al., 2014).

Acute normovolaemic hemodilution (ANH), also termed intraoperative hemodilution, is another preoperative autologous transfusion method, wherein blood is collected from the patient immediately before surgery and the lost volume replaced with a colloid or crystalloid. The collected blood can be transfused back into the patient once the patient is hemostable. This serves to minimize the blood volume lost during the surgery. The amount of blood that can be removed is limited and varies with the size of the patient. ANH cannot be used if the patient has already lost a large amount of blood, and is therefore not applicable in emergent situations involving heavy bleeding. Unlike PAD, ANH is more cost effective than allogenic transfusion. The main reasons for this are that the costs of testing, cross matching and storing the blood are eliminated (National Health Services, 2006).

The final type of autologous transfusion is intraoperative blood salvage (IBS), which can also be termed intraoperative autologous transfusion. In this method, blood is collected during surgery, processed, and returned to the patient. Processing methods vary, and can involve simple filtration or centrifugation and washing. Simple filtration transfuses whole blood back into the patient, while centrifugation and washing transfuses only packed red blood cells.

2.4.2.1 Acute Normovolemic Haemodilution

As mentioned above; before some operations begin, doctors remove some blood and replace it with other fluids. After surgery, the blood that was removed may be returned to the patient ("alternatives 2006," WHO).

2.4.2.1.1 Advantages

The technique provides up to 4 units of blood, which will cover many elective operations and eliminate the need for bank blood. The risks of viral transmission and immunologically mediated haemolytic, febrile or allergic reaction are virtually eliminated provided the patient only receives autologous blood. Immune-modulation seen after allogenic transfusion does not occur. This may decrease the risk of postoperative infection and recurrence of cancer. ("Alternatives of BT - 2006," WHO.; Babb & Mrcp, 2006)

2.4.2.1.2 Disadvantages

The system requires a great deal of logistical planning well ahead of surgery. This may be a particular problem where surgery is rescheduled at short notice. Pre-donated blood must be clearly labelled in the blood bank and the risk of clerical or human error remains. Up to 50% of pre-donated blood is unused. (Jacobsson, WHO.)

2.4.2.1.3 Precautions and contradictions

The patient must be able to tolerate repeated phlebotomy and the resultant haematological and cardiovascular challenges this entails. Patients are excluded if they have pre-existing anaemia, cyanotic heart disease, ischaemic heart disease, aortic stenosis or uncontrolled hypertension. (Babb & Mrcp, 2006; Blood et al., WHO.)

2.4.2.1.4 Complications

All the usual complications of blood donation/storage may occur, including bacterial contamination at collection and haemolysis because of improper collection, handling, storage or transfusion technique (Babb & Mrcp, 2006).

2.4.3 Intraoperative Autologous Blood Transfusion

The main advantage of this method over the previous two auto transfusion methods is the capacity to provide large quantities of autologous blood very rapidly. As the vast majority of ruptured ectopic pregnancy surgeries are performed in emergent situations, intraoperative salvage is the most suitable type of autologous transfusion for these patients (Babb & Mrcp, 2006). It is also becoming more common in orthopaedic surgery, such as knee and hip replacements ("alternatives 2016," WHO.). Below are the autologous blood transfusion devices on market:

CURRENT SOLUTIONS

Autologous Blood Transfusions the CELL SAVER

(intra-operative blood salvage, uses centrifugal forces to separate RBCs from blood plasma and adds nutrients before returning blood to patient)

Cost of buying **\$5000**

Cost of buying transfusion kit for each patient **\$85**

Cost of preparation of one unit of blood **\$150**

Annual Maintenance Costs **\$1000**



Eichert, I., Isgro, F., Kiessling, A. H., & Saggau, W. (2017). Cell Saver , Ultrafiltration and Direct Transfusion : Comparative Study of Three Blood Processing Techniques Cell Saver , Ultrafiltration and Direct Transfusion

Figure 4 Current Solutions: Cell Saver and its cost implications

2.4.3.1 Technique of centrifugation by Cell Saver

This method uses the principle of blood separation from plasma and water during centrifugation. The volume remained in the extracorporeal circuit is pumped into a centrifuge bowl in which the cellular components are separated. The remaining red cells are washed to remove debris, anticoagulant and plasma, and the resulting red blood cell product is pumped into a collection bag for return to the patient(Eichert et al., 2017).

2.4.3.2 Technique of Ultrafiltration of Hemosep Cell Salvage

This technique uses the removal of water electrolyte and small molecules across a semipermeable membrane by hydrostatic pressure. Large molecular substances such as blood cells, and protein remain preserved.

CURRENT SOLUTIONS



Autologous Blood Transfusions

the HEMOSEP CELL SALVAGE

(intra-operative blood salvage for open heart and orthopaedic surgery, absorbs RCBs & some platelets from salvaged blood and returns them to patients)

Cost of buying \$4000

Cost of consumables per use \$300

Annual Maintenance \$550



Eichert, I., Isgró, F., Kiessling, A. H., & Saggau, W. (2017). Cell Saver, Ultrafiltration and Direct Transfusion : Comparative Study of Three Blood Processing Techniques Cell Saver, Ultrafiltration and Direct Transfusion

Figure 5 Current Solutions: Hemosep Cell Salvage and its cost implications

Centrifugation is a key step in this process to remove all the waste in the blood, creating a red blood suspension which will be delivered back to the patient. Air detection before transfusion is very important since air embolisms want to be avoided. Although the blood obtained from this technique is safe to use, there is a major concern due to potential contamination with amniotic fluid, activating clotting factors, and other debris that could appear during labour. As a result, further filtering is of the essence as it increases patient safety. Candidates for this technique must have blood loss greater than 1,000mL; thus, women that have PPH are ideal candidates for this technique.

2.4.3.3 Advantages of autologous blood filtration techniques

Red blood cells which would have been lost are scavenged and reinfused. The technique provides a supply of red blood cells in proportion to the losses and theoretically an unlimited amount of blood may be collected, processed and returned to the patient. It is therefore the technique of choice when large blood losses are expected and becomes increasingly cost-effective with large volume losses. It has an excellent long-standing safety record. It utilizes simple and inexpensive collection and re-transfusion devices. This provides a cost-effective means of reducing the requirement of allogenic blood transfusion.(Eichert et al., 2017; Jacobsson, WHO.)

2.4.3.4 Disadvantages of autologous blood filtration techniques

The cell saver requires complex specialized equipment resulting in high initial capital expenditure and ongoing costs of disposables. A high level of training is required for the operator. The process is complex and can result in serious complications. The blood salvaged may contain cell debris, free haemoglobin and micro-aggregates(Babb & Mrcep, 2006).

2.4.3.5 Complications of autologous blood filtration techniques

When large volumes of salvaged blood are re-transfused, significant changes in haematological parameters may occur including the following: Electrolyte disturbances such as increased concentration of sodium and chloride and reduced magnesium, calcium and albumin, Dilutional coagulopathy as washed blood does not contain platelets or clotting factors; this may require blood-component therapy, and salvaged blood syndrome(Babb & Mrcep, 2006).

Incorrect use of washing and filtration devices may result in red cell destruction. There is potential for air embolism. Pyrexia and shivering are often reported following re-transfusion of unwashed salvaged blood, occurring with an incidence ranging from 1.5 to 12%. The exact cause is unknown but may be because of activated cytokines in the salvaged blood(Babb & Mrcep, 2006).

2.4.4 Associated Risks of Autologous Transfusion

2.4.4.1 Haemolysis and Coagulopathy

The main risks associated with autologous transfusion are coagulopathy (clotting disorders), haemolysis (rupture of red blood cells) and infection. Haemolysis can occur and cause subsequent coagulopathy if the blood is subjected to excess mechanical stress or if the blood is contaminated with bacteria. To avoid this, autologous transfusion should not exceed 4000 millilitres and should be done within four hours of removal (Salvage, 2009). Using the correct amount of anticoagulant can further reduce this risk. Coagulopathy can also occur due to the presence of thromboplastic substances (proteins necessary for clotting) and other coagulation system components present in whole blood, which has led to the belief that transfusing whole blood is riskier than transfusing packed red blood cells (Vamvakas & Blajchman, 2018). However, interviews with expert physicians at CoRSU have indicated that transfusing whole blood is preferable in many cases due to the fact that whole blood contains many other substances (clotting factors, platelets, plasma, shown in Figure below) that can positively influence a patient's prognosis.

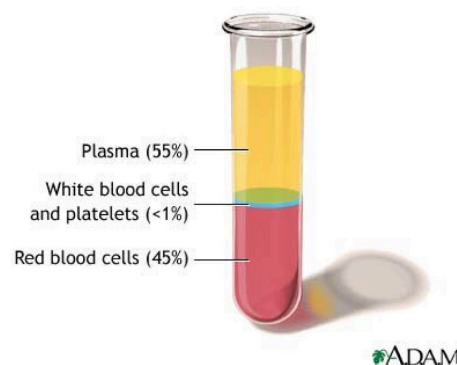


Figure 6 Components of Whole Blood

The ongoing wars in central Asia have convinced a new generation of clinicians that whole blood (WB) benefits bleeding patients (John B & Donald H, 2019). A survey done in August 2018 shows that 19 leading trauma centres in the US are using this approved product as their first line transfusion, with some starting pre-hospital and continuing into the Emergency Department (ED) and Operating Room. John B & Donald H report a retrospective, observational study of their recent experience of transfusing WB, performed in a rigorous fashion, with appropriate analysis and without overstating their results. They show that civilian trauma patients receiving WB plus components did as well or better than patients matched by propensity score who received components and no WB. There were trends toward lower mortality and faster lactate normalization in the low titer group O WB (LTOWB) group, as well as early and higher (closer to 1:1) transfusion ratios in the LTOWB group. Previously, this same group has shown that the fears of haemolysis are unfounded, similar to the results from the military studies, albeit with larger number of transfused WB units. Additionally, infections can occur if any part of the device is exposed to the environment. Prophylactic antibiotics are commonly used to prevent infection (Debas, Gosselin, & Mccord, 2004).

2.4.4.2 Air and Fat Embolisms

Air embolisms (air bubbles entering the veins) as shown in Figure 3 can occur during any transfusion procedure (allogenic or autologous) if proper protocols are not followed or devices are misused. Severe air embolisms can be catastrophic for the patient and cause complications in any organ system. Modern autologous transfusion devices have in-line air detectors which are used to prevent air embolisms. Most blood transfusion kits also have a mechanism to prevent air from entering the bloodstream during transfusion. Any new device must account for air embolisms as a potential side effect when considering design variables. Fat embolisms, while less likely to occur than air

embolisms, can also cause complications during transfusion. Fat embolisms can be prevented by removing micro aggregates from the blood(Bilgili et al., 2014).

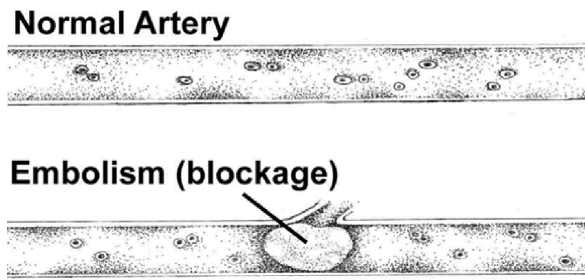


Figure 7 Embolism in an artery

2.4.4.3 Salvaged Blood Syndrome

Salvaged blood syndrome has been reported primarily in cases of transfusing packed red blood cells, though the theoretical risk exists for whole blood as well. The mechanism for the development of this syndrome is not well understood, but activation of platelets and white blood cells appears to be the cause. In this syndrome, the patient develops disseminated intravascular coagulation (DIC) and/or increased capillary permeability in the lungs(Bilgili et al., 2014). DIC causes haemorrhage and thrombosis (blood clots), producing an array of complications that must be treated by transfusing platelets and clotting factors(Blood Safety Program, Services, Health, & Bhutan, 2013; Highmore et al., 1970). Increased capillary permeability can cause pulmonary edema and shortness of breath. These symptoms are difficult to treat and often only treatment of the underlying disease will result in cessation of symptoms(Salvage, 2009). This syndrome can be prevented by using citrate as the anticoagulant as well as avoiding aspirating blood that has been heavily diluted by surgical fluids(Bilgili et al., 2014; Eichert et al., 2017).

2.4.4.4 Hypotension

The rare but serious risk of severe hypotension has been reported in isolated cases. When receiving autologous blood, some patients have experienced a life-threatening drop in blood pressure that returned to safe levels only when the transfusion was halted. No antibodies or other abnormal features were found in the blood that could have been responsible for the drop in blood pressure. This phenomenon remains unexplained, though it is hypothesized that the bedside leukocyte filter used during many autologous transfusions passes the blood through a pressurized tube, which could result in the excretion of vasodilation agents. The FDA reported in 1999 that severe hypotensive events occur in approximately 80 out of 20 million (0.004%) transfusion cases(Salvage, 2009).

3 Criteria for Success

Success is the ultimate goal of this design project, however due to the ambiguous definition of project success and the different perceptions of team members toward this concept, we set factors that will set basis for our success criteria away from the usual time, cost, and quality. These factors were closely consulted during the design process for the first functional prototype at the end of the designated time for implementation. At the end of the design project, we aimed to achieve a simple to use suction method and a device that is **easy to clean, affordable, reusable/disposable, collapsible, compact for transportation, sterilisable(if reusable), easily understandable and operable by only one person**. Being aware of blood flow properties, we carried out tests to choose the most efficient diameter of suction tube and pore size of the mesh filters to ensure that the process of recycling the blood is as short as possible maintaining output quality.

Material selection to build device. The materials selected should exhibit the required mechanical properties; the design in this project will comprise of different components which will each require different mechanical properties. Since we are dealing with blood, the materials used should be biocompatible in order to transport blood without having unintended effects. They should be sterilisable/easy to disinfect being that the team looked to design a device that comes into contact with sensitive body tissue-blood; considering that some of the components will be re-useable on

patients. Furthermore, the materials used should be safe to the environment that is, they should be easy to degrade or possibly be recyclable. Materials selected should be easy to fabricate as per the selected fabrication method.

Availability of materials to build device. These play a major role in the cost of the project in terms of acquiring the materials and fabricating them into different forms or shapes to suite the design. Using the locally available vernacular materials may result into a smaller budget; in the case where local materials cannot be acquired, cheapest but most effective material should be acquired. In the event of shipping materials, we needed to find a Freight Air Shipping service which has a 5-day delivery period from any part of the world to be used to acquire the materials unless otherwise. Therefore, the materials selected should be of appropriate pricing but effective especially if they cannot be re-useable. Available materials will be screened as per the design requirements and ranked according to pre-chosen factors.

Desirability of the product. The device produced at the end of this project should not only be profitable but also benefit the primary and secondary customers. The secondary consumers identified so far are health facilities offering surgery services. The primary beneficiaries are patients in health facilities that are prone to blood loss both in and out of operating theatres. The device should satisfy the consumer's immediate and long-term needs. We must therefore carry out a value proposition survey from the customer perspective to know what our customers really want and expect. At the end of the project, the device should be comparably cheaper to purchase than all existing marketed solutions, easy to use, cheap to maintain in terms of acquiring consumables and servicing and cover most of the consumer expectations.

Efficacy of the device. During the design process, we ensured that the device will work to fulfil its intended purpose. We should therefore ensure that the solution concept is legally and technically feasible as well as economically justifiable. A feasibility study should be done during solution screening, it should contain the following; technical feasibility – assessing the technical resources available to the project and the technical ability of the team, economic feasibility involving a cost-benefit analysis, legal feasibility investigating any aspect of the proposed solution conflicts with legal requirements, scheduling feasibility to assess if project will be completed in time, and an operational feasibility to see if solution satisfies the requirements discovered during the needs finding. The design and development team in this context includes all outsourced service providers, consultants and mentors.

Viability of the device. The project outcomes should have the ability to have a significant impact as regards the stated problem statement among other factors. The project viability mirrors the project feasibility. Therefore, the device from this project should be able to have a significant impact on haemorrhaging in a hospital environment in terms of being an attractive alternative to allogeneic blood transfusions and being the best choice for low resource environments for autologous blood transfusion.

Usability of the product. The solution propagated from this project should be easy to use, in the context of both a human centred and user centred design. If the device has computer based interactive system should meet the ISO 9241-210:2010 which provides recommendations for human centred design principles and activities through the life cycle of computer based interactive systems. The device should be an active product and thus for passive use; once started, it should operate with without much of the user's technical intervention. Active use of the product should be an option only if the users are equipped with the technical knowledge and want to customise the operation of the device to suite a special need. In addition, user training for both users should be comparably simple; this will make the device easy to use across all backgrounds of users. Failure to achieve ease of usability of the product immediately compromises the patient safety and an avalanche of challenges like shunning of device, loss of market, continuous break down of equipment to mention but a few.

Size and appearance of the device. Dimensions and appearance of a product have a significant impact on its desirability. Therefore, in comparison to the existing solutions for autologous blood transfusions, our device should be more mobile thus smaller. This coupled with other factors in comparison to existing solutions like power requirements will increase the desirability of our product.

Safety of the user and patient. The design should promote both user and patient safety by carrying out biocompatibility tests for the different components of the device. Patient safety, tests will be done of the device according to its classification; if the device is electrical, it would fall under class CF. If the device is electrical, tests for Protective Earth Continuity, Insulation, Earth leakage current, Enclosure leakage current, Patient leakage current, Patient auxiliary current should be performed. In doing all this, the device must conform to ISO 13485: 2016 for quality management systems related to medical devices, ISO 7153 -1:2016 for surgical instruments and other standards to ensure that all necessary precautions have been taken to ensure patient safety. Blood compatibility is to be evaluated for all blood contacting devices irrespective of the contact duration. According to ISO-10993, thrombogenicity, haemolysis, and immunology (complement activation) testing has to be performed for these devices.

4 Brain Storming & Idea Selection Matrix

This is the approach we used to generate numerous solution ideas that can be applied to efficiently and effectively manage the problem of blood haemorrhages during surgeries focusing on the autologous methods of blood transfusion, we considered ideas that will efficiently filter blood and yet are purchasable, maintainable and cheap to use. The generated solution ideas were reviewed and filtered to determine the most appropriate using an engineering matrix selection criterion. The biggest decision to make was whether to go for whole blood transfusion, or transfusion of only Red blood cells; we carried out intensive research as can be seen under the “Justification” coupled by the decision matrix as seen below and unanimously decided to go with whole blood transfusion.

Table 1 Decision matrix for either WB or RBC transfusion

Factors Solutions	Usability (out of 5)	Simplicity Design (out of 5)	in Cost Implication	Total (out of 15)
Whole blood transfusion	4	4	5	13
RBC transfusion	3	1	2	6

We decided that designing a device for the low resource countries in Africa that will foster autologous transfusions with the capability of blood recycling after it is harnessed from a bleeding patient during any medical procedure will be impactful in the development health sector. This device in the likeness of the Auto Transfusion System (ATS), Cell saver and Ultrafiltration machines would save a country like Uganda more than UGX 5 billion shillings annually. The process further has a reduced risk of disease transmission and transfusion reactions, minimal compatibility testing, and reduces demand on blood bank inventory.

The team unanimously decided that the device deemed – **hemoSAVE** has to be mechanically powered to suite health facilities with power issues and in so being the centrifugal method of blood recycling was eliminated. Therefore, the team had to choose a mechanism of operation that would avail suction of blood and pushing it through a haemofilter.

Table 2 Solution Matrix

Factors Solutions	Usability (out of 5)	Simplicity Design (out of 5)	in Cost Implication	Total (out of 15)
Use of a syringe Pump	4	3	2	9
Use of foot pump	5	2	3	10

Use of a siphon	5	3	4	12
Use of an electric Pump	5	2	1	8
Use of Squeeze pump	2	2	3	7
Use of a Hand clamped pump	2	2	4	8

5 Justification for Whole Blood Transfusion

The ongoing wars in central Asia have convinced a new generation of clinicians that whole blood (WB) benefits bleeding patients(John B & Donald H, 2019). As with many changes in civilian trauma care, the use of WB has transitioned from a wartime practice to the civilian world, becoming routine at many centres. A survey done in August 2018 shows that 19 leading trauma centres in the US are using this approved product as their first line transfusion, with some starting pre-hospital and continuing into the Emergency Department (ED) and Operating Room. John B & Donald H report a retrospective, observational study of their recent experience of transfusing WB, performed in a rigorous fashion, with appropriate analysis and without overstating their results. They show that civilian trauma patients receiving WB plus components did as well or better than patients matched by propensity score who received components and no WB. There were trends toward lower mortality and faster lactate normalization in the low titer group O WB (LTOWB) group, as well as early and higher (closer to 1:1) transfusion ratios in the LTOWB group. Previously, this same group has shown that the fears of haemolysis are unfounded, similar to the results from the military studies, albeit with larger number of transfused WB units.

These results are not only the justification for **haemoSAVE** but they also encourage other donor centres, blood banks, and clinicians caring for bleeding patients to collaboratively establish WB programs. The WB story is a fascinating example of evolution of clinical care! WB was the standard transfusion product for 50 years and was a balanced approach to transfusion(John B & Donald H, 2019). In the early 1970s it essentially disappeared from clinical use, replaced with unbalanced component therapy, in which plasma to red blood cell (RBC) ratios often reached 1:10, with platelets given even less often. This drastic change occurred without supporting outcome data in bleeding patients. Interestingly, it was during this era that acute respiratory distress syndrome, multiple organ failure, abdominal compartment syndrome, and profound coagulopathy became common(John B & Donald H, 2019). Over the last decade clinicians around the world have reversed this iatrogenic resuscitation error and are now transfusing bleeding patients in a balanced fashion, with amounts of plasma, platelets, cryoprecipitate, and RBCs that attempt to replicate WB(John B & Donald H, 2019). At the same time, the deleterious effects of even small amounts of crystalloid have become widely recognized, and plasma is used as the primary resuscitation fluid(Salvage, 2009). However, blood banks and bedside clinicians all report difficulty with coordinating the preparation, thawing, checking, delivering, and transfusing all these products at the same time and in the correct order(John B & Donald H, 2019); frankly it's just hard to do.

WB is easier and exposes the recipient to far fewer donors potentially making it safer from a number of angles, including human error. All indications suggest that WB is a superior product. It is one component that delivers plasma, platelets, fibrinogen, and RBCs in the correct ratio, in one bag, at one time, with a shelf life that can extend to **35 days**(John B & Donald H, 2019). Placing RBCs and thawed/liquid plasma on ambulances and in the ED has been associated with improved survival; however, with different expiration dates this has proved cumbersome to manage. Platelets have even shorter expiration dates (4 days) and different storage requirements than plasma and RBCs, while cryoprecipitate requires thawing before it can be transfused(John B & Donald H, 2019). WB eliminates these issues, providing one component, minimally “processed,” stored in its native milieu that delivers all these critical elements in one bag, greatly simplifying the storage, delivery transfusion, and administrative issues surrounding transfusion of the bleeding patient. WB is easily carried prehospital, for the first time in two generations providing for patients the highest quality of all elements in blood critical to haemorrhage control within minutes of injury.

The logistical advantage of WB versus attempting to recreate WB with component therapy is clear. The nursing personnel that “check the blood” at the bedside are some of the strongest proponents of WB, as they must contend daily with the paperwork and order of transfusion chaos that exists at the bedside while attempting to “recreate” WB from components. WB simplifies these issues by decreasing the paperwork and eliminating the ratio/order question. It is well known that administrative errors are the most common transfusion misadventure and WB will likely decrease those errors.

However, there is great concern about alloimmunization with WB. The bedside clinicians are not cavalier about this issue; however, there are studies being carried out trying to weigh a risk-to-benefit equation of alloimmunization in patients that at best have a 25% mortality within the next 105 minutes(John B & Donald H, 2019). For example, only a small minority of female patients of childbearing age are transfused. The risk of alloimmunization by transfusing O+ LTWB to a Rh- woman of child bearing age is commonly reported at 22% (3%– 30%) and an even smaller risk for her future child. If she is in haemorrhagic shock and requires a laparotomy, her mortality is more than 40%(Salvage, 2009). Therefore, WB is not the answer for all patients. As bleeding slows and transfusion becomes guided by laboratory values, component therapy can be utilized. **Using WB early will result in earlier haemostasis and decrease the overall number of blood products transfused.**

Other arising issues with the use of WB with the computer systems, cost, impact on other products, supply of O- versus O+ LTWB, the right titer, what is the right titer method, leukoreduced or not, platelet-sparing filter or not 21-day or 35-day storage, and what to do with expiring WB. While challenging, as UgHealth we are convinced that these issues are answerable. Further challenges arise when it comes to training bedside clinicians in the use of WB. **HaemoSAVE** will therefore be impactful in blood transfusion!

Section II

6 User Requirements and Specifications

6.1 Process to Obtain User Requirements

The project requirements were determined during the observations at CoRSU Hospital. Interviews were conducted with surgeons, anaesthesiologist, and technicians. Based on the results of these interviews, we developed a preliminary list of user requirements. We then distributed surveys ([Appendix 1](#)) to some hospital personnel both within CORSU and outside, asking them to rank the user requirements. The aim of this was to collect qualitative data to help us in the design process. With the four returned surveys, it was possible to rank the user requirements in order of descending importance.

6.2 Ranking System

The survey responders were asked to rank the identified user requirements by their perceived importance: a rank of 1 was the highest priority, a rank of 3 was medium priority, and a rank of 9 was lowest priority. These rankings were then summed, with the lowest numbers representing the most important requirements. The results are a clearly delineated ranking system, shown in Table 4.

Table 3 Results from survey for user requirements

Device Requirement	Raw Score
Removes particulates and blood clots	7
Minimizes contamination from environment	14
Minimizes risk of cross contamination between patients	17
Can be used in any clean cavity of surgery	20
Prevents air embolisms	24
Device is low maintenance	27
Doesn't require user to use their hands during suction	27
Alerts user when malfunctioning	28
Durable and long lasting	28
Easy to operate by any staff in surgical setting	29
Device is low cost	30
Connects to existing blood transfusion kit	32
Can contain large amounts of blood loss	33
Measures amount transfused to patient	35
Quick transition to backup power	36
Main power source is electrical	43
Device can be operated quickly	43
Device is portable	48
Device is small	50
Can change transfusion rate	50
Measures amount of blood lost by patient	52
Backup power source is mechanical	56
Device is quiet	57

6.3 Translating to Engineering Specifications

These user requirements were then translated into engineering specifications, either through direct literature research or through interviews which were then verified with the literature whenever possible as shown in *the* detailed specifications. Table 5 below shows a modified list of user requirements matched to engineering specifications. The preliminary user requirement list was modified based on

new findings from literature research. The exact process for obtaining each engineering specification is described in the “Detailed Specifications” section. The current list of user requirements reflects the team’s efforts to accurately represent the needs expressed by our end users. The team’s current engineering specifications are shown in Table 2 below. The double line in the table separates critical requirements from those which are considered non-critical, based primarily on the results of the customer survey distributed, as well as additional literature research. All of the requirements above the line must be addressed; those below the line. The items below the line are those our team considers optional; ideally, they will be included if possible, but since it is unlikely that we will be able to design a device which meets all of the requirements, those below the line can be sacrificed to achieve the more critical requirements.

Table 4 Ranked user requirements

	User Requirement	Engineering Specifications
Quality	Removes particulate matter	$\geq 170 \mu\text{m}$ in diameter Filtering efficiency of 98%
	Does not damage blood cells	$< 150 \text{ mmHg}$ pressure
Safety	Closed system	0 openings to environment
	Noticeable if device malfunctions	Force on plunger $> 45 \text{ N}$
	Durable	Withstand drop from 2 m
Function	Can manage significant blood loss	$\geq 2 \text{ L}$ blood loss
	Flow rate removes blood sufficiently	$\geq 0.5 \text{ L/min}$
	Measures total blood collected	$\leq \pm 10 \text{ mL}$ accuracy
	Easy to operate	Training time $< 30 \text{ min}$ 1 operator required < 5 steps for operation Force applied $\leq 48 \text{ N}$ Diameter of grip $\leq 3 \text{ in}$ Can be operated with foot pedal
	Low cost	\$25-\$30
	Compatible with or replaces blood transfusion kit	$\geq 20 \text{ drops/min}$ infusion rate $\leq 450 \text{ mL}$ blood bag volume Compatible with 3mm tubing on blood bag
	Quick to operate	Set-up time of $< 2 \text{ min}$ Time to first transfusion is $\leq 10 \text{ min}$
	Small and portable	$\leq 15.5 \text{ kg}$ filled
	Quiet Operating level	$\leq 30 \text{ dB}$

6.4 Detailed Specifications

6.4.1 Removes particulate matter:

This requirement was consistently ranked one of the most important by all the clinicians and staff surveyed. Anecdotal interviews suggested that clots can be seen as large as 20 cm (Jacobsson, 2018). Further research indicated that clots and particulates must be filtered to a level of 170 μm to reach a satisfactory risk level for transfusion. The standard level of efficiency for filters of any pore size is 98% (Association for Surgical Technologists, 2018; Jacobsson, 2018).

6.4.2 Does not damage blood cells:

Literature research indicated that a vacuum pressure greater than 150mmHg would result in increased cellular destruction of the whole blood(Blood Safety Program et al., 2013), making the transfusion process ineffective or potentially harmful for the patient. Therefore, a maximum vacuum pressure of 150 mmHg is indicated as the engineering specification(Blood Safety Program et al., 2013; Eichert et al., 2017). Additionally, all of the materials the blood comes in contact with must be biocompatible.

6.4.3 Closed system:

To ensure patient safety, contamination of blood from the surrounding environment should be minimal. To this end, Dr. Antonio Loro – orthopaedic surgeon at CoRSU expressed that he would like to minimize health care providers' physical contact with the blood by developing a closed system which would transport the blood from the patient, through a filtration system, and either into a blood bag or directly to the patient for transfusion.

6.4.4 Noticeable if device malfunctions:

An alert of some kind to notify the surgical staff if the device was malfunctioning was requested by a senior resident. He stated that the volume of a cell phone ring tone should be loud enough to get the attention of the surgeon. However, after subsequently reviewing the requirements, we decided that the alert not be restricted to an auditory mechanism. Therefore, the specification was changed to indicate the point at which a clinician should be notified that the device is malfunctioning. Since moving to a purely mechanical, disposable system, this specification had to be redefined. Because the operator is using their own mechanical power to operate the device, they should be able to determine if the device is becoming more difficult to operate because of clogging. This will be anecdotally proven during functional testing. The value of 45 N was theoretically measured as the maximum force (with error) needed to operate the device with no clogging present.

6.4.5 Durable:

The durability of the device is best described as its ability to withstand the impact force of being dropped from a certain height, since that is the most probable method of damaging a handheld device. Two meters was chosen as that height because it is representative of the average height of an adult man (North Carolina State University, 2006).

6.4.6 Can manage significant blood loss:

A haemorrhage is defined as blood loss exceeding 150 ml/min(Jones, 2017). Anecdotal evidence from literature indicates a maximum blood loss from ruptured ectopic pregnancies of 2500 mL (Hall, 1979). The device should be able to remove 2-2.5 L of blood without becoming clogged.

6.4.7 Flow rate removes blood sufficiently:

That flow rate of a cell saver machine is estimated at 3.5-6 L/min(Bilgili et al., 2014). However, in additional conversations with Dr. Antonio Loro, he stressed that the blood must be removed within 5 minutes of opening the patient's wound site so that the surgeon can begin repairing the haemorrhage. With a maximum blood loss of 2-3 L, this results in a much lower minimum acceptable flow rate, in the range of 0.5 L/min since haemorrhages are further described as blood loss exceeding 150 ml/min.

6.4.8 Measures total blood collected:

It is important for the physician to be able to estimate both the amount of blood that the patient has lost and the amount that has been transfused in order to determine the proper course of treatment; an accuracy of ± 10 mL in measuring this value was determined by the team to be acceptable. We are currently brain storming on the best way to carry out this measurement.

6.4.9 Easy to operate:

There is a serious human resource shortage in sub-Saharan Africa, especially in the area of skilled health workers(World Health Organization, 2016). Therefore, this device should be designed such that anyone in the operating theatre can use it with minimal training. Limited personnel are available and only one person is required to operate the suction machine currently in use; therefore, the number of personnel needed should be minimal. Benchmarking with the current suction machine yielded a maximum 5-step set-up process. A maximum training time of 30 minutes was recommended by a

senior clinician. Additionally, the female 5th percentile force that can be applied in a position needed to operate the device is 48 N, so we set the maximum force to this value so that most users will be able to operate the device. In addition, the device should be operable when attached to a custom foot pedal or even with a hand crank. Since the device has up to three methods of operation, we deduced anecdotally that it'd be easy to use and perfect for under staffed health facilities.

6.4.10 Low cost:

We have had to estimate the ideal cost, at least for the time being. We do know that currently from the Uganda Radio Network, a safe unit of blood costs UGX 79800/= which corresponds to approximately \$20. We would like to be in this range of costs for a disposable device, around \$20-25. Costing of the pump assembly will be done separately. We estimate the assembly to cost \$25, but this is bought once. Additionally, the issue of cost is vital when considering scaling of this particular mechanical design, since cost is an important prohibitive factor in the purchase of any new technology, especially in emerging economies.

6.4.11 Compatible with or replaces current blood transfusion kit:

The current blood transfusion kit has two ports on it that could be used as transfer points in the bag (Blood Safety Program et al., 2013). The device will use standard tubing that can be attached to either port. We decided that this requirement be met; since the staff is already familiar with the use of the current transfusion kit, this would also serve to make the device easier to use. In addition, the exit nuzzle is compatible with an infusion pump input. This will enable better equipped hospitals add saline solution to the blood before transfusing it back to patient.

6.4.12 Quick to operate:

The requirement that the device be quick to operate can be defined in multiple ways. We were able to quantify this concept in terms of the time needed to set up the machine (< 2 minutes) and the time between the first use of the machine on the patient and the availability of blood for transfusion (< 2minutes-30 minutes). These values were the result of clinician interviews. Further research into transfusion protocol in trauma situations indicated that the fastest possible time to transfuse blood in emergencies in U.S. hospitals was in the range of 10-15 minutes (Blood Safety Program et al., 2013) (Association for Surgical Technologists, 2018). The time to reach haemostasis can be up to 18-29 minutes without adverse effects for the patient (Association for Surgical Technologists, 2018; Blood Safety Program et al., 2013). The time to first transfusion has thus been set to 10 minutes.

6.4.13 Small and portable:

With the change to a handheld design (substitutable with foot pedal attachment), the main limitation for this requirement is the total weight. Anthropometric data showed a 10th percentile female isometric arm lifting strength of 22.8 lbs or 10.3 kg (North Carolina State University, 2006). This should be the maximum weight of the device when it is filled with blood. Additionally, the device need not be held as it can be fitted onto a pump assembly. However, this is not portable. Therefore, the foot pedal structure should be able to withstand weights of up to 20kg. Blood has a density of 1.06 g/mL (Quarteroni & Formaggia, 2004) and we plan to have a reservoir with a maximum volume of 500 mL, so the maximum weight of the remaining materials is 10 kg. Additionally, the device should be small enough that it can be operated by anyone; the primary limiting factor is the diameter of the reservoir. We set the maximum diameter of 2.5 in. to fit the 5th percentile female hand size of 6.4 in (North Carolina State University, 2006).

6.4.14 Quiet:

In discussions of operating volume, hospital staff indicated that the operating volume of the current suction machine was acceptable. We carried out a benchmarking procedure through literature research (Bilgili et al., 2014; Highmore et al., 1970) and found an operating volume of similar machines to be in the range of 50 dB. We anticipate that the device will not produce energy higher than 30dB.

7 Design Decisions

7.1 Concept Generation

The team's first step in concept generation was to create a functional decomposition diagram ([Appendix 2](#)) breaking up the tasks the device was required to perform. The categories that we included were precursory removal of large clots; insertion of the device into the open wound site cavity; withdrawal of blood from the cavity; transportation to a container (reservoir); removal of clots, particulates, and micro aggregates; prevention of new clots; and transportation of blood back into the body. These steps must also occur in the order outlined above, with the exception that the blood not necessarily be filtered before it is transported to a reservoir, but it must be filtered before it is transfused. We also created a category purely to analyse suction methods, since that was the basis of movement of blood throughout the system.

In terms of collecting blood, we concluded that suction of a siphon would be the top choice, which would be paired with a gravity driven filter for clots. We later discarded the siphon technique when the group realized the flow would stop if the device was not fully submerged in the blood, which would make it extremely difficult for the surgeon to use. We also determined that silicon could be used within the device to help prevent the formation of new clots (Eichert et al., 2017). The final issue was the decision of where or whether to inject additional anticoagulant, which is already present in the current blood bag.

1.1 Concept Selection

In evaluating ideas generated within the team and by the rest of the design class, we developed three complete systems. We chose the system that integrated the most highly ranked components, was most feasible within the scope of the team's engineering skills, and most fully addressed the user requirements by making a pros and cons list for each design ([Appendix 3](#)). The initially chosen concept was designated as the "easy siphon" but was set aside due to the reasons mentioned above and in the ([Appendix 3](#)).

During brainstorming, we had initially overlooked simple system designs, instead focusing on generating components which could be combined into a whole system. This methodology resulted in very complex systems. While evaluating the pros and cons of each system, the simple "Giant Syringe" concept emerged. This is a self-contained, man-powered system with no expensive pump necessary, composed essentially of a large-scale syringe with an internal filter. To our dismay, such a system already existed, hence we had to add a novelty around the same concept. The need for a user to free their hands and attend to the patient in the operating theatre came up. Use of other pumps would additionally boost the suction rate and require the operator less energy.

The concerns that the team believes we can address in the future development of the prototype are the blood volume capacity, flow rate, pump run by an electric motor and being prone to clogging. The device could feed directly into a blood bag, so the volume would not need to be larger than 450 mL, but would have to expand several times to collect all the blood in the cavity. The device could also be designed such that it would withdraw enough blood in one expansion to fill multiple blood bags.

7.2 Final geometry

The final geometry of the design was driven by two elements: functional needs and associated human factors. The main functional driver behind the dimensions of the reservoir was the minimum volume specification of 450 mL. We aimed for a volume of 500 mL to allow for the possibility of accidentally aspirating air into the device; the final geometry yields a 488 mL reservoir. We are currently brainstorming on how to solve the air embolism issue with the pump assembly. The other dictating factor in the final geometry was the 5th percentile adult female hand size, which limited the maximum diameter to 2.5". Similarly, the handle size on the plunger was dictated by the need to maintain the structural integrity of the piece while accounting for the 95th percentile adult male hand size. The diameter of

the inlet valve was dictated by the maximum diameter of readily available duckbill check valves. The outlet diameter was chosen to interface with the standard blood bag tubing size. Please find diagrams in the [Appendix](#).

7.2.1 Check valves

In designing this device, we investigated several different types of check valves. We began by looking at umbrella valves, but found that they didn't allow a large enough area for blood to flow through at the inlet. At the outlet, they did not allow for flow in the correct direction. We then moved to duckbill valves, which allow for a larger diameter at the inlet and a different attachment mechanism at the outlet. Until this point, we planned to place the inlet valve above the filter; however, the adoption of the duckbill valves necessitated movement of the valve. The largest diameter duckbill valve we were able to obtain has an outer diameter of 0.63". A filter of this size would clog too rapidly for the intended purpose, meaning that the diameter of the filter would need to be larger than that of the duckbill valve. Therefore, we switched the locations of these two components. This change necessitated the addition of a third check valve above the filter to prevent flow of filtered blood backwards through the filter on the down stroke of the plunger. Because we were unable to find an appropriate manufactured check valve, we had to design and fabricate a simple rubber swing check valve.

7.2.2 Tapered tip

We chose to add a tapered tip to the design for a number of reasons. First, the tip will now be used to store large clots that are filtered out by the first, coarse internal filter. This function means that we needed to have an enclosed volume at the tip of the device. Rather than simply extending the cylindrical body of the device, we chose to modify the tip, which provides this storage volume without further obstructing the user's view of the operating field.

7.2.3 Reusable vs. disposable

One of the major changes in the team's final design compared to previous iterations is that it is entirely disposable. Early designs were intended to be reusable with a few disposable parts. To justify this decision, we completed a preliminary cost analysis comparing the cost per unit to produce a reusable and a disposable device with the same geometry. Additionally, it is worth noting that the design for a reusable device would be slightly different from that for a disposable device; in the reusable version, the filters would need to be removable. This factor has the potential to further complicate the manufacturing process.

8 Engineering Background

In this chapter, we looked at the basic engineering principles of to consider in order to ensure safe blood transfusion before we can carry out the engineering analysis. Before we consider blood as a Newtonian fluid we have to ensure that vessel diameters for the intended device are greater than 0.3 mm, and above shear rates of 100 sec^{-1} . We therefore study blood biochemistry to find out the components of blood that influence its viscosity after which we use fluid mechanic analysis to deduce the shear rate of blood. However, this chapter is only a preamble for the actual calculations that lie under "*Engineering analysis*."

8.1 Blood Biochemistry

Blood is made up of cells (and cell fragments) suspended in a liquid called plasma (Guyton & Hall, 2000). The plasma contains dissolved proteins, metabolic wastes, and other molecules being moved between organs. There are two main types of cells present in blood, erythrocytes, or red blood cells, and leukocytes, or white blood cells. Erythrocytes make up 99% of the blood cells and are responsible for carrying oxygen through the circulatory system (Johnson, 1991). Leukocytes are part of the immune system and help protect the body against infection and cancer. The cell fragments present in blood are called platelets and function in clotting when blood vessels are damaged.

The components of blood can be separated by centrifugation. The erythrocytes sink to the bottom of the centrifuge tube, and the plasma rises to the top. Platelets and leukocytes form the “buffy coat” between the layers of plasma and erythrocytes(Johnson, 1991). If the blood is allowed to clot, the remaining fluid is termed serum. Serum is similar to plasma but lacks the protein fibrinogen(Guyton & Hall, 2000; Johnson, 1991). There are several different methods to measure the amounts of each blood component. The percentage of blood volume that is intact red blood cells is defined as the haematocrit level. Normal levels of haematocrit are 45% in men and 42% in women. Haemoglobin concentration measures the concentration of the major oxygen-carrying pigment haemoglobin in whole blood. Normal levels of haemoglobin are 15 g/dL in men and 13.8 g/dL in women. The actual number of erythrocytes in a specific volume of blood (termed the RBC count) can also be calculated. Normal counts in men are 5.2 million cells/ μL , and 4.6 million cells/ μL in women(Johnson, 1991).

Anaemia is a medical condition defined as a reduction in one of the measurements previously discussed. Anaemia can be caused by a very wide variety of factors. Surgery patients are almost always present with anaemia due to haemorrhage. There is no exact lower limit to what is considered a normal haematocrit/ haemoglobin/ RBC count and what is anaemic. The World Health Organization criteria for anaemia are haemoglobin levels of <13 g/dL for men and <12 g/dL for women. However, these levels were intended to be used for nutritional evaluation rather than for a standard in the diagnosis of anaemia(Guyton & Hall, 2000). Haemolysis occurs primarily through mechanical injury to the cells caused by air bubbles that expand and collide with the cells, generating mechanical stresses. Thus, aspiration of air should be avoided whenever possible to reduce the incidence of haemolysis. Dilution of the blood with saline is an option to consider. Adding saline in a ratio with blood of approximately 1:1 reduces the incidence of haemolysis by 55-60%, even at suction pressures of 300 mmHg (Association for Surgical Technologists, 2018).

8.2 Fluid Mechanics

Fluid mechanics will be the most important relevant scientific field related to the function of the device. As the device will be dealing primarily with blood, it is important that we fully understand the fluid dynamics of blood for the device to function as needed.

8.2.1 Hemodynamics:

Although whole blood is technically a non-Newtonian fluid(Baskurt, Ph, Meiselman, & Sc, 2003), a good approximation is that it may be considered a Newtonian fluid at vessel diameters greater than 0.3 mm, and above shear rates of 100 sec^{-1} (Highmore et al., 1970; Salvage, 2009). We will be using tubing significantly larger than 0.3 mm in diameter; however, we do not yet know if we will be applying a shear rate greater than 100 sec^{-1} .

8.2.2 Blood Viscosity:

Whole blood has an average viscosity of about 4 centipoise and is incompressible (constant density)(Duncker, Vranckx, & Hasan, 2002). This is about 4 times higher than the viscosity of water (1centipoise) (Baskurt et al., 2003). As whole blood is a non-Newtonian fluid, the viscosity is dependent on the shear rate. Specifically, whole blood is a shear-thinning fluid, as apparent viscosity decreases with increasing shear rate. There are two factors that contribute to this: cell aggregation at low shear rates and erythrocyte deformation at high shear rates. Erythrocyte aggregation occurs in the presence of fibrinogen and globulin, two plasma proteins. The erythrocytes stick together to form aggregates called rouleaux. These rouleaux are broken up as the blood flows at faster rates, decreasing the particle size and lowering the overall viscosity. Experiments have shown that the rouleaux are broken up into single cells at a shear rate of 10 sec^{-1} (Figure 8, middle panel). As the shear rate continues to increase, the apparent viscosity continues to drop. This phenomenon is attributed to the elongation of erythrocytes at high shear rates, which further decreases the viscosity (Figure 1, bottom panel) (Duncker et al., 2002).

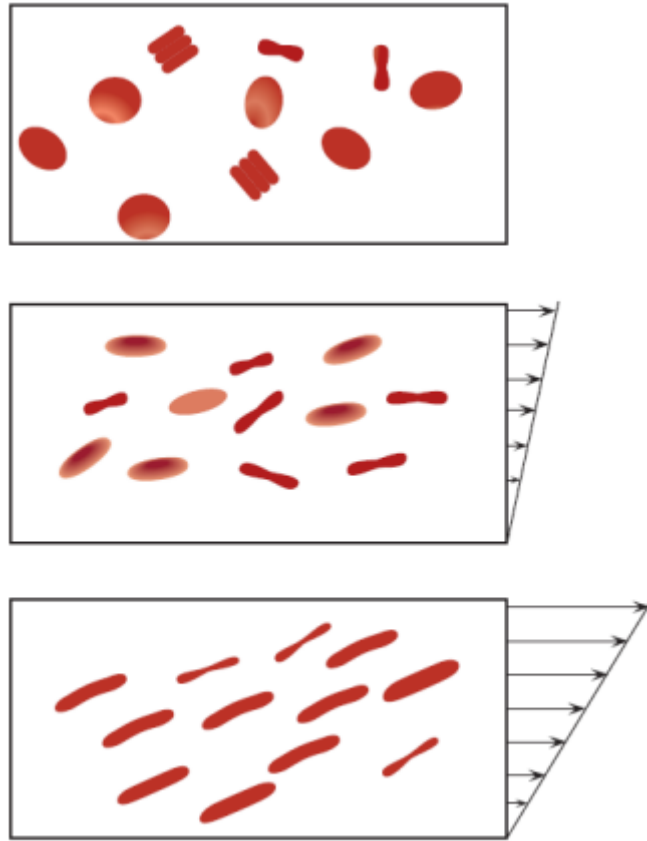


Figure by MIT OCW.

Figure 8 Physiologic changes during increasing shear rates

The viscosity of blood is also a function of haematocrit. The number of erythrocytes present in blood changes how the blood will respond to an applied force. We can compile these factors influencing the viscosity of blood into a relationship that we can use to calculate the viscosity in a given circumstance to a more accurate level than simply using the average, 4 centipoises. If the shear rate is above 100s^{-1} , the relationship is Newtonian and the viscosity is given in centipoise by:

$$\mu N = (0.00221) \left(e^{\frac{1965}{T}} \right) (e^{2.31f})$$

T is the absolute temperature of the blood in Kelvin and f is the fractional haematocrit value. If the shear rate $\dot{\epsilon}$ is below 100 s^{-1} (non-Newtonian behaviour), the viscosity is calculated as:

$$\mu = \frac{T_y}{\dot{\epsilon}} + 2\sqrt{\frac{T_y + \mu_N}{\dot{\epsilon}}} + \mu_N$$

Here, $\dot{\epsilon}$ is the strain rate, μ_N is the Newtonian velocity, given by the same equation used if the strain rate is above 100s^{-1} , and τ_y denotes the yield stress of the fluid expressed in dyne/cm^2 . The value of τ_y is determined through the equation:

$$T_y = (f - 0.1)^2 (c_f + 0.5)^2$$

In the above relation, f is the fractional haematocrit of the blood, and c_f is the concentration of fibrinogen expressed in g/dL (Baskurt et al., 2003). These relationships will be important to consider as we further examine the operation of the device. In order to perform any type of velocity, flow or pressure calculation, we will need to know the viscosity of the fluid we are working with. We will need

to perform an analysis of the flow dynamics of the device, regardless of the form of the final design, to ensure that it meets all relevant engineering specifications. Flow rate and pressure will be the two most important parameters to consider. The flow rate must meet the specification of 10 L/min without exceeding the maximum pressure of 150 mmHg that can damage the red blood cells. The balance between these two parameters is both the design driver and the most difficult challenge. We will need to make decisions regarding the dimensions, force, volume, suction pressure that comprise the device in order to ensure these two specifications are simultaneously met.

8.2.2.1 Classification of Flow

There are several different fluid dynamics principles we will need to utilize to characterize the flow of blood through the device. First, we will need to determine if the flow is laminar or turbulent. This is accomplished by calculating the Reynolds number, which is an expression of the inertial to viscous forces. Reynolds number is calculated using the expression:

$$Re = \frac{\rho v L}{\mu}$$

where ρ is the fluid density, v is a characteristic velocity, μ is the fluid viscosity and L is a characteristic length. When analysing flow in a tube, as we will be for our device, the characteristic velocity is the average velocity and the diameter of the tube is the characteristic length. In cylindrical tubes, the flow is defined as laminar when $Re < 2300$. The intermediate region is termed the transitional flow region, where the flow is unstable and intermittently turbulent (Quarteroni & Formaggia, 2004).

8.2.2.2 Bernoulli Equation

The Bernoulli Equation relates parameters of a fluid flow along the same streamline. The use of the equation is restricted to certain flow situations. Viscous effects are assumed to be negligible, the flow is assumed to be steady and incompressible and the equation must be applied along a streamline. The general Bernoulli equation is expressed as:

$$p + \frac{1}{2}\rho v^2 + \rho gh = \text{constant}$$

Depending on the final calculation of the Reynold's number, the Bernoulli equation may or may not be a reasonable approximation of the flow. High Reynold's number flows are dominated by inertial forces, and the viscous forces can be considered negligible. If the Reynold's number of the flow is large, the Bernoulli equation would be a reasonable approximation to the flow and we can forgo attempting to estimate the exact viscosity of the blood. If the Reynold's number turns out to be small, viscous forces will dominate the flow and we will have to use one of the following equations to characterize the flow (Quarteroni & Formaggia, 2004).

8.2.2.3 Conservation of Mass

We can also use the principle of conservation of mass. The conservation of mass holds for any type of flow and any type of fluid, and thus will be relevant no matter what results from the previous flow and viscosity calculations. Blood is an incompressible fluid, so we can write the conservation of mass as:

$$\oint_{cs} \vec{v} \cdot d\vec{a} = 0$$

8.2.2.4 Conservation of Momentum

We can also utilize the conservation of momentum, commonly called the Navier-Stokes equation. Like the conservation of mass, Navier-Stokes can be applied to any flow conditions and any type of fluid. The general form of the Navier-Stokes equation is:

$$\rho \frac{d\vec{v}}{dt} + \rho(\vec{v} \cdot \nabla) \vec{v} = -\nabla p + \mu \nabla^2 \vec{v} + \rho \vec{g}$$

The fluid density is denoted ρ , the viscosity μ , the velocity vector $\vec{v}$, and the gravity vector $\vec{g}$. The complete Navier-Stokes equation is rarely used without simplifying assumptions, as very few exact solutions have been found (Quarteroni & Formaggia, 2004). Poiseuille Flow One of the exact

solutions to the Navier-Stokes Equation holds for laminar flow in a tube. If we determine the flow through the device to be laminar, we will be able to use Poiseuille's Law to characterize the flow. Poiseuille's Law relates the flow rate to the pressure drop for rigid tubes.

$$Q = \frac{\pi a^4}{8\mu l} (P_a - P_b)$$

Here, a represents the radius of the tube, μ represents the viscosity; P_a and P_b represent the pressure at two different points along the streamline, with Δl being the distance between them (Baskurt et al., 2003; Duncker et al., 2002).

9 Material Selection

This section will describe the materials that were chosen for the prototype and the final design.

9.1 Prototype Materials

Since the prototype will demonstrate the function of the device only, we chose a material that would be easy to machine and is clear. This material did not need to be of medical grade as the initial prototype will not be tested on patients and will only serve as a proof of concept. We chose ABS to manufacture the prototype device. ABS is not medical grade and cannot withstand sterilization cycles but is easy to 3D print, inexpensive, and comes in standard stock sizes.

10 Engineering Analysis

The analysis of the device parameters was completed using the material properties of medical grade polypropylene, shown in Table 6 below.

Table 5 Parameter analysis of materials

Density	0.92
Yield Strength	33MPa
Young's Modulus	2068MPa
Flexural Modulus	1380MPa
Hardness	100MPa
Impact Resistance	690J/m

Fusion 360 Material Library

10.1 Whole Device

10.1.1 Impact Force:

Because the entire device is handheld, it has the potential to be dropped onto a hard floor and break due to the impact force. We can treat the device as a mass, m , falling from a height, h , onto a structure (the floor) which deforms to absorb the energy of the mass. The maximum velocity at which it impacts the floor can be easily calculated using the principle of conservation of energy.

$$\Delta KE + \Delta PE = 0 \rightarrow mgh = \frac{1}{2}mv_f^2 \rightarrow v_f = \sqrt{2gh}$$

Assuming a straight-line collision (no change in angular momentum), the net work done is:

$$F \cdot d = \Delta KE = \frac{1}{2}mv^2 = mhg \rightarrow F = \frac{mgh}{d}$$

where d is the distance the device travels after impact with the floor. This distance is dependent on the material properties of the floor. A second method for determining the impact force uses the definition of force as the change in the momentum of the device.

$$F = \frac{\Delta p}{\Delta t} = m \cdot \frac{v_f}{\Delta t} = \frac{m\sqrt{2gh}}{\Delta t}$$

Here the problem is in estimating the time needed for the device to stop moving. As yet we have been unable to find a method to estimate this value. The method for determining the deformations of the floor also depends on estimates of the strain of the floor, and since we would also be choosing a floor material arbitrarily, this equation also results in unsubstantiated quantities for the impact force. Therefore, we have chosen to disregard this analysis with the assumption that our device will be manufactured from material that is already being used in handheld, disposable medical devices that has undergone rigorous testing in this area. The components of our device most prone to failure due to an impact force are the tip, the exit valve to the blood bag, and the handle of the plunger. The tapered support in the current tip design should help minimize the adverse effects of an impact force. The other two areas remain vulnerable.

10.2 Plunger

10.2.1 Torsion:

The plunger could be subject to torsion while it is in the extended position. The 95th percentile force for an adult male hand torque is 7.4 N-m (North Carolina State University, 2006). The plunger can be modelled as a beam with a cross sectional area shown in Figure 2 and corresponding polar moment of inertia, J , derived below.

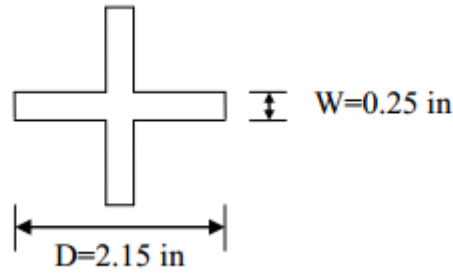


Figure 9 Model of plunger for analysis

$$J = \int A r^2 dA = I_x + I_y = 2I_x = \frac{1}{6} \cdot W \cdot D^3 = \frac{1}{6} \cdot W^4 = 0.419 \text{ in}^4$$

The maximum shear stress occurs at the outer surface of the plunger and is:

$$\tau_{max} = \frac{T \cdot c}{J} = 7.4 \cdot 0.05461 / 1.744 \times 10^{-7} = 2.3 \text{ MPa}$$

The maximum shear stress can then be translated to the plane stress using the principles of Mohr's Circle, such that $\tau_{max} = 2 \cdot 2.3 \text{ MPa} = 4.6 \text{ MPa}$. The yield strength of the material is 33 MPa, giving a safety factor of 7.2. This models the behaviour of the plunger if it were rigidly attached to the reservoir tube. In reality, the plunger will rotate in torsion, with a frictional force created by the interference fit of the rubber ring. The maximum torque will be lower than this value, resulting in an even larger safety factor.

10.2.2 Bending:

The position at which the plunger has the largest bending moment is when it is fully extended from the reservoir, supported only by the O-ring at the end. If a perpendicular force is applied to the end of the plunger and it is modelled as beam which is rigidly attached at one end, the bending stress is

$$\sigma = \frac{M \cdot y}{I_x} = \frac{F \cdot H \cdot \frac{D}{2}}{0.5J} = \frac{199.2 \cdot 0.214 \cdot 0.044}{0.872 \cdot 10^{-7}} = 21.5 \text{ MPa}$$

with F as the 95th percentile adult male pulling force (North Carolina State University, 2006).

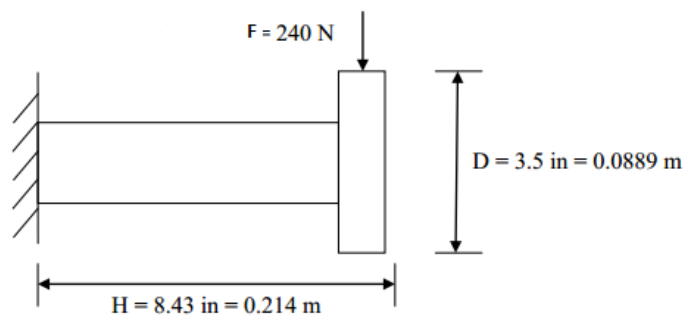


Figure 10 Model of plunger when subjected to perpendicular force

Because the reservoir tube and the plunger are composed of the same material, it is only necessary to analyse the failure of one of these. These results yield a safety factor of 1.3. While this is a low value, it is unlikely that the total 240 N force will ever be exerted completely perpendicular to the plunger; **there will likely always be a parallel component**, reducing the bending moment.

10.3 Reservoir

10.3.1 Hoop Stress:

The reservoir will be subject to a hoop stress applied by the user in gripping the reservoir during operation of the device. That stress was modelled using the following assumptions:

- grip force of 622 N (95th percentile of adult males)
- Uniform pressure around the reservoir. The hoop stress is then:

$$\sigma = \frac{pr}{t}$$

with a wall thickness of 1/8" and an external diameter of 2 1/4". The pressure can be calculated as:

$$p = \frac{F}{SA} = \frac{F}{2\pi r H} = \frac{622}{2(0.029)(0.1651)} = 20.9kPa$$

$$\text{Thus: } \sigma = \frac{pr}{t} = \frac{20.9kPa \cdot 2.25in}{0.125in}$$

Converting the dimensions into metres, $\sigma = 376.2kPa$. 376.2 kPa is well below the yield strength of 33 MPa (with a safety factor of 88), so the reservoir will not fail.

10.3.2 Check Valve

We were unable to find a large check valve that could interface with the large inner diameter (2.25") of the device. Therefore, we decided to manufacture a custom swing check valve out of rubber that will fit the large tube diameter in the reservoir. However, to **ensure that the valve will open under the negative pressure in the reservoir tube**, we performed a beam deflection calculation with one end fixed and a point load centred in the middle of the beam.

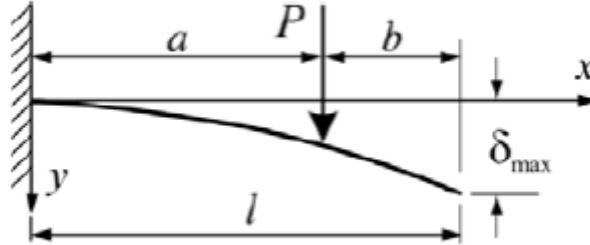


Figure 11 Beam deflection analysis; to study opening of check valve under negative pressure(Quarteroni & Formaggia, 2004)

$$\delta_{max} = \frac{Pa^2}{6EI} (3l - a)$$

The specifications do not dictate a minimum force on the plunger, only that the maximum force should be less than 43 N. Therefore, we chose a representative small force (P) of 11.121N = 2.5 pounds (a pressure of 1 psi in the reservoir tube over an area of 2.5in²). The disc was simplified as a square of uniform cross section (1.5" x 1.5") for the calculation of beam deflection. The corresponding a value was 0.75" and the l value was 1.5". The moment of inertia (I) of the beam was calculated as $\frac{1}{12}lt^3$, where t is the thickness of the rubber (1/8"). The Young's modulus (E) provided by the manufacturer of the rubber was 5500psi. The resulting maximum deflection was determined to be 3.6", which means that the valve will open under a pressure of 1psi, and will therefore open with much larger applied forces on the plunger.

10.4 Dowel Pins

The plunger will apply a shear force (F) on contact to the two dowel pins. The dowel pins we would like to use are made from stainless steel which has a shear strength of 186 MPa. To calculate the force, F, required to shear the dowel pins we use $\tau = F/A$ where A is the area of the two dowel pin

surfaces in shear and τ is the shear strength of the stainless steel. The area for the two dowel pins is calculated to be 35.63 mm². Therefore, the force required to shear the dowel pins is 6600 N which greatly exceeds the forces that will be applied on the plunger.

10.5 Fluid Flow in the Device

There are several different parts of the device in which we must characterize the fluid flow. We begin with the basic force equation, $F = ma$. We are going to make the simplifying assumption that the applied force to the plunger is constant, although few people would be able to apply a truly constant force. Examining the forces on the plunger we can draw the free-body diagram.

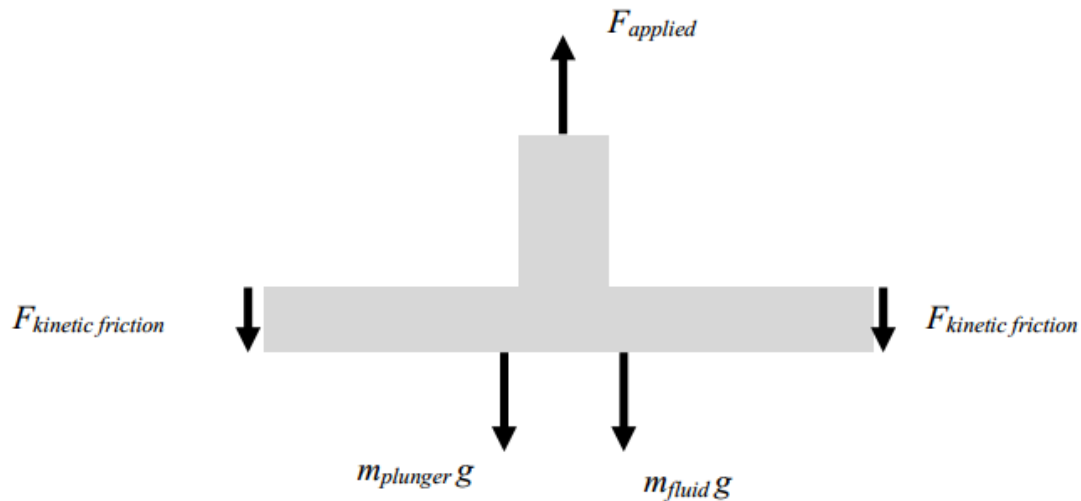


Figure 12 Analysis of forces on plunger with free body diagram(Hibbeler, 2010)

As the weight of the fluid is much more significant than the weight of the plunger, we will neglect the weight of the plunger for now. We will also neglect kinetic friction. It is difficult to determine the kinetic friction in this case using the normal equation $F_k = \mu k N$. There is no normal force due to the weight of the plunger, as the friction force acts completely perpendicular to gravity. Rather, the sealing pressure of the O-ring around the plunger caused by the interference fit creates the normal force. Additionally, the coefficient of kinetic friction is dependent on the velocity of the plunger, and is not constant in time. Assuming a constant plunger velocity of 100 mm/min, the friction force of a typical 3-piece syringe traces a curve of:

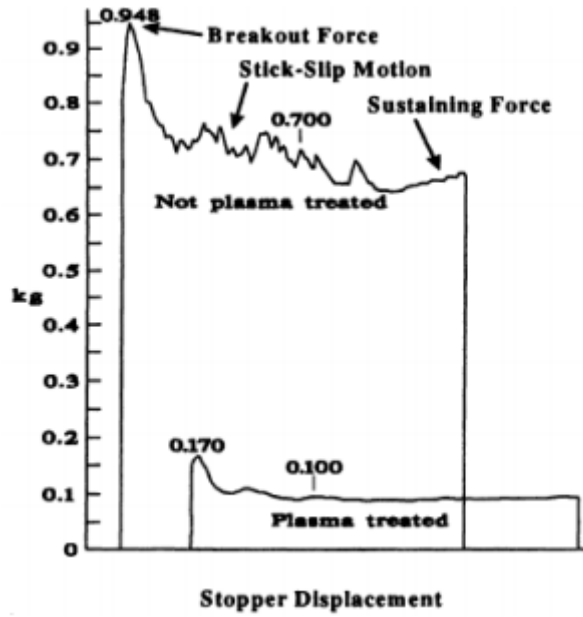


Figure 13 Friction force in a Friction force ((Tsukruk & Bliznyuk, 2006)

In Figure 14, the top curve shows the friction force when using a basic silicone lubricant. The bottom curve shows the forces generated when the syringe barrel is treated with plasma to crosslink the lubricant and reduce the force. Inclusion of kinetic friction when examining the plunger introduces a high degree of complexity. Friction forces normally have to be experimentally determined, and are something we will have to consider when performing validation tests. However, friction will have the ultimate effect of lowering the velocity of the plunger (and subsequently the fluid) so we do not anticipate that it will cause a harmful increase in pressure. Returning to the basic force equation, we now are examining only two forces, the applied force in the +y direction and the weight of the fluid in the -y direction. As the mass of the fluid changes as the plunger is pulled back, we must produce an equation for the mass of the fluid as a function of time. This mass will be a piecewise function, as the suction tube fills prior to the barrel. We will define the first phase of filling as the time before the suction tube is full, and the second phase of filling as the time after the suction tube has filled and the barrel is filling.

$$m = \rho V = \rho \pi r^2$$

$$m = \rho (\pi r_1^2 h_1)$$

$$m = \rho (\pi r_1^2 h_1 + \pi r_2^2 h_2)$$

Here, parameters with a '1' subscript denote the suction tube, while those with a '2' denote the barrel. m_1 denotes the mass of the fluid in the suction tube, which does not change in time once full. The heights are related to the velocity of the plunger. We know that h_2 increases at the same rate as the plunger speed v , which means that h_2 can be expressed as $v \cdot t$. The speed at which h_1 increases is also related to the velocity of the plunger v . We can equate these parameters using the flow rate of blood through the device:

$$Q = A_1 V_1 = A_2 V$$

$$\pi r_1^2 v_1 = \pi r_2^2 v$$

Thus $v_1 = \frac{r_2^2}{r_1^2} v$; this means that we can express h_1 as a function of v .

We can then take this mass and return it to the equation for acceleration: $A = F/m$. Using the definition of acceleration as the time rate of change of velocity, we can integrate this equation to obtain the velocity of the plunger as a function of time. Looking first at the first phase we have:

$$a = \frac{dV}{dt}$$

$$\frac{dV}{dt} = \frac{F}{\rho \pi r_2^2 V t}$$

$$V dV = \frac{F}{\rho \pi r_2^2 t} dt$$

$$\int V dV = \int \frac{F}{\rho \pi r_2^2 t} dt$$

$$\frac{1}{2} V^2 = \frac{F}{\rho \pi r_2^2} \ln t + C$$

We can disregard the negative case, as it does not make sense to have negative velocities of the plunger. We then get:

$$V = \sqrt{\frac{2F}{\rho \pi r_2^2} \ln t + C}$$

We would like to be able to use the initial condition that the fluid starts out as stationary ($V(0)=0$), but as the natural logarithm of zero is undefined we cannot. Therefore, in order to determine an approximate value of the constant of integration C , we will choose a small value of t ($t=0.1s$) and assign the velocity at that time to be zero. We then solve for C and obtain:

$$V = \sqrt{\frac{2F}{\rho \pi r_2^2} \ln t + 4.605F/\rho \pi r_2^2}$$

For the second phase of filling, we can repeat the same procedure,

$$a = \frac{dV}{dt} = \frac{F}{M} = \frac{F}{\rho \pi (r_1^2 h_1 + r_2^2 vt)}$$

This differential equation is not separable, and we must use numerical methods to find an approximate solution. This can be accomplished through the MATLAB function ode45. This function accepts a differential equation, time interval and initial condition as inputs and outputs a vector of numerical solutions. In our case, the initial condition is the speed of the fluid in the suction tube when it enters the barrel at some non-zero time.

At this point, we can use a range of radii and heights for both the barrel and suction tube to see what kinds of fluid velocities we obtain based on the geometries. We will then be able to relate the velocities to the pressure in the fluid to determine we are exceeding the maximum pressure limit of 150 mmHg, which could constrain what geometries we can use in the design of the device. We determined an initial reasonable range of geometries shown in Table 7.

Table 6 Anticipated Geometries before engineering analysis

Geometry	Minimum(cm)	Maximum(cm)
----------	-------------	-------------

Suction tube radius (r_1)	0.5	2
Suction tube height (h_1)	3	7
Barrel radius (r_2)	2	5
Barrel height (h_2)	5	20

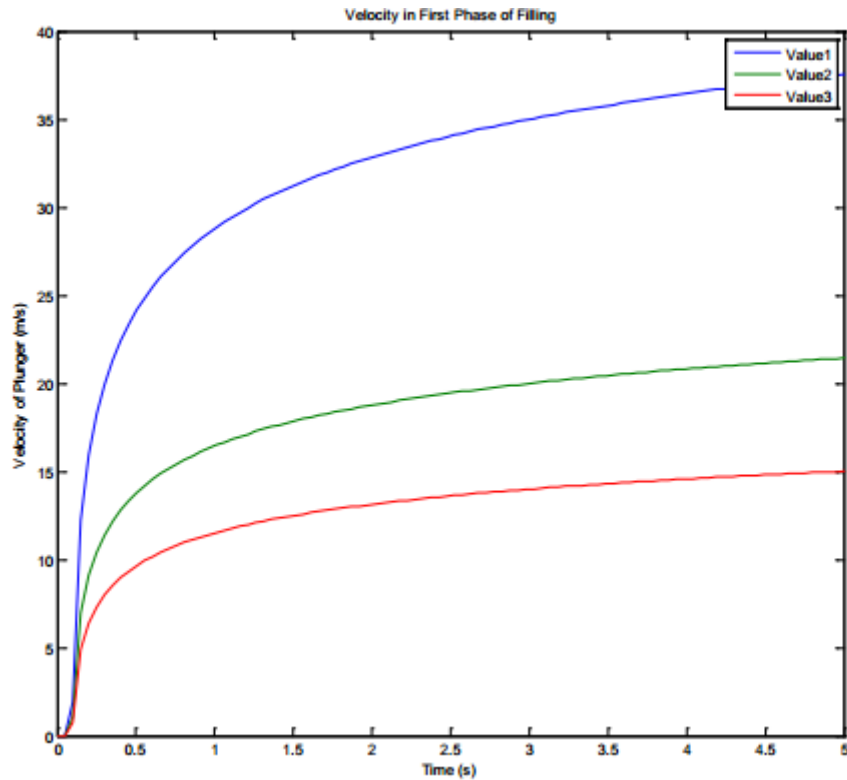
We can use these ranges to create a vector in MATLAB to find the range of velocities of the plunger based on the specific geometry. We can also input a range of values for the applied force.

Based on the evaluations of anthropometric data, the maximum force exerted on the plunger (95th percentile of male pulling force) is 199.2 N (North Carolina State University, 2006). Returning to the first equation where the suction tube is filling, there are three variables that influence the plunger velocity; r_2 , F and t . This makes plotting the influence of all three at the same time impossible without creating an animation in time. Thus, we will choose three representational values (Table 6) of the geometries and one force value in order to examine the effect of time on the plunger speed. We will choose the minimum, maximum and average geometries to ensure that we are analysing the full range of possibilities.

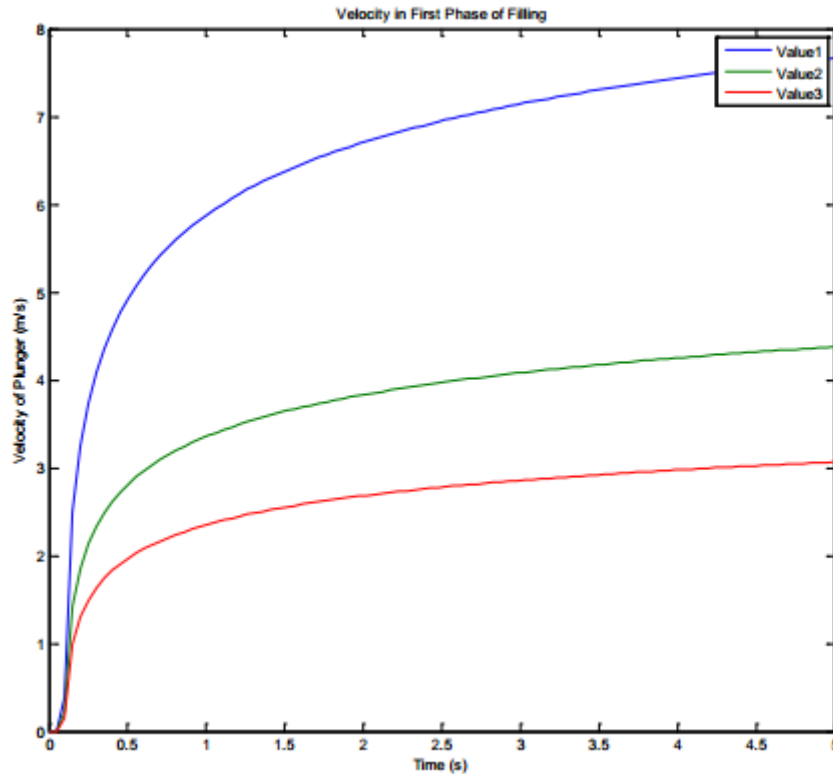
Table 7 Representational \values to use in MATLAB analysis

Geometry	Minimum(cm)	Middle Point(cm)	Maximum(cm)
Suction tube radius (r_1)	0.5	1.25	2
Suction tube height (h_1)	3	5	7
Barrel radius (r_2)	2	3.5	5
Barrel height (h_2)	5	12.5	20

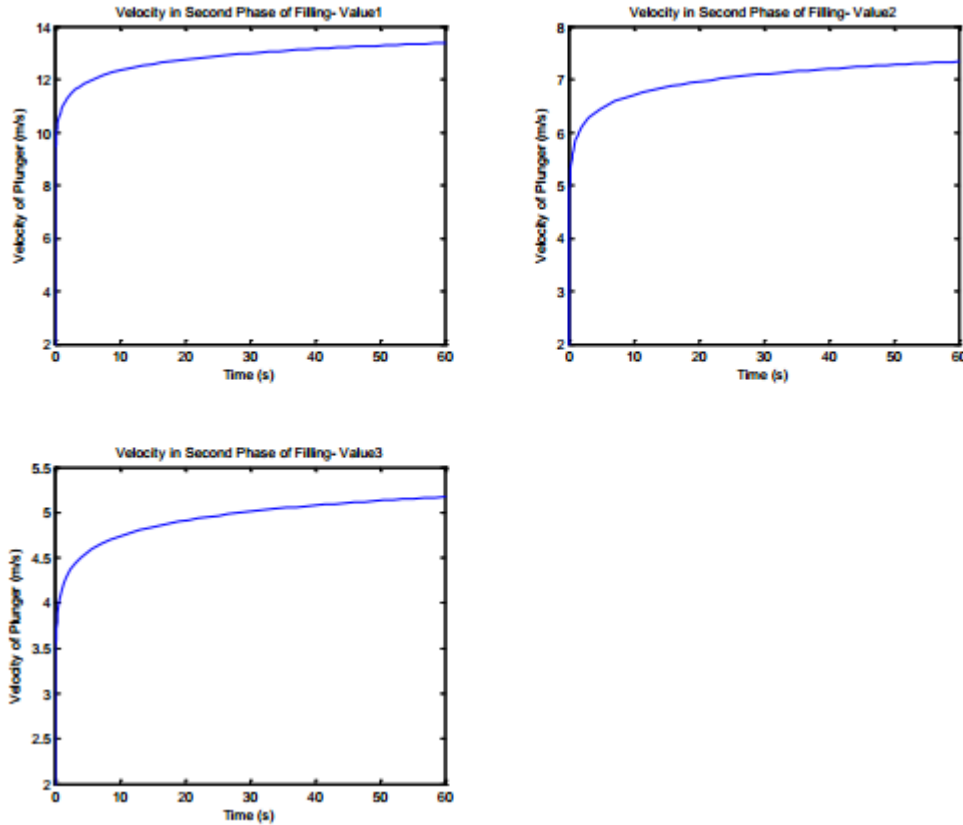
We will use 199.2 N as the chosen force, as it represents the maximum that theoretically could be applied to the plunger. Computing the velocities in MATLAB, we obtain:



As expected, smaller geometries result in higher velocities of the plunger. We also note here, that the analysis produces extremely high velocities of the plunger. It is not reasonable to expect a user to pull back the plunger at 35 m/s or even 5 m/s. This large magnitude of error could come from one of two primary sources. First, we neglected kinetic friction, which contributes significantly to the force opposing the movement of the plunger. Second, using the maximum human pulling force of approximately 240 N is also not physically realistic. Applying a 240 N force is equivalent to putting a 25kg weight on the end of the syringe, a truly huge force considering the situation. If we run the code again using a more reasonable 10 N force, we obtain:



These speeds of the plunger are significantly slower, but still are quite high, even for the larger geometries. This error can again be attributed to neglecting the kinetic friction between the rubber O-ring and the interior of the device barrel. We will continue with the analysis, however, to examine relationships among the parameters. We can now take the asymptotic values of the velocity of the plunger at the end of the first phase and use them as the initial condition for the second phase. This is where we return to the equation for the velocity of the plunger that we must solve using numerical methods. The MATLAB codes are provided in the [Appendix 4](#). As MATLAB assigns the number of steps and step sizes used by the function, we cannot graph the solutions from the different value groups on the same plot. We must plot them separately:



As we saw with the first phase, increased size of the device reduces the velocity of the plunger. These velocities are again much higher than we would expect, which is likely due to the contribution of kinetic friction. We would expect the user to pull the plunger back at a velocity of about 1 cm/s, which is several hundred orders of magnitude lower than we obtained from the analysis.

We can now take the velocity of the plunger and work the different fluid parameters. Due to the no-slip condition, we can assume that the velocity of the fluid against the plunger is the same as the plunger velocity. We start by characterizing the flow using the Reynolds number.

$$Re = \frac{\rho v L}{\mu}$$

In this formulation, ρ is the fluid density, v is a characteristic velocity, μ is the fluid viscosity and L is a characteristic length. When analysing flow in a tube, the characteristic velocity is the average velocity and the diameter of the tube is the characteristic length. In cylindrical tubes, the flow is defined as laminar when $Re < 2100$. Turbulent flow occurs when $Re > 4000$. The intermediate region is termed the transitional flow region, where the flow is unstable and intermittently turbulent (Hibbeler, 2010). When $Re \ll 1$, the flow is dominated by viscous effects, and when $Re \gg 1$, it is dominated by inertial effects.

The density of blood is 1060 kg/m^3 (Quarteroni & Formaggia, 2004) and we will choose 3.5 cm as the tube diameter (average of upper and lower range). We will estimate on the high side and choose 1 m/s as the characteristic velocity to account for the increased velocity in the smaller-radius suction tube (as well as the entry to the blood bag). We will use the average density of blood, measured at .004 Poise (Baskurt et al., 2003). This gives us a Reynolds's number of 9275, which is in the laminar region where inertial effects will dominate the flow. This means that we can reasonably approximate the fluid as inviscid and model it using the Bernoulli equation. The Bernoulli equation relates two points on a streamline. We can consider a point in the blood still contained in the body cavity (subscript 0), a point in the suction tube (subscript 1), and a point in the barrel of the syringe (subscript 2) as being along the same streamline and related by:

$$p + \frac{1}{2}pv^2 + pgh = \text{constant}$$

$$p_o + \frac{1}{2}pv_o^2 + pgh_o = p_1 + \frac{1}{2}pv_1^2 + pgh_1 = p_2 + \frac{1}{2}pv_2^2 + pgh_2$$

When the blood is still in the body cavity, it has no velocity and we can define the pressure and height there as 0. This simplifies the equation to:

$$0 = p_1 + \frac{1}{2}pv_1^2 + pgh_1 = p_2 + \frac{1}{2}pv_2^2 + pgh_2$$

If we assume that the device is held straight up, we can use the vector of heights from the previous analysis as input to h_1 and h_2 . The previous analysis also gave us the velocity of the fluid in the barrel v_2 . This means that we can solve for the fluid pressure in the barrel after rearranging the previous equation:

$$-p_2 = -\frac{1}{2}pv_2^2 - pgh_2$$

Using MATLAB, we can plot the pressure as a function of the height of the tube and the velocity. We will use the same range as provided in Table 6 and add the height of the suction tube since we have set the zero to be at the bottom of the suction tube. As previously discussed, the velocities we obtained from the analysis of the plunger were not physically realistic, so we will use a range of velocities of the plunger from 0 – 0.5 m/s to ensure we are including all possible velocities. We get a 3D plot of pressures:

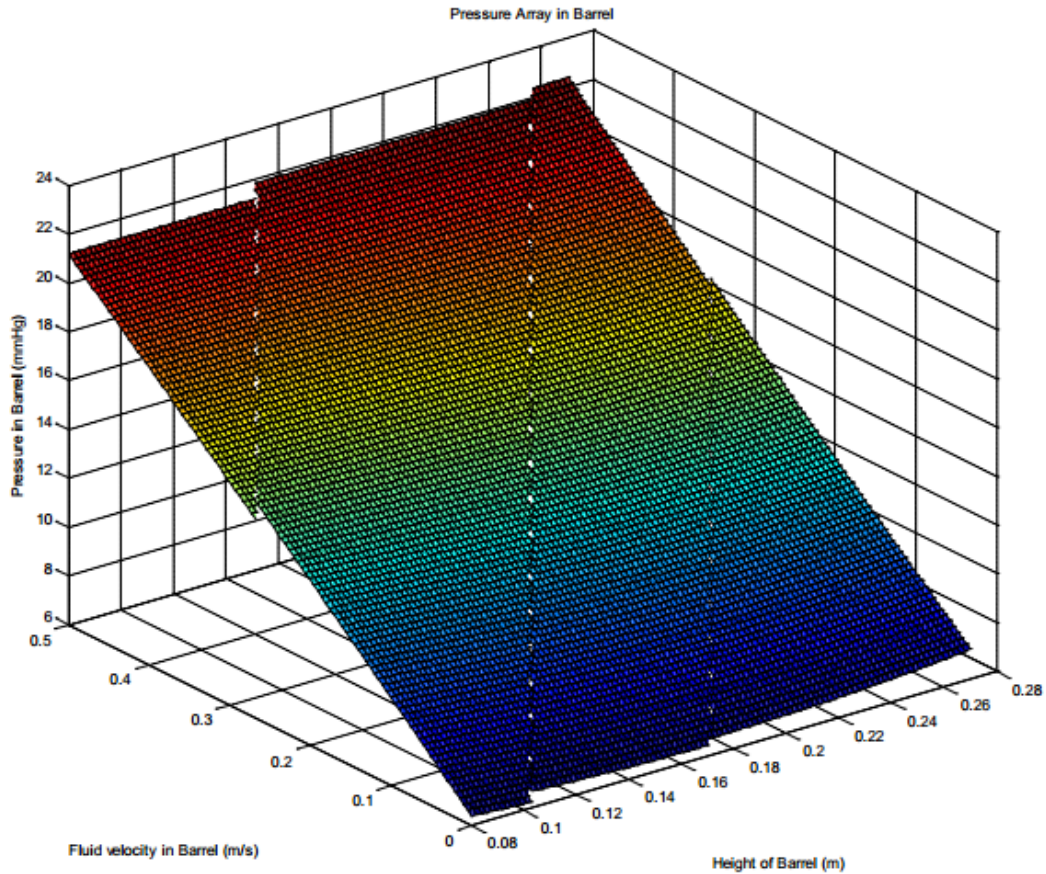
$$Q = A_1V_1 = A_2V_2$$

We can take the range of areas based on the range we set for the radii of both the suction tube and the barrel and the velocity range we used for v_2 and obtain the range of velocities v_1 in the suction tube to be 0 – 3.125 m/s. We can then rearrange the Bernoulli equation to find the pressure in the suction tube:

$$0 = p_1 + \frac{1}{2}pv_1^2 + pgh_1 = p_2 + \frac{1}{2}pv_2^2 + pgh_2$$

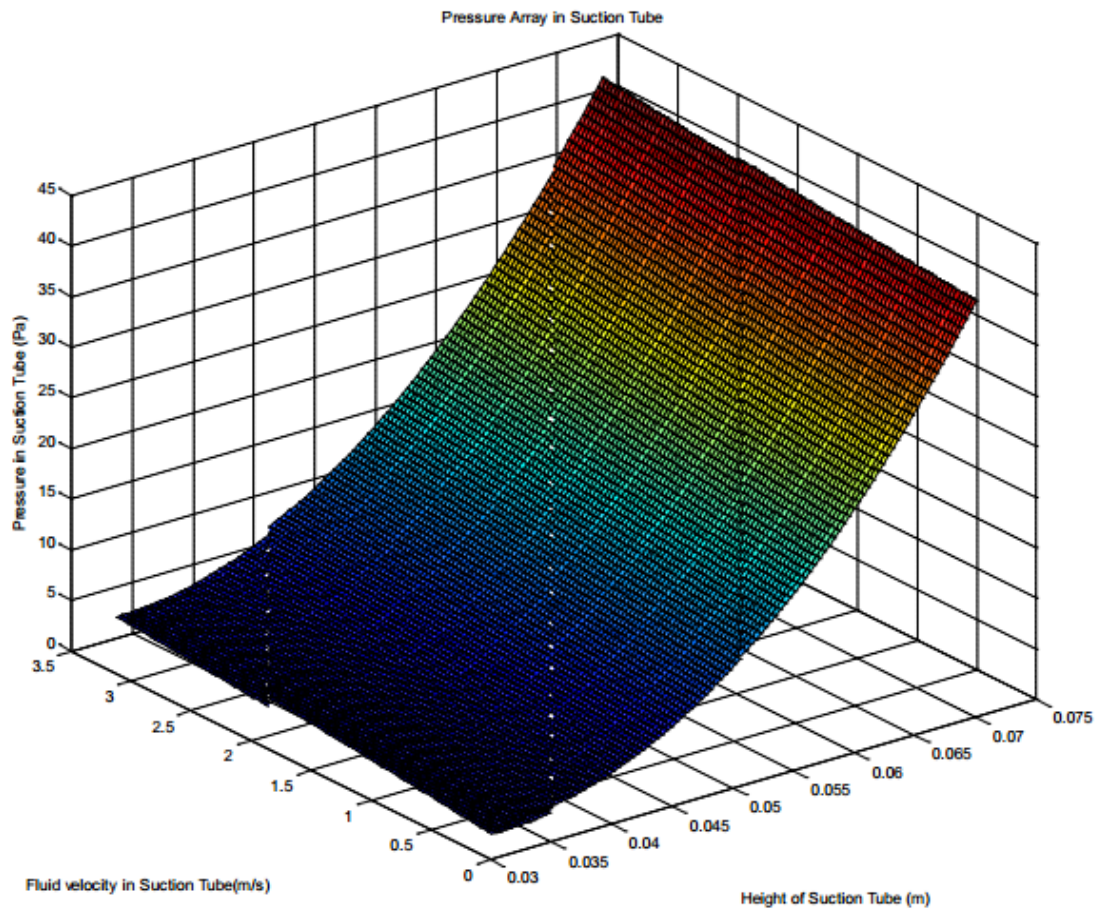
$$-p_1 = -\frac{1}{2}pv_1^2 - pgh_1$$

Creating a similar plot in MATLAB of the pressure as a function of the velocity and the height, we get:



We can see here as well that for all the possible fluid velocities and geometries the pressure is still well under 150 mmHg. This means that we can freely choose dimensions of the device based on human factors within our ranges without exceeding the pressure limit.

We can also evaluate the pressures generated in the connection to the blood bag. We have to reset the zero point in the Bernoulli equation, as the blood in the IV tubing is not on the same streamline as we used previously. The two points we are now comparing are a point in the barrel and a point in the IV tubing, which we will denote with the subscript '3.'



We can see here that even at the smallest geometries and highest velocities we are well under the pressure limit of 150 mmHg. We can repeat the procedure for the pressure in the suction tube. We must first relate the velocity in the suction tube to the velocity in the barrel through the flow rate:

$$p_3 + \frac{1}{2} \rho v_3^2 + \rho g h_3 = p_2 + \frac{1}{2} \rho v_2^2 + \rho g h_2$$

We can choose a point in the barrel such that $h_2 = h_3$. We then can rearrange the equation for p_3 :

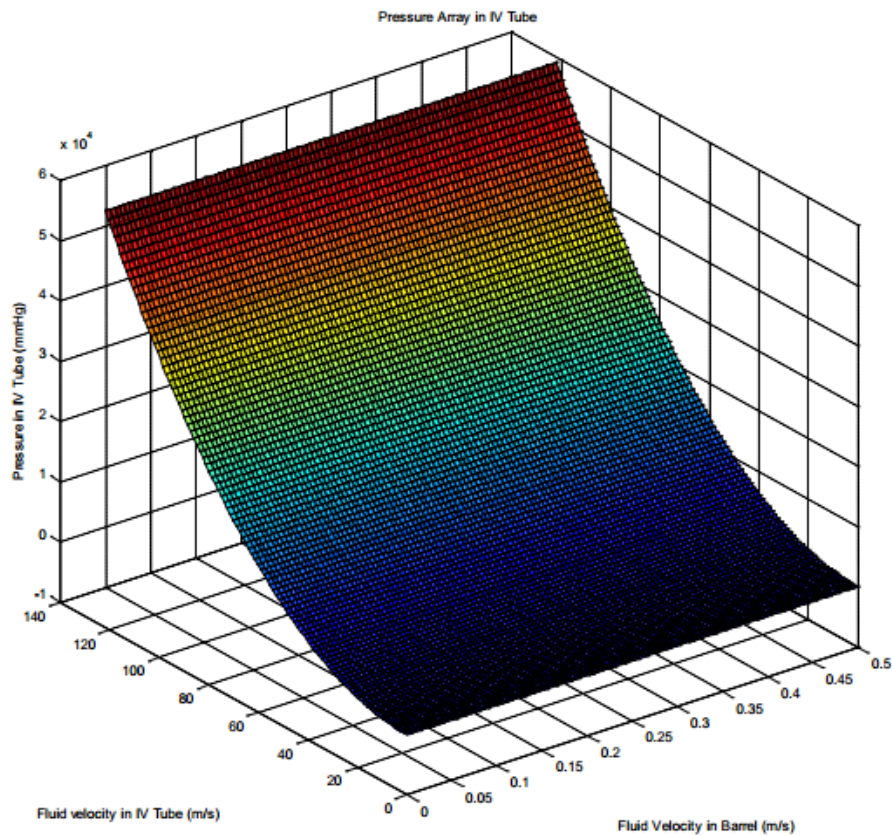
$$p_3 = p_2 + \frac{1}{2} \rho v_2^2 - \frac{1}{2} \rho v_3^2$$

$$p_3 = p_2 + \frac{1}{2} \rho (v_2^2 - v_3^2)$$

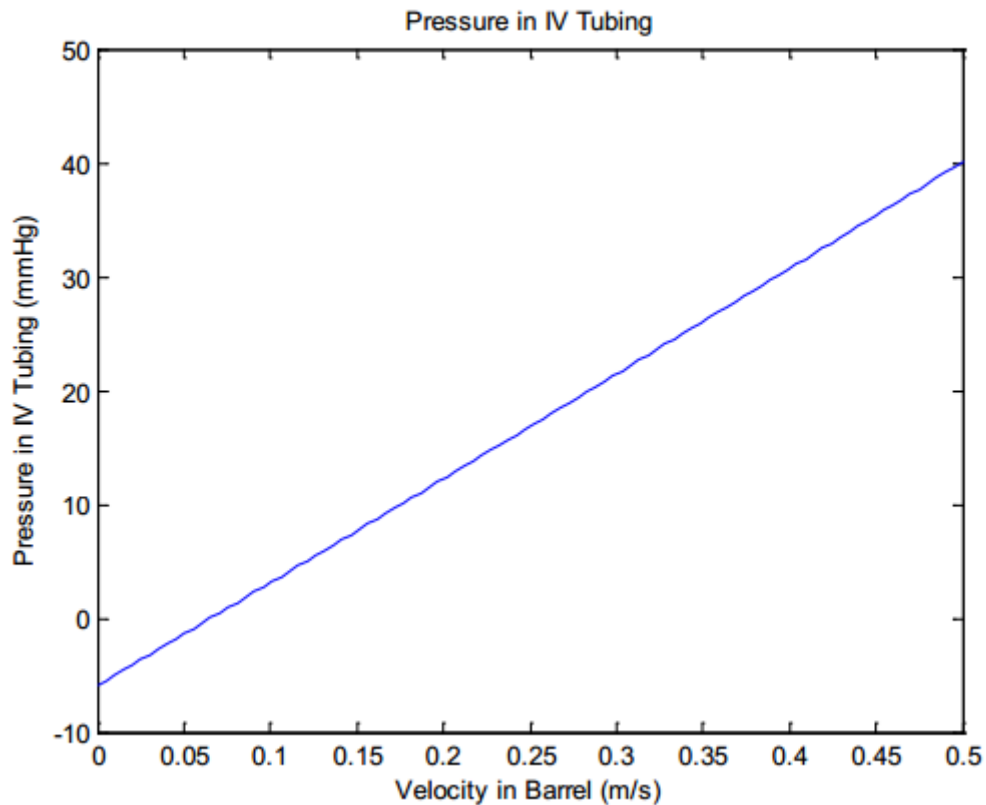
For p_2 , we can input the pressure array we got previously, which gives us a range of about 0-24 mmHg. We will use the same range of velocities of v_2 , and can relate them to v_3 through the flow rate:

$$Q = A_3 V_3 = A_2 V_2$$

The diameter of standard IV tubing ranges from 3-6.4 mm, which we can use to calculate a minimum and maximum area of A_3 . We get that v_3 can range from 0-122.07 m/s. This upper limit is quite fast, which is not unexpected as the diameter of the IV tubing is so small. Plotting the pressures in MATLAB, we get:



The pressures generated in the IV tube are much higher than those that occur in the suction tip or in the barrel, and some exceed the limit of 150 mmHg. We will need to keep the diameter of the tubing as wide as possible to reduce the velocity through the tube. If we use the upper limit of the tubing size, 6.4 mm, we can calculate the velocity of the fluid in the tubing (using the same procedure as previously) as 1.22 m/s, a much more reasonable value. If we use this value and vary just v_2 , we can plot the resulting pressure:

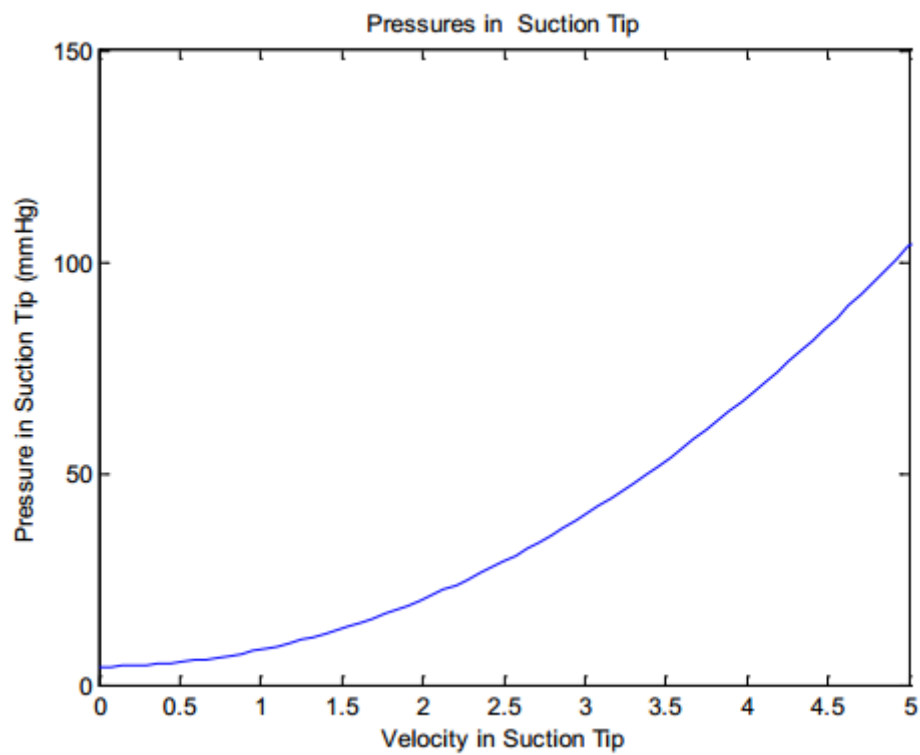
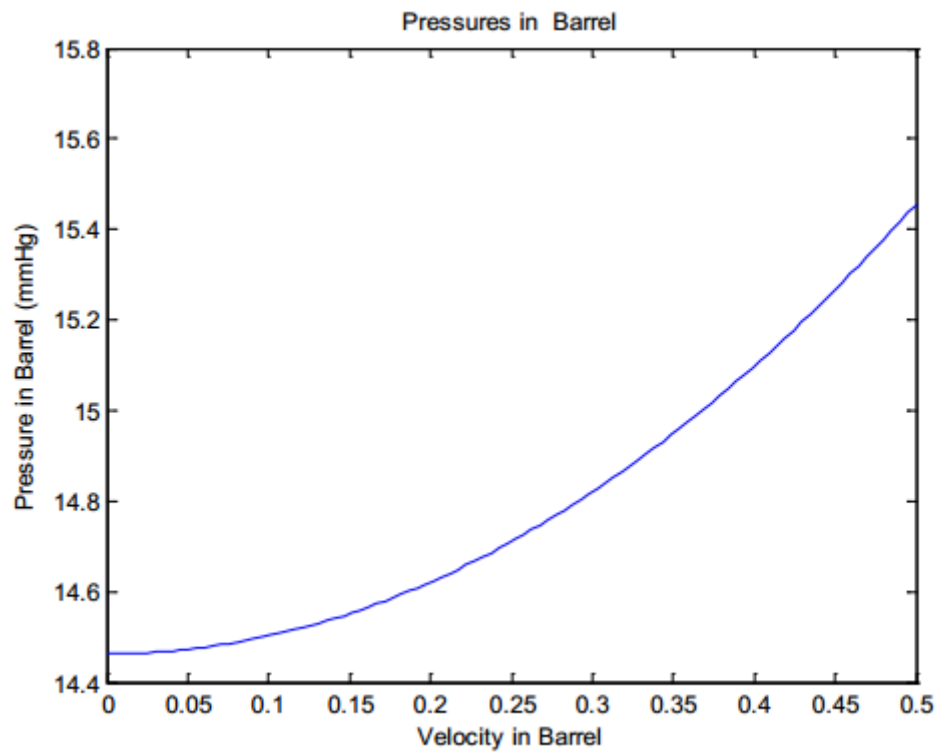


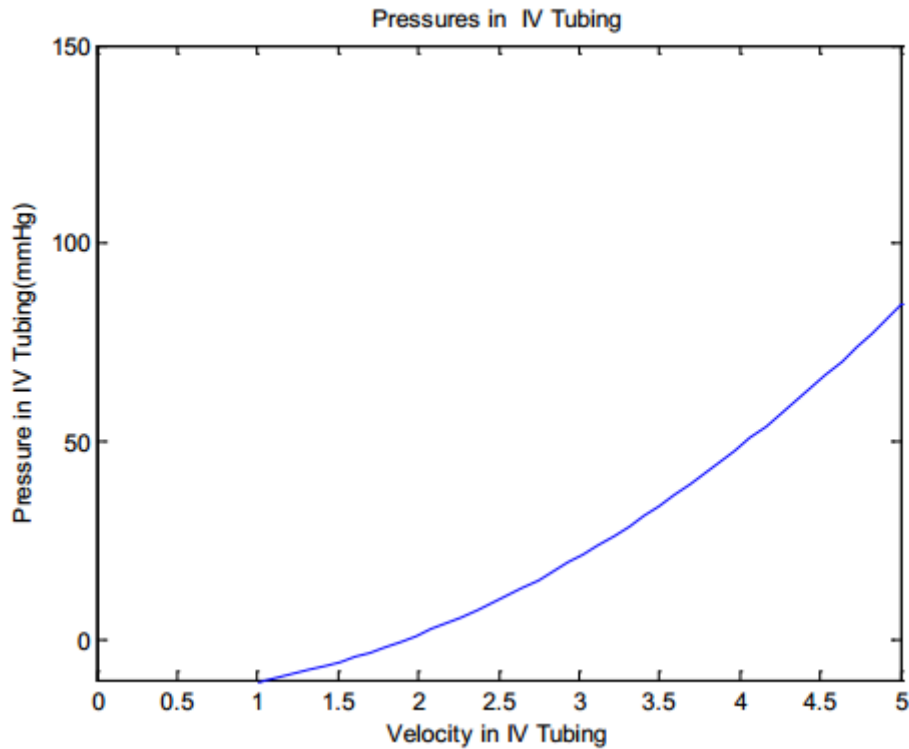
This shows that as long as we use the maximum size tubing in the IV line, we should not generate pressures greater than 150 mmHg.

The final parameter to examine is the overall flow rate of blood. We have used the flow rate to equate the different velocities, but have yet to calculate it for the whole device. As the flow rates through the various parts of the device are equal, we can choose any one of them to work with. Let us choose the syringe barrel. As stated previously, we have a radius range of 2-5 cm and a velocity range of 0-0.5 m/s. Returning to the equation for flow rate, we have:

$$Q = A_2 V_2$$

If we plug in the maximum values for the area and velocity, we end up with a flow rate of 23.6 l/min, which is greater than the flow rate defined in the engineering specifications. If we use the smallest area of the barrel and a minimum velocity of .01 m/s, we obtain a flow rate of .75 l/min, which is lower than the defined specification but still a fairly significant rate. As the user will vary the pressure on the plunger, meeting the flow rate specification should not be much of an issue for the geometries used here. After finalizing the dimensions of the device based on human factors and available stock sizes of materials, we run the analysis again using our specific values. We get:





These final plots illustrate the pressures occurring in the various parts of the device. We can see that the pressures are under the 150-mmHg limit. We must realize however, that the analysis does make simplifying assumptions and it is still vitally important that we perform validation tests to experimentally determine that the fluid pressure never gets too high.

10.6 Foot Pedal & Hand Crank Pump

We would use 199.2 N as the chosen force, as it represents the maximum that theoretically could be applied to the plunger as deduced from anthropometric data but having deduced that 10N is more feasible, we will use that value coupled with an average 5ms^{-1} speed. We will carry out reverse analysis having known the amount of force and speed that we require to move the plunger to deduce the required dimensions of the driving wheels, and piston rod length.

Using kinematics analysis, with pin point, we deduce the figure below with P-piston pin, N-Crank pin, I-rod length, A-Crank Angle, X-distance OP. Using Cosine rule of triangles;

$$l^2 = r^2 + x^2 - 2rx\cos A$$

Assuming $A=45^\circ$, $l=150\text{mm}$, $r=100\text{mm}$,

$$x = r\cos A + \sqrt{l^2 - r^2\sin^2 A}$$

We find the velocity with respect to the crank angle; first derivative $\frac{dx}{dA}$

$$\frac{dx}{dA} = -r\sin A - \frac{r^2\sin A\cos A}{\sqrt{l^2 - r^2\sin^2 A}}$$

Velocity is negative when X decreases with time, and $A < 100^\circ$ and positive when $A > 100^\circ$. The magnitude of the second term is less than $r\sin A$ and doesn't affect the sign if $l > 2r$. Substituting the terms, the magnitude of the term $\sqrt{l^2 - r^2\sin^2 A}$ and neglecting the force input, we deduce the "ideal speed" of the piston as 0.048ms^{-1} . This value is the most realistic, even when using the hands to pull

the plunge. Furthermore, a motion simulation with Fusion 360 proves that the system works with the estimated dimensions. With all this, we decided to proceed with the estimated dimensions. However, we will change this after subjecting the first functional prototype to experiments and applying a more accurate analysis.

10.7 Filter Design

In collecting whole blood components for transfusion, it is desirable to minimize the presence of impurities or other materials that may cause undesirable side effects in the recipient. For example, to reduce the transmission of disease and non-specific febrile reactions, it is generally considered desirable to remove substantially all of the leukocytes from whole blood prior to transfusion, storage or separation into its clinically proven components. In blood banks and hospitals. The most common way to remove leukocytes from whole blood is by filtration using a leukodepletion filter. Currently available leukodepletion filters employ various filtration media as will be expounded on shortly in the preceding sections.

10.7.1 Biological Background

Leukodepletion is a technical term for the removal of leucocytes from blood components using special filters. White blood cells, also known as leucocytes, are immune cells that circulate in the blood and in the lymphatic system. There are 5 main types of leucocytes; neutrophils – main action against bacterial and fungal infections, Monocytes – main action against bacterial infections, Eosinophils – main action against parasitic infections, Basophils – responsible for responses to allergens, and Lymphocytes – main action against viral infections. Neutrophils, eosinophils, and basophils are also known as granulocytes since they contain granules that can digest microorganisms. Lymphocytes and monocytes are known as agranulocytes since they lack granules in their cytoplasm(Johnson, 1991).

Neutrophils are granular leucocytes formed from the myeloid cell line within the bone marrow. They are the most common leucocyte, making up around 40-70% of those found in peripheral blood. They are primarily involved in the immune response against bacterial infection and their presence in tissue is associated with acute inflammation. They are typically 9-16µm in diameter and have a multi-lobed nucleus. The cytoplasm contains granules which contain degradative enzymes, which are released during phagocytosis. They have a relatively short lifespan of 2-3 days.

Monocytes are formed from the myeloid cell line within the bone marrow. They are primarily involved in the immune response against bacterial infection and make up roughly 5-10% of circulating leucocytes. They have a kidney bean shaped nucleus. Monocytes are circulating leucocytes which typically remain in the blood for around 8 hours before migrating into tissue where they differentiate into macrophages. Macrophages then form the main population of phagocytic cells within tissues and have a much longer lifespan than neutrophils of months or even years. In some tissues the resident macrophages have specific names e.g. Kupffer cells in the liver and osteoclasts in the bone. They are also much larger than neutrophils, with a diameter of 25-50µm and have a single-lobed, round nucleus. They secrete cytokines to modulate the immune response.

Eosinophils, named so because they histologically stain with eosin, are granular leucocytes formed from the myeloid cell line within the bone marrow. They typically make up 1-3% of circulating leucocytes and are mainly found within tissues, generally only spending around an hour in peripheral blood. They have a diameter of 12-17µm and have a bi-lobed, sausage shaped nucleus.

Basophils are granular leucocytes formed from the myeloid cell line within the bone marrow. They are 14-16µm in diameter and have a bi-lobed, S-shaped nucleus. These cells are found in the peripheral blood and have a lifespan of roughly 2 weeks. They are very similar in function and appearance to mast cells, which are found within tissues. Basophils contain granules containing histamine and they cause local inflammatory responses through interactions with IgE. Their role in the immune system is poorly understood but it is thought that they mediate type I hypersensitivity reactions alongside mast cells, such as asthma and anaphylaxis.

Lymphocytes are agranular leucocytes formed from the lymphoid cell line within the bone marrow. They are primarily involved in the immune response against viral infection. These are the smallest leucocytes, with a diameter of 6-15µm. They have round, densely staining nuclei and sparse

cytoplasm. They circulate between tissues, peripheral blood and the lymphatic system. Their lifespan also varies depending on the subtype that they differentiate into. There are three major types of lymphocytes; Natural killer cells, T cells and B cells.

		
	Erythrocyte	Leukocyte
	5-7	7-15

Cell Type					
	Neutrophil	Lymphocyte	Monocyte	Eosinophil	Basophil
Size (µm)	12-15	7-10	15-25	12-15	12-15
% of Pop	60-70	20-45	2-10	1-3	0.5-1

Figure 14 Size of RBCs vs WBCs

The leucocytes present in blood for transfusion play no therapeutic role in transfusion and may be a cause of adverse transfusion reactions. The roles and/or products of these white blood cells in salvaged blood are highlighted in the table(Chu, 1999) below:

In Body		In salvaged Blood
Granulocytes	• Phagocytic cells engulf and destroy foreign material • Responsible for first line of defence	• Micro-aggregates • Releases Cytokines • Compete with stored cells for energy sources
Lymphocytes	• CMI • AMI	• Major reservoir for viruses • Alloimmunization • Release Cytokines
Monocytes	• Major Antigen Presenting Cells	• Initiate Immune Reaction leading to alloimmunization • May carry CMV

Clearly, the Removal of leucocytes has a number of potential benefits for transfusion recipients. Other potential benefits not highlighted in the table above include; reduced risk of platelet refractoriness, reduced risk of febrile non-haemolytic transfusion reactions (FNHTR), reduced risk of CMV transmission, reduction in storage lesion effect, reduction in the incidence of bacterial contamination of blood components, possible reduced risk of transfusion-associated graft vs host disease (TAGVHD), possible reduction in transfusion related immuno-modulatory (TRIM) effects, and the reduced risk of transmitting variant Creutzfeldt-Jakob Disease.

10.7.2 Engineering Background

There are several methods of Leucodepletion as listed below:

- Filtration
- Washing
- Freezing
- Buffy coat removal
- Micro-aggregate filtration
- Specific leucodepletion filters
- Low leucocyte apheresis devices

The most effective & efficient method for reducing the number of leucocytes in a unit is by filtration (Campbell, MacKenzie, Yentis, Sooranna, & Johnson, 2012). Specific leucocyte depleting filters are made of:

- Cellulose Acetate (Erpur-G by Organon Technika)
- Polyester (Sepa Cell R-500, by Asahi)
- Tightly Packed Fibres of combed cotton (Imugaurd, Terumo, Haemonetics)
- Pall RC 50 & RC 100

Cotton Wool and Cellulose Acetate are more effective (Fujioka et al., 2019) and the former provides the cheapest design for a filter. Filtration systems are significantly less expensive than other methods like automated cell washing, freezing and deglycerolization.

The generic Structure and Design of leucocyte depletion filters consists of layers of asymmetrical non-woven synthetic fibres. This structure allows for the filtration depth filtration & absorptive mechanism and it is supported by the adherence properties of blood components i.e monocytes, PMNs, platelets, and lymphocytes have higher adherence than RBCs; they are therefore easily trapped within the filtration system. Other mechanisms of action for leucodepletion filters include; blocking, bridging, and interception as shown in the image below.

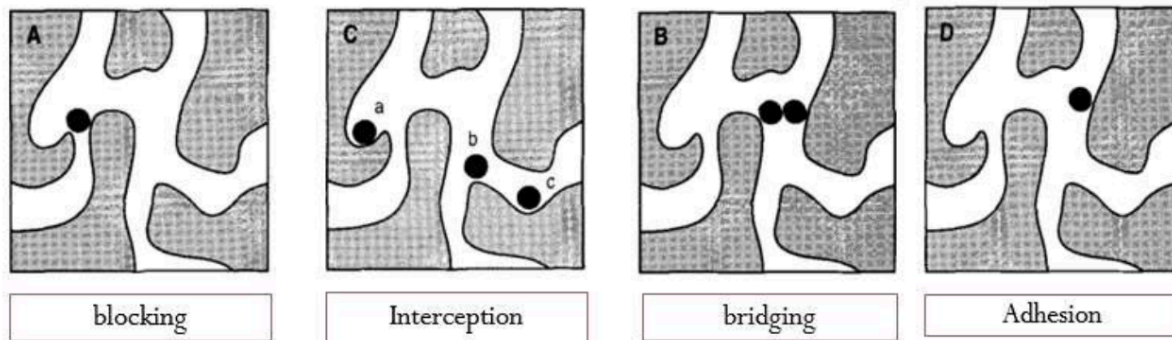


Figure 15 Mechanisms of Action of LD filters

Leukodepletion filters can be classified on basis of their maximum log efficiency for the removal of WBC. The types of Leucocyte Filters are as follows:

- 1st Generation: Removes 90% leucocytes / Log 1
- 2nd Generation: Removes 99% leucocytes / Log 2
- 3rd Generation: Removes 99.9% Leucocytes / Log 3
- 4th Generation: Removes 99.999% Leucocytes / Log 4

Leukodepletion filters can also be classified by their pore size and the filter's filtrate composition. Some of the pore sizes are as listed below:

- 170-240 micro meter: Large clot and particulate debris
- 40 micro meter: Micro-aggregates of fibrin, leucocytes, platelets (one log reduction)
- 7-10 micro meter: Micro-aggregate, cells, (three log reduction)

Nonwoven filters have an irregular and roughly shaped porous structure, with a relatively broad distribution of pore sizes. Although large structural differences exist between membrane filters, the specific filter surface of various nonwoven filters is comparable to the specific filter surface of membrane filters. Asymmetric filter compositions may be illustrated schematically by their pore size distributions throughout the filter as shown in figure 16. These figures represent an idealized pore size distribution with a continuous decrease in pore size, while in practice there is a stepwise decrease of pore sizes throughout the filter.

There are two attributes of a leukodepletion filter that determine its ability to remove leukocytes from blood: the intrinsic leukodepletion efficiency of the filter media and the leukodepletion capacity of the filter. The intrinsic leukodepletion efficiency is a measure of the optimum performance of a given filter media when challenged with a minimal number of leukocytes. The observed degree of leukodepletion is a function of the filter media architecture and surface composition. The second attribute, the leukodepletion capacity of a filter, describes the quantity of leukocytes that can be removed by a given filter assembly at the intrinsic efficiency of the media before allowing leukocytes to pass through the filter at a lesser leukodepletion efficiency and appear in the filtrate blood.

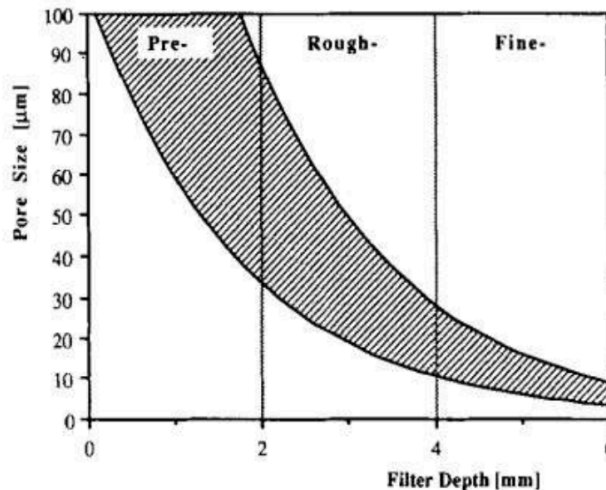


Figure 16 Ideal scheme of pore size gradient in the asymmetrical non-woven filter. The marked are represents the distribution of pore sizes as a function of filter depth(Bruil et al., 1991).

Conventional filter structures, composed of packed fibres, have a broad pore size distribution, which is poorly defined. In contrast to nonwovens, membranes are composed of a continuous porous matrix, usually with a well-defined structure. Most of the techniques to prepare membranes offer unique possibilities to adjust the pore structure. Open cellular structures, with a narrow pore size distribution may be obtained. Other factors affecting filtration are; number of leucocytes, temperature (viscoelasticity), flow rate / Speed of filtration, pressure, presence of HbS, number & function of platelets, plasma content of cell suspension media, and the clogging of cells on membrane.

In conclusion, polyurethane membranes make the best filters, pore size distribution has considerable effect on filtration efficiency and therefore must be controlled to deduce an advantage. It is also clear that adhesion can be increased indirectly by reducing size of pore to increase surface area properties of leucocytes however, very small pore sizes lead to clogging. The clogging can be prevented by gradual reduce in pore size, or the use of an asymmetrical filter. In any filter design, both adhesion and sieving mechanisms are involved but cell adhesion play a predominant role.

10.7.3 HaemoSAVE Filter

The HaemoSAVE filter includes glass fibre filter pads and non-woven polyester fibre filter pads sealed within a filter housing. The filter is designed such that whole blood, is conducted through the glass fibre filter pads before the non-woven polyester fibre filter pads.

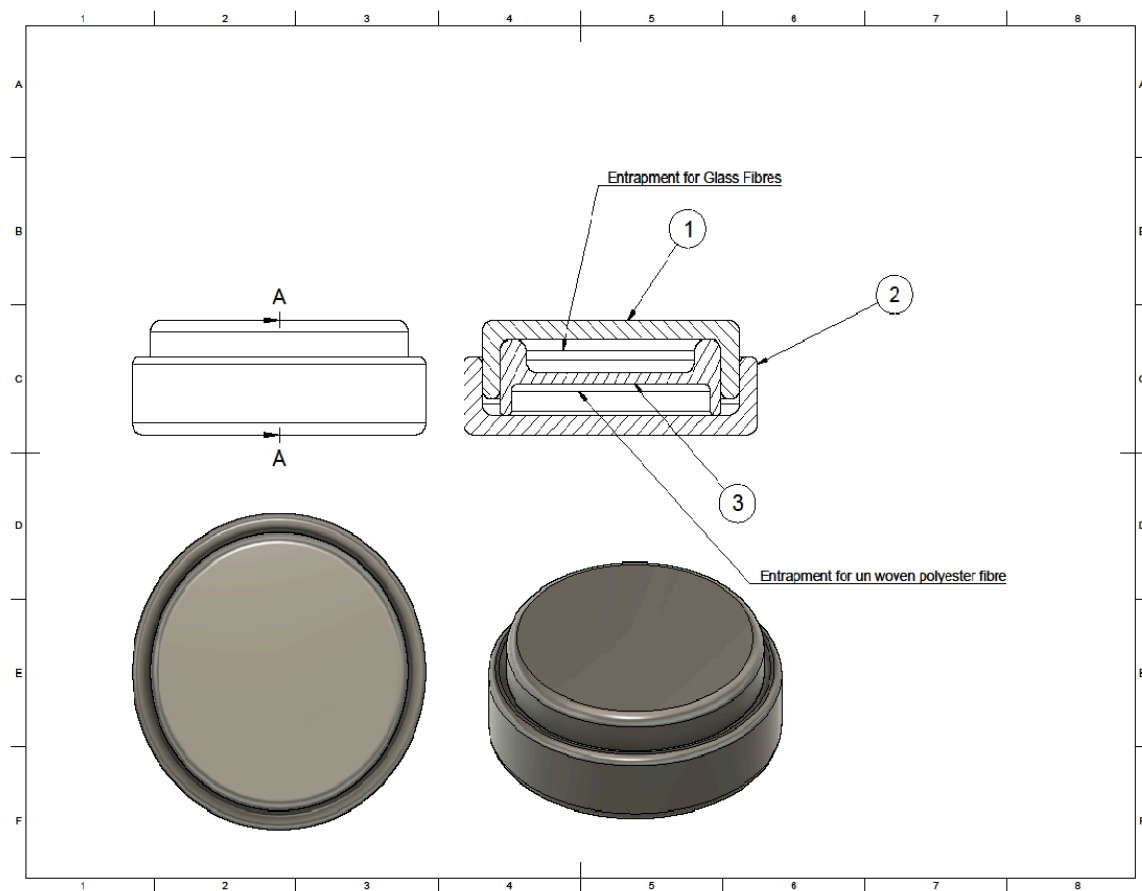
The filter includes a filter housing having an open space within. The housing has a filter inlet for conducting a body fluid into the open space and a filter outlet for conducting filtered body fluids out of the open space. A plurality of glass fibre filter pads are sealed within the open space of the filter housing. Preferably, the glass fibres have a mean diameter of from about 0.1 to about 5.0 micrometres. A plurality of non-woven polyester film filter pads is also sealed within the open space of the filter housing. The non-woven polyester fibres have a mean diameter of from about 0.1 to about 5.0 micrometres. In one embodiment, the glass fibre filter pads and the polyester fibre filter pads are sealed within the open space such that the body fluid which is conducted into the open space first contacts and passes through the glass fibre filter pads before contacting and passing through the polyester fibre filter pads. The filter design should provide both good intrinsic leukodepletion efficiency and high capacity in warm, freshly-drawn blood for leukocytes. The leukodepletion filter should remove leukocytes equally well from warm, freshly-drawn blood as well as from blood which has been cooled because of its extended scope of application in emergency cases.

Accordingly, it would be advantageous to provide a leukodepletion filter which would have its maximum intrinsic leukodepletion efficiency in warm blood, thereby obviating the step of cooling the blood. The step of cooling the blood is costly in both time and equipment and excludes leukodepletion of whole blood with recovery of non-activated platelets. Furthermore, it would be advantageous to

provide a leukodepletion filter which has an increased leukodepletion capacity whereby units of blood containing an excessive number of leukocytes could be filtered through a single filter.

Polyester-based filters selectively remove lymphocytes from fresh, warm blood with both great efficiency and capacity for lymphocytes; but not for granulocytes(Campbell et al., 2012). The glass filter media should effectively remove both granulocytes and lymphocytes from blood immediately after collection with great efficiency. Based on the efficacy of this arrangement past literature(Bodensteiner, 1990; Fujioka et al., 2019; Jamal, Rus Mazeni, Noor, & Hussin, 2000), we have combined polyester filter pads and glass filter pads in a filter, or in a series of filters, to remove the two components of leukocytes with great efficiency and great capacity.

Furthermore, the ratio of the filter media may be manipulated to improve the performance of the filter on both classes of leukocytes(Campbell et al., 2012). Maximum leukodepletion capacity for a given filter design may be achieved by adjusting the relative quantities of the two media included in the filter Assembly, such that both lymphocytes and granulocytes are detected in the blood filtrate in equal numbers when the capacity of the filter is exceeded.



The filter housing includes an open space within. The casings 1 and 2 are perforated with holes of pore size 170 μm while the third casing has pores of 500 μm . The three parts fit into each other. The open space is designed for receiving and sealing the filter media of the filter membranes. The filter housing includes a filter inlet space for conducting the whole blood into the open space of the filter. The filter housing also includes a filter outlet which conducts the body fluid (after filtration) out of the open space of the barrel.

A plurality of glass fibre filter pads are sealed within the open space of the filter housing. A seal extends peripherally about the plurality of filter pads and hermetically seals the filter pads into the filter housing such that no blood may pass around the filter pads. The glass fibre filter pads are fibrous, single-layer sheets made by a wet-laid paper-making process. The glass fibres should

preferably have a mean diameter of from about 0.1 to about 5 micrometres. Glass fibre sheets are commercially available. A plurality of non-woven polyester fibre filter pads are also sealed within the open space of the filter housing. The non-woven polyester fibre filter are made from melt-spun polyester fibres. Commercially, melt-spun polyester fibres and polyester fibre filter pads are available. As discussed above, the ratio of the glass filter pads to the polyester filter pads may be varied to more efficiently leukodeplete. Preferably, the weight ratio of the glass fibre filter pads to the polyester fibre filter pads is from about 3:1 to about 1:20(Fujioka et al., 2019).

10.8 General Description of HaemoSAVE

The heamoSAVE is a self-contained, dual pump mechanically/electrically powered system for intraoperative whole blood salvage device. We hope to make it commercially available in order to avail its use in hospitals for both elective and emergency surgery with significant blood loss and in the management of major traumatic or obstetric haemorrhage.

Blood lost into the surgical field is filtered to remove particulate matter and aspirated into a collection reservoir where it is anticoagulated. If sufficient blood is collected and the patient loses sufficient blood to require transfusion, the salvaged blood can be transfused directly back to the patient. Alternatively, if the health facility has ample resources as predefined by us, they can centrifuge and wash the salvaged blood in a closed system and suspend red cells in a sterile saline solution; this light blood must be transfused to the patient within 4 hours of processing. The reinfusion bag should be labelled in the operating theatre with the minimum patient identifiers derived from a patient's ID band. The blood salvage is transfused through a leucodepletion filter. The transfusion should be prescribed, documented and the patient monitored in the same way as for any transfusion.

It is composed of a large-scale syringe with an internal filter; the syringe plunger can be assembled onto a foot pedal pump or an electric motor. Two check valves direct flow of blood into the reservoir of the syringe and then subsequently into an attached blood bag through an outlet valve. An O-ring provides an air tight seal between the plunger and the reservoir barrel housing. The internal surface of the reservoir barrel is coated with silicon to avoid blood coagulation. The hollow tapered tip is joined to the reservoir barrel by an o- ring and threaded joint, the tip provides storage for larger clots which are caught by a coarse internal filter before blood passes through an additional fine internal leucodepletion filter. The leucocytes present in donated blood play no therapeutic role in transfusion and may be a cause of adverse transfusion reactions. Some of the benefits of the system include the lack of an expensive pump and the ease of maintenance due to a small number of parts and a simple design. However, the design also requires very high tolerances in manufacturing in order to create the necessary vacuum pressure to draw blood into the reservoir and is prone to clogging from blood clots.

10.8.1 Prototype Design

10.8.1.1 Operation of device (Path of flow)

The device operates by creating a negative pressure differential on the upward stroke of the plunger, which draws blood through the tip (A) and into the syringe reservoir (D), passing through the first duckbill valve (I), the two internal filters (B and C) and the swing check valve (E). The plunger is then forced downwards (down stroke), at which point the positive pressure closes the swing check valve and opens the duckbill valve at the exit to the blood bag. The blood then exits the main reservoir and is transferred into a blood bag which is connected to the outlet valve (H). This process is repeated in a continuous cycle until the blood intended for auto transfusion is completely evacuated from the patient's cavity.

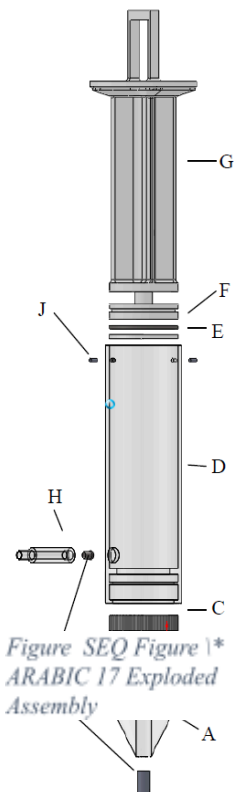


Figure SEQ Figure 1*
ARABIC 17 Exploded
Assembly

11.2.1.2 Part-by-part Description

The tip (A) includes a rigidly attached internal filter (B) with a maximum pore size of 200 μm . This coarse filter will be used to remove larger clots before they reach the fine internal filter. The filter will be glued onto an internal lip (0.25" width) and has a diameter of 2.25". The tip also includes a hollow space beneath the filter, which is meant to store clots that are caught by that filter and reduce clogging.

The second filter (C) has a maximum pore size of 10 μm and is attached in a rigid housing element with a height of 0.5" inside the main reservoir housing. The height of the housing element can be varied as needed to accommodate the filter, but is currently set to 1.5". The next element the blood will encounter is a rubber swing check valve with a 2.25" diameter (E), which will be glued to a 0.125" lip in the housing of the main syringe. The valve will function like a torsional spring, opening on the up stroke of the plunger and closing on the down stroke.

The handle on the plunger allows the user to fully grasp the plunger when pulling upwards. When the plunger is extended in the open position, dowels pins (J) prevent it from being pulled out of the barrel completely.

10.9 Device Specifications

1. Dimensions (mm ³):	520 mm x 140 mm x 1000mm
2. Weight (kg): (empty filled)	0.5 kg 10 kg
3. Consumables:	Foot Pedal, Electric Motor, Hand Crank
4. Estimated life time	2 Years
5. Estimated shelf life	5 Years
6. Portability	Mobile (between ORs and ERs) Portable (hand-held)
7. Use:	Reusable
8. Maintenance Requirements	Cleaning and Sterilisation every after use
9. Energy requirements	Mechanical energy (manually powered)
10. Facility requirements	Sterilization Any kind of sterilisation method is viable

Section III

11 Testing Protocol

Testing may be defined as subjecting a device to conditions that indicate its weaknesses, behaviour characteristics, and modes of failure(Paul H. King & Fries, 2015). It is a continuous operation throughout the development cycle that provides pertinent information to the development team. Testing may be performed for three basic reasons:

- Basic information
- Verification
- Validation

Basic information testing may include vendor evaluation, vendor comparison, and component limitability. Verification is the process of evaluating the products of a given phase to ensure correctness and consistency with respect to the products and standards provided as input to that phase. Validation includes proving the subsystems and the system meet the requirements of the product specification(Paul H. King & Fries, 2015).

Testing is an essential part of any engineering development program. If the development risks are high, the test program becomes a major component of the overall development effort. To provide the basis for a properly integrated development test program, the design specification should cover all criteria to be tested including function, environment, reliability, and safety. The test program should be drawn up to cover assurance of all these design criteria. The ultimate goal of testing is assuring that the customer is satisfied. It is the customer who pays the bills, and if we are to be successful in business, we have to solve their problems. We aim for quality, but quality is not just an abstract ideal.

We, UgHealth aims to design a whole blood transfusion device that conforms to the both FDA standard 21 CFR868 5830 and ISO 1135-5:2015. We have taken into consideration the WHO & Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee Standards for intraoperative whole blood transfusion guidelines during this test protocol(Paul H. King & Fries, 2015).

11.1 Fundamental Testing objectives

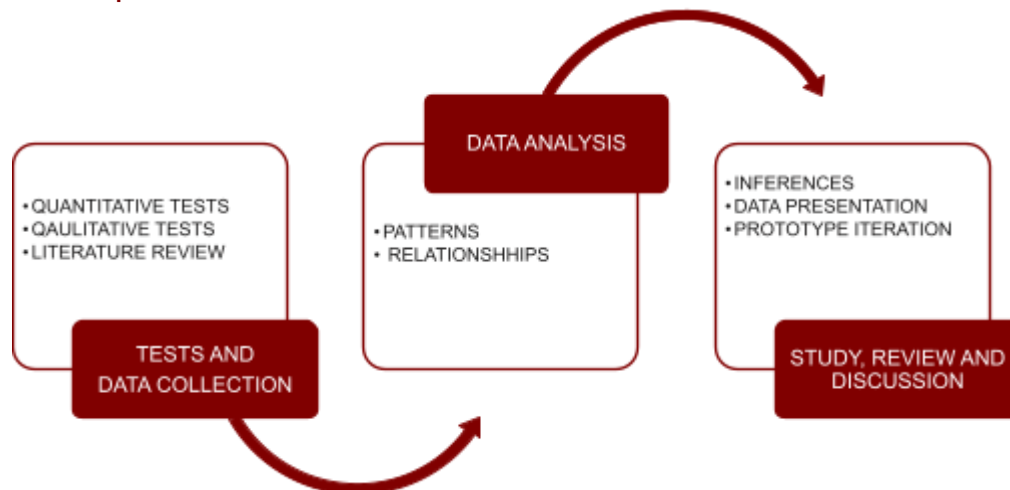
1. To test for Bio toxicity/Patient Safety,
2. To validate the Mechanical Integrity of the device,
3. To test Environmental safety of device,
4. To validate human Ergonomics.

11.2 Methods

11.3 Study Design

The protocol was implemented as a cross sectional field-based study. The study employed a mixed methodology, containing both qualitative and quantitative methods as well as a combination of data analysis techniques. The protocols herein were implemented as part of two groups, user interaction tests and non-user interaction tests.

11.4 Conceptual Framework



11.5 Parsing Test Requirements

For all the tests the team conducted, there was a certain requirement to be validated by the result of the test. We began by placing all the requirements into a database where they were sorted by a variety of attributes. The purpose of the database was to ensure that all requirements are addressed in the test protocol as well as providing a convenient tracking system for the requirements. We sorted the requirements by the following attributes:

- Requirement number (among all requirements)
- Statement of requirement
- Paragraph number in the document which contains the requirement
- Requirement number within that paragraph
- Author of the requirement
- Team member responsible for ensuring the requirement is addressed
- Type of test to address the requirement

With the requirements listed, we used them to develop the various test protocols necessary for testing. (Paul H. King & Fries, 2015)

11.6 Test Protocols

For each test performed, the following details were populated:

- The name of the device or part of the device under test
 - The type of test being performed
 - The purpose of the test
 - A definition of potential failures during the test
 - The expected results
 - Any special requirements
 - The number of units on test
 - The length of the test in hours or cycles
 - A detailed procedure for running the test or reference to a procedure in another document, such as a standard
 - The parameters to be recorded
- (CDC, 2019)

11.7 Non User Interaction Tests Methodology

The tests we carried out can be roughly divided time testing, event testing, stress testing, environmental testing, and failure-related testing. We analysed the results with this classification.

11.7.1.1 Time Tests

Time testing was conducted primarily to determine long-term reliability parameters, such as failure rate and mean time between failures (MTBF). By carrying out time testing, we were able to determine what part or component fails, when it fails, the mode of failure at that particular time, the mechanism of failure and how much more or less life the equipment has that is required for operational use. This allowed us to prioritise the areas that were critical for reliability improvement the coming iterations of prototypes.

11.7.1.2 Event Tests

Event testing consisted of repeated testing of equipment through its cycle of operation until failure. We carried out these tests to deduce the number of cycles to failure.

11.7.1.3 Stress Tests

We took precaution to find the optimal stress levels to subject haemoSAVE to. This was because too much stress would cause the test results to be inconclusive, as overstress may precipitate a failure that our device would not normally experience during normal usage. We subjected our design to a stepwise stress to determine where in the progression the failure occurred.

11.7.1.4 Environmental Tests

The environmental testing mimicked the environment of application of the device during normal operation, storage, maintenance, and disposal.

11.7.1.5 Failure Related

A test may be conducted until all test units/ part of the device or a certain percentage of units/a number of parts of the device have failed. This guided us to calculate MTBF from the test data.

All tests, were performed at a confidence level of 90%. We are 90% confident that the reliability parameters established in these tests will be characteristic of units in the field. A 90% confidence level also yields a risk factor of $(1 - \text{confidence level})$ or 10%. The limit was important in determining the number of test units and the length of test time. In this protocol, we ignored the number of test units since we had only one for field tests.

11.8 Failure Definition

For each test and for each, a failure was defined. This definition depended on the intended application and the anticipated environment. What is considered a failure for one component was not considered be a failure for other parts. The test protocol details the definition of the failure for each test carried out.

11.9 Determining Sample Size & Test Length

After determining the simulations and in vitro tests we had to carry out, we needed to determine the test sample size of units and the length of time necessary to accomplish the testing goals. Sample size of units and test time are were dependent upon the MTBF goal. The formula for determining the sample size and test time is derived from the following equation(Paul H. King & Fries, 2015):

$$(Sample\ size)(Test\ time) = MTBF\ goal\ (X^2_{\alpha; 2r+2})/2$$

To complete the equation we used the chi-square chart. As mentioned earlier, the risk factor was derived from the confidence level:

$$Confidence\ level = 1 - \alpha, \text{ where } \alpha \text{ is the risk factor.}$$

Using the 90% confidence level, $\alpha = 0.10$. The r in Equation is the number of failures. When calculating sample size and test time, we that assumed there will be no failures, we derived the minimal test time. Thus, $r = 2(0) + 2$. Looking at the chi-square chart in, go across the top row of the chart and find 0.10, or *. Go down that column to the line for $v = 2$. There you will find the number 4.605. Inserting the MTBF goal into the equation and solving it yields the unit test time or (sample size) (test time) as follows:

$$Thus\ test\ time \approx 11\ cycles\ per\ test\ unit$$

11.10 User Interaction Tests Methodology

The studies were carried out in Kampala and Entebbe. Our primary data sources were predominately qualitative; observations of respondents carrying out tasks and structured surveys. The inclusion criteria for hospitals was hospitals specialised in surgeries. We ranked them according to the number of surgeries carried out per week, and the number of emergency cases they receive daily. We choose the top 4 hospitals; CoRSU hospital, Mulago Specialised Women & Neonatal Hospital, Nakasero Hospital and Kawempe Women's Hospital. We interfaced with the longest working staff at the facilities.

Our methodology was directed towards the development of a testable hypothesis. In hypothesis testing, the null hypothesis is the basis of the research. This is the hypothesis that there will be no difference, and once rejected then the alternative is automatically accepted. For each of the guided interviews, we had both a null and research hypotheses that we investigated.

In this research design, the usability and desirability of HeamoSAVE are validated. HeamoSAVE has been designed by means of an extensive Human Factors engineering process (in Design I & II). The particular approach followed is situated Cognitive Engineering, a systems approach(Schmettow, Schnittker, & Maarten, 2017) for developing design concepts for complex environments. Initially, autologous blood transfusion was analysed and described on the basis of available literature, user interviews and task analyses. Next, user requirements were elicited which guided the device design. Consequently, the device was developed in an iterative fashion using paper prototyping and 3D printing.

Usability is defined as 'the extent to which HaemoSAVE can be used by specified users to achieve cell salvaging and transfusion with effectiveness, efficiency and satisfaction(Schmettow et al., 2017).

Due to its relevance for efficient and effective operational processes in healthcare, usability engineering is increasingly incorporated in public guidance reports. In our research, the desirability of the device is dependent on its usability.

In our study, we triangulated data collection and evaluation methods in order to overcome the lack of a profound analysis of the user-device interaction by mainly reporting coarse outcome measures rather than tracing the interaction process as in contemporary tests. Another shortcoming of contemporary validation studies is the limited-duration interaction with the studied medical device. In particular, the rate of performance improvement with practice cannot be assessed in single-encounter studies. Our protocol rests on two extensions to the FDA's proposal recommendation: a method for a more fine-grained representation of the user's task completion process. In essence, it assesses the degree by which a user deviates from an optimal path for task completion. Second, a longitudinal research design is implemented, where participants go through multiple sessions with variants of a task set, making it possible to trace progress in performance.

11.11 Study Setting

Kampala and Entebbe have 68% of Uganda's health service centres (UBTS, 2018), other areas have a gross shortage of these services. Health facilities specialised in major surgeries can only be found in the central region. We crudely estimated that all health services provided in these urban areas are superior to those offered in rural areas, therefore the qualitative and quantitative data collected in these urban areas will be extrapolated to give us a picture of rural areas.

11.11.1 Study Population

The study population involved health facilities and their surgical staff. Their selection criteria is outlined below.

11.11.1.1 Selection Criteria

Our selection criteria was based on the following attributes:

- Rate of population
- Current and projected population density
- Proximity to commuter taxi routes
- Distance from other hospitals
- Anticipated impact on existing hospitals
- Existing infrastructure and availability of services
- Placement of hospital in country's health facility structure.
- Revenue streams of hospital
- Governing body ~ religious body, other NGOs, or government

11.11.1.2 Inclusion Criteria

- Hospitals specialised in child birth and/or orthopaedic surgery
- Hospital staff serving for >2 years at health facility
- Health facilities which are either non for profit or public
- Hospital staff working in more than one health facility

11.11.1.3 Exclusion criteria

- For profit health facilities
- Staff refusing to sign consent forms
- Staff employed in for profit health facilities
- Health facilities un reachable on commuter taxi routes

11.11.2 Sample Size Determination

We deployed two techniques to avail us calculate the sample size for user interaction: the Krejcie and Morgan sampling frame and the Kish Leslie formula.

11.11.2.1 The Kish Leslie formula

$$N = \frac{Z^2_{\alpha/2} p(1-p)}{d^2}$$

Where;

Z-alpha is standard normal value corresponding to the set confidence level of 95% which is 1.96.

N is the required sample size of both health facilities and staff

d is the tolerable sampling error (precision) which we put at 10%.

p is the estimated percentage of the mortality in surgeries in Africa;

We deduced our "p" from the estimated deaths in surgery in Africa due to haemorrhages interpolated by 58% of the total occurrences in the world. Therefore $p = 58\% (1.5m/17.2m) = 5.05\%$

N = 18

11.11.3 Sampling Procedure

We employed homogeneous purposive sampling to recruit the hospitals, officers and doctors, as this sampling technique focuses on particular characteristics of a population that are of interest, which will best enable us to address the research questions and meet the objectives. We invited the key informants to participate in the study through, emails, phone calls and consequentially visits at the facilities.

11.11.4 Hypotheses & Research Questions

The quantitative approaches are directed toward the development of a testable hypothesis. In hypothesis testing, the null hypothesis is the basis of the research. This is the hypothesis that there will be no difference, and once rejected then the alternative is automatically accepted. The null hypothesis (H_0) was that:

The different methodologies and devices currently used to combat haemorrhages in trauma are efficient, there is no need to develop a novel better suited for the landscape in LMICs

The alternative hypothesis (H_1) was:

Designing a device which can recycle blood for patients in trauma against the landscape in LMICs will increase the availability of safe blood and reduce mortality rates in surgery

The alternative hypothesis (H_2) was:

In relation to the design, performance and functionality, can the proposed device be used in a hospital setting?

12 Ethical Guidelines Observed during Testing

Research involving human participants pertains to a broad range of scientific enquiry aimed at developing generalizable knowledge that improves health, increases understanding of a phenomena and is ethically justified by its social value. Every research has some inherent risks and probabilities of harm or inconvenience to participants/communities. Therefore, protection of participants should be built into the design of the study. Do no harm (non-maleficence) has been the underlying universal principle guiding health care in all systems of medicine around the world.

While conducting biomedical and health research, the four basic ethical principles namely; respect for persons (autonomy), beneficence, non-maleficence and justice have been enunciated for protecting the dignity, rights, safety and well-being of research participants. These four basic principles have been expanded into 12 general principles (Council & Medical, 2017) described below, and are to be applied to this test protocol.

12.1.1 Principle of Essentiality

Whereby after due consideration of all alternatives in the light of existing knowledge, the use of human participants is essential for this protocol. This should be duly vetted by an ethics committee (EC) independent of the proposed research. However, due to the lack of access to one, we had our

protocol reviewed by an experienced professor; Dr. Kaweesa Joseph Lenon an experienced surgeon from Nakasero Hospital, Uganda.

12.1.2 Principle of Voluntariness

Whereby respect for the right of the participant to agree or not to agree to participate in research, or to withdraw from research at any time, was paramount. An informed consent process ensures that participants' rights are safeguarded. All human participants were informed of the purpose of their participation in the study and the aim of the entire project.

12.1.3 Principle of Non-exploitation

Whereby research participants were equitably selected so that the benefits and burdens of the research are distributed fairly and without arbitrariness or discrimination. In this protocol, the participation of the human subjects was optimally defined to avoid fatiguing the participants with a lot of work.

12.1.4 Principle of Social Responsibility

Whereby the research was planned and conducted so as to avoid creation or deepening of social and historic divisions or in any way disturb social harmony in community relationships.

12.1.5 Principle of Ensuring Privacy & Confidentiality

Whereby to maintain privacy of the potential participant, her/his identity and records were and are being kept confidential and access is limited to only those authorized.

12.1.6 Principle of Risk Minimization

whereby due care was taken by all stakeholders at all stages of the research to ensure that the risks are minimized and appropriate care and compensation is given if any harm occurs. Fortunately, no event occurred during the implementation of this protocol that required compensation, all decisions taken in this study had the least risk attached.

12.1.7 Principle of Professional Competence

Whereby the research was planned, conducted, evaluated and monitored throughout by persons who are competent and have the appropriate and relevant qualification, experience and/or training.

12.1.8 Principle of Maximization of Benefit

Whereby due care was taken to design and conduct the research in such a way as to directly or indirectly maximize the benefits to the research participants and/or to the society.

12.1.9 Principle of Institutional arrangements

Whereby institution – Makerere University where the research was being conducted, have policies for appropriate research governance and they took the responsibility to facilitate research by providing required infrastructure, manpower, funds and training.

12.1.10 Principle of Transparency & Accountability

Whereby the research plan and outcomes emanating from the research will be brought into the public domain through this report while safeguarding the right to privacy of the participants. All stakeholders involved in this research were asked disclose any existing conflict of interest. The research was conducted in a fair, honest, impartial and transparent manner to guarantee accountability. Related records, data and notes have been retained for the required period for possible external scrutiny/audit.

12.1.11 Principle of Totality of Responsibility

Whereby all stakeholders involved in research were responsible for their actions. The professional, social and moral responsibilities compliant with ethical guidelines and related regulations are binding on all stakeholders directly or indirectly.

12.1.12 Principle of Environmental Protection

Whereby the researchers were accountable for ensuring protection of the environment and resources at all stages of the research, in compliance with the existing national environmental guidelines and regulations. This protocol does not in any way whatsoever harm the environment. All environmental safety tests were conducted based on past literature and analysis software.

13 Technical Tests

The table below summarises tests we carried out, and the methodology we deployed for each test. We grouped the requirements in order to carry out one test that captures the tests of an entire group.

Statement of Requirement		Part of device under test	Methodology of test	Type of test
1.	Removes particulate matter, $\geq 170 - 240 \mu\text{m}$ in diameter Filtering efficiency of at least 90%	Coarse filter	Lab Test	FUNCTIONALITY TESTS
2.	Removes of leucocytes & amniotic fluid, $\geq 7 - 10 \mu\text{m}$ in diameter Filtering efficiency of 99.99%	Fine filter	Literature Review	
3.	Closed system ,zero openings to environment	Whole Device	Bubble Leakage Test	
4.	Noticeable if device malfunctions, Force on plunger $>45 \text{ N}$	Plunger	Field Test	
5.	Noticeable if device malfunctions, Transparency of material	Whole Device	Visual Inspection	
6.	Durable, Withstand free fall drop test	Whole Device	Simulation	
7.	Material Reusability, Number Autoclave Sterilisation Cycles before degradation of material	Whole Device	Analysis using CES - Cambridge Engineering Selector	
8.	Can manage significant blood loss, $\geq 2 \text{ L}$ blood loss	Barrel Reservoir	Mathematical Modelling	
9.	Minimum amount of blood for suction $\geq 10\text{mL}$	Suction Tip	Mathematical Modelling	
10.	Flow rate removes blood sufficiently, $\geq 0.5 \text{ L/min}$	Whole Device	Mathematical Modelling	
11.	Measures total blood collected , $\leq \pm 10 \text{ mL}$ accuracy	Barrel Reservoir	Mathematical Modelling	
12.	Easy to operate ,Training time $< 30 \text{ min}$ for 1 operator	Whole Device	Field Test	USABILITY TESTS
13.	Easy to operate, 1 operator required	Whole Device	Field test	
14.	Easy to operate , Force applied $\leq 48 \text{ N}$	Plunger	Mathematical Modelling	
15.	Easy to operate , Diameter of grip $\leq 3 \text{ in}$	Reservoir Barrel	Measurement	
16.	Quick to operate , Set-up time of $< 2 \text{ min}$	Whole Device	Field Test	
17.	Quick to operate, Time to first transfusion is $\leq 10 \text{ min}$	Whole Device	Field Test	
18.	Small and portable , $\leq 15.5 \text{ kg}$ filled	Whole Device	Mathematical modelling	
19.	Compatible with 3mm tubing on blood bag, infusion pump and other blood transfusion devices	Blood Bag Connector	Field test/literature review	
20.	Toxicity, Cytotoxicity	Whole Device	Literature Review & virtual lab	PATIENT SAFETY / BIOCOMPATIBILITY TESTS
21.	Toxicity, sensitisation	Whole Device	Literature Review & virtual lab	
22.	Toxicity, Irritation or Intractaneous Reactivity	Whole Device	Literature Review & virtual lab	
23.	Toxicity, Systemic Toxicity (acute)	Whole Device	Literature Review & virtual lab	

24.	Mechanical Integrity, Torsion Tests for plunger	Plunger	Mathematical Modelling	MECHANICAL INTEGRITY TESTS
25.	Mechanical Integrity, Bending Test	Plunger	Mathematical Modelling	
26.	Mechanical Integrity, Hoop Stress Test	Barrel Reservoir	Mathematical Modelling	
27.	Mechanical Integrity, Check valves functionality	Check Valves	Mathematical Modelling	
28.	Mechanical Integrity, Shear force for dowel pins	Dowel pins	Mathematical Modelling	
29.	Does not damage blood cells, Fluid (blood) flow in device	Reservoir Barrel	Mathematical Modelling	CELL SALVAGE QUALITY
30.	Fluid Flow in device, Protein Adsorption	Reservoir Barrel	Literature Review, Mathematical modelling & virtual lab	
31.	Does not damage blood cells , < 150 mmHg pressure	Reservoir Barrel	Mathematical Modelling	ENVIRONMENTAL SAFETY TESTS
32.	Environmental Impact of device materials on disposal by burning	Whole Device	Environmental Impact with Sima Pro and CES - Eco Audit Tool - understand the environmental impacts of plastic chosen	
33.	FDA (21 CFR868:5830)	Whole Device	Literature Review	CONFORMANCE TESTS
34.	ISO (DTR 23128 – Medical Devices Transfusion Set & Blood Bag Compatibility Methods)	Whole Device	Literature Review	
35.	TC76 – Transfusion, infusion & injection and blood processing equipment for medical and pharmaceutical use	Whole Device	Literature Review	
36.	MTBF - mean time between failure	Whole Device	Field Testing, Mathematical Modelling	RELIABILITY TESTS
37.	MTTR - mean time to repair	Whole Device	Field Testing, Mathematical Modelling	
38.	MTTF – mean time to failure	Whole Device	Field Testing, Mathematical Modelling	
39.	MTBB – mean time between breakdowns	Whole Device	Field Testing, Mathematical Modelling	
40.	MTBR – mean time between replacements	Whole Device	Field Testing, Mathematical Modelling	

13.1 Micro Aggregate Filter Integrity Test

Statement of Requirement Purpose of Test	Part of device under test	Type of test
Test a filters with mesh size of 170 µm to deduce its filtering efficiency to remove particulate matter (clots, flesh, etc.)	Coarse filter	Lab test
Test Pass Fail Criteria	Test Entry / Exit Criteria	Test Deliverables
The test will be successful if it's able to remove undissolved particulate ranging from 2-0.02cm from a sample solution without clogging and / or adsorption and having an efficiency of 90%	Recordings will be taken after passing the analytical solution through the filter	Table of concentration of residue, water recovery and pressure build.

Ultra sonicated samples should not show more than a 2% increase in dissolved sample material when compared to the non-sonicated sample If the filter requires more than 150mmHg, the filter is clogged and has passed the test			Trace of post measured pressure build for sample against water recovered.
Test Suspension Resumption Criteria		Parameters to be recorded	Test materials/ Environmental / Staffing / Training Needs
Test was to be abandoned if any of the filters got an irreversible damage.		Pressure Amount of residue % of water recovered	Filters Silicon tubing Pressure gauge 300mL syringe Deionised water
Number of units under test	3	Detailed Procedure	
Length of Test	N/A	Prepare a sample solution of approximately 50% of deionised water and concentration of bits of paper. Filter three sample aliquots through separate filters 30mL syringe.	
References	FDA(Services, Administration, (CDER), (CBER), & (ORA), 2004)	Dispense the samples individually into test tubes and analyse according to the analytical method as follows: Sample 1 – Analyse immediately. Sample 2 - mix for 5 minutes, mix well, and analyse. Sample 3 - mix for 10 minutes, mix well, and analyse. <i>* Analysis for presence of paper bits was done by drying up the samples on soak sheets in a drying oven. The amount of paper was ranked from 0 -4.</i>	
Results		Post-filtration samples were compared using paired t-tests with P <0.05 indicating statistical significance. The null hypothesis assumed that the true mean difference between the paired samples is zero. Draw air into the syringe and then attach it to the filter syringe adaptor on the pressure gauge. Push air into the filter and mark the highest pressure recorded.	
The amount of residue from the aliquots decreased with mixing. This indicates that the filter lets some particulate <170 micro meters. This is not worrying because the filter has not only filtered out dangerous clots but has also emulsified the clots. The mean deviation of the amount of residue in the paired t – tests decreases with mixing. This indicates that some particulates adhere into the filter essentially making it a better filter but putting it closer to imminent failure due to the pressure build. The pressure build shows how much force is required to break the adherence between the particulate and the mesh. However, the smallest of the particulates may be being trapped into the mesh pores causing the bigger particulates t elute faster. More investigation needs to be done around this. Raw data from this test can be found in the Appendix.			

13.2 White blood cells / amniotic fluid filter integrity test

Statement of Requirement Purpose of Test	Part of device under test	Type of test
Filter for use with terminally ill patients where injection of whole blood puts them at risk of immune reactions. And also for women undergoing caesarean birth surgery.	Fine filter	Literature Review
Test Pass Fail Criteria	Test Entry / Exit Criteria	Test Deliverables
The test will be successful if it's able to remove leucocytes with diameter ranging from 7-15 micro meters from a sample solution without	Recordings will be taken after passing the analytical solution through the filter	Table of the presence of amniotic fluid and leucocyte

clogging and / or adsorption and having an efficiency of 99.999%		components before and after filtering.
Test Suspension Resumption Criteria	Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test was to be abandoned if any of the filters got an irreversible damage.	Concentration	N/A
Number of units under test	1	Detailed Procedure
Length of Test	N/A	Blood from a caesarean delivery was collected. Four samples were collected: pre-wash, post-wash, post-filtration with a leukocyte depletion filter. Each sample was analysed for amniotic fluid markers of zinc coproporphyrin-1 and sialyl-Tn, for fetal haemoglobin, and the sample underwent pathological examination for white blood cells and squamous cells. Post-filtration samples were compared using paired t-tests with $P < 0.05$ indicating statistical significance.
References	(“Efficiency of leukocyte depletion filters and micro-aggregate filters following intra-operative cell salvage during cesarean delivery - ScienceDirect,” n.d.)	
Results		
Zinc coproporphyrin-1 and sialyl-Tn were negative at almost all sample points. Squamous cells decreased by 59.1% post-wash and 91.2% post-filtration using a leukocyte depletion filter. Leukocyte depletion filters removed 99.7% of white blood cells and were more effective in removing white blood cells than micro-aggregate filters ($P=0.02$).		

13.3 Bubble Leakage Test

Statement of Requirement Purpose of Test	Part of device under test	Type of test
The system should be closed; zero openings to environment to avoid contamination in the transfusion process.	Whole Device	Visual Inspection/water dip test
Test Pass Fail Criteria	Test Entry / Exit Criteria	Test Deliverables
Test will be successful if there are no leakages found.	Test starts after pressure differential is achieved and ends when no observation is made in 20mins.	Leak Detection Leak Location
Test Suspension Resumption Criteria	Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test to be abandoned in case there is unrepairable damage on prototype.	Leak Location	BLT Thermometers Silicone gel Air compressor
Number of units under test	1	Detailed Procedure
Length of Test	10mins	Clean device; Remove dirt, slag, or any foreign debris.
References	(Gamblin & Services, 2018)	Consideration of the cleaning chemical must be taken in consideration for compatibility with BLT solution.
Results		Create pressure differential by pushing air into the device using an air compressor. After blocking the blood bag tube connector with silicone gel.
Leakages were detected and located at the joint between the plunger's O-ring and the walls of the reservoir barrel. This leakage was also seen during usability testing.		Temperature should be checked prior to applying the BLT solution to see that it is between the BLT temperature limits. Flow solution over test area, not creating bubbles in the process.

There is need to find better methodology to maintain a closed system for the filter to be a closed system and avoid blood spills. However, these spills and leakage could be due to the fact that the tested prototype had no dowel pins, the dowel pins in this device prevent the plunger from moving out “unsafe regions.”	Allow a dwell time of 10mins Inspect body of device for formation of bubbles. Increase lighting Better position to keep view angle at 0°-15° If possible, improve temperature, wind, humidity
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13.4 Durability test

Statement of Requirement Purpose of Test		Part of device under test	Type of test
The device durability is important to increase user desirability. Durability will be implemented with free fall drop test.		Whole Device	Simulation / Mathematical Modelling
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
Test will considered to be passed if device is not damaged at 1.5m impact.		Test exited after reaching maximum possible height of human deduced from anthropometric data.	Analysis of deformation and stress in the device with different impact.
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test will be abandoned if device gets destroyed.		Stress Distribution Deformation location	Auto desk Fusion 360
Number of units under test	1	Detailed Procedure Loaded device will be placed, prior to release, in a position that will ensure correct orientation, within 2 degrees upon impact, for flat-face drops or flat drops on ends or sidewalls of cylindrical containers, and within 5° upon impact for drops on chimes of the reservoir barrel. Release mechanism that does not impart vertical, rotational, or sideways forces to the device. Provide an impact surface, horizontal and flat, massive enough to be immovable and rigid enough to be non-deformable under the test conditions. The impact surface shall be of concrete, stone, or steel. If the dropping surface is a steel plate, it must be at least 1/2 in. (13 mm) thick and must be anchored firmly to the mass. The impact surface shall be integral with a mass at least 50 times that of the loaded device (10kg) to be tested. Neither the depth nor width of the mass shall be less than half the length. Perform falls at 90°, 180°, and 270° for a fully loaded, half loaded and empty device for 0.5, 1, 1.5, and 2m.	
Length of Test	N/A		
References	(Selecting, Ista, & Procedures, 2018)		
Results			
Visual Stress assessment of the simulated results was carried out. There is need to strengthen the “high risk areas” such as; the blood bag connector and the suction tip. The stress wave and displacement wave of the internal components were also monitored to reveal weak joints. There is need to find a joining mechanism to ensure that there is no displacement of components during the fall. More research needs to be done to find biocompatible material matrix with higher tensile strength properties.			

13.5 Usability & acceptability tests

Statement of Requirement Purpose of Test	Part of device under test	Type of test
In order to achieve a high desirability, we need to test the ease of use of the device by investigating the following aspects: Training	Whole Device	Field test

time < 30 min for 1 operator, 1 operator required, requires < 5 steps for operation, Force applied to move plunger ≤ 48 N, Diameter of grip ≤ 3 in, quick to operate (set up time, time for transfusion), size and finally carry out qualitative data analysis about the use of the device. In the past, device dimensions was done basing on anthropometric data and simulations, there's a need to validate this in the field.			
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
If the answers from the questionnaire are mainly negative, then it means the device has been rejected by the users and therefore, this test will have been failed.		N/A	We will be able to know the views of the users about our device through written feedback
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
If results from the user acceptance survey are negative and unsatisfactory, the test is to be suspended.		Acceptability of device Amount of time to process two litres of water Mean flow rate	Well written and straightforward questionnaires
Number of units under test	1	Detailed Procedure	
Length of Test	No time bounds	Identified hospitals that would be ideal for carrying out the research.	
References	(Schmettow et al., 2017)	Acquired introductory letters from the head of the physiology department that were to be taken to selected institutions so as to be allowed to carry out the research	
Results		research	
It was discovered that the device will be willingly accepted into medical field as an alternative to current methods of counteracting hemorrhage. Out of 18 participants, 16 ranked the device highly in terms of their interaction with the prototype as very easy to handle and operate, not requiring a lot of user training, ideal size and generally comfortable with the design of the device.		Structuring of test protocol. Invited willing participants through emails, phone calls and also through visits to the facilities. An acceptability questionnaire was administered to the respondents prior to usability testing. Functional tests were performed by two separate groups. In the first, a sub group of 3 trained users processed 2L of water through the device 10 times, while the other members of the subgroup where given up to only 3 tries. The time to process was recorded, and the mean flow was calculated by mathematically dividing the time taken by the amount of fluid processed. Procedure was repeated ten times for each user. The second group processed 2L of water thrice without any training. In order to test reliability parameters, water with small bits of water was used to simulate failure amongst other events.	

13.6 Peripheral device compatibility verification

Statement of Requirement Purpose of Test		Part of device under test	Type of test
The device openings should be compatible for use with other peripheral devices like blood bags, and infusion pumps.		Blood bad connector, Suction Tip	Mathematical Modelling / Field test
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
Test fails if connection with peripheral device tubing is incompatible		N/A	N/A
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test will be abandoned if peripheral devices are unavailable			
Number of units under test	1	Detailed Procedure	
Length of Test	N/A	Attach the blood bag connector to a blood bag tube Attach blood bag connector to infusion pump tube Attach suction tip to conventional silicon ¼” tubes	
References	N/A		
Results			
The dimensions used in the designing of the device match with the ISO recommended sizes of blood tubing. Our physical tests to fit our device openings to and infusion pump and blood bag where successful.			

13.7 Bio-compatibility/toxicity tests

Statement of Requirement Purpose of Test		Part of device under test	Type of test
The purpose of toxicity testing is to generate information about a substance's toxic properties so that the patient is safe. The models used in this testing are fully compliant with ISO 10993 standards as well as FDA. The models are therefore efficient guinea pigs of sensitivity levels in a human.		Whole Device	Literature Review
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
Detection of bio toxicity due to the use of any of the device materials dictates the failure of a test.		N/A	N/A
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
N/A		N/A	N/A
Number of units under test	N/A	Detailed Procedure	
Length of Test	<24	Materials to be used in device are gathered; polypropylene and PMMA. Materials are put into contact with a blood species for anticipated times of contact during the scope of its application.	
References	(Biolalabs, 2013; Book, 2006; Laboratories, 2019)		
Results			

Both medical grade PMMA and polypropylene are not bio toxic. Since we plan to acquire readymade medical grade polymers, we do need to re test on our own. We therefore reviewed literature of experiments done against FDA and ISO standards. Both materials are biocompatible for use in invasive devices with contact less than 24 hours.	The in contact samples aliquots are tested for cytotoxicity, sensitisation, irritation/intracutaneous reactivity, and systemic toxicity. Quantitative and qualitative data reports are deduced. Analyse and test data – Test of significant Toxicity. The percent minimum significant difference is calculated. The results are separated into linear and nonlinear responses in order to use probabilistic methods to further determine point estimates in toxicity in future times that were not tested. A t-test approach is used as a control to confirm results.
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13.8 Mechanical integrity tests

Statement of Requirement Purpose of Test		Part of device under test	Type of test
To ascertain mechanical Integrity, we modelled the following tests on different part of the devices to determine their resilience; Torsion Tests for plunger, Bending Test, Hoop Stress Test , Check valves functionality, and Shear force for dowel pins		Whole Device	Mathematical Modelling & Simulation
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
Test will fail under any one of the following conditions: Tarsal Shear strength of plunger < Tensile strength of material Safety factor of bending test <1 Deduced hoop stress < tensile material of material If deflection of the check valves cannot occur at 50mmHg = 1psi If the model applied force on plunger exceeds the shear stress of dowel pins		N/A	Torsion Shear strength of plunger Bending stress of plunger Deflection of check valve at 50mmHg Shear stress of dowel pins
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test is abandoned if it cannot be mathematically modelled.		Maximum Shear stress of plunger Bending stress of plunger Hoop stress Moment of inertia of swing check valve Shear stress of dowel pins	n/a
Number of units under test		Detailed Procedure	
Length of Test		<u>Torsion</u>	
References		(Hibbeler, 2010)	
Results		The plunger could be subject to torsion while it is in the extended position. The plunger is modelled as a flat double T-section with a known cross-sectional area. The maximum shear stress on the outer surface of the plunger is calculated. This value of shear stress is then translated to the plane stress to deduce the probable torsion force acting on the device.	
The maximum shear stress was 4.6MPa whilst the yield strength of the material is 33MPa thus giving a safety factor of 7.2. In reality, the plunger will rotate in torsion, with a frictional force created by the interference fit		<u>Bending</u>	

of the rubber ring. The maximum torque will be lower than this value, resulting in an even larger safety factor. The results of the bending test yield a safety factor of 1.3. While this is a low value, it is unlikely that the total 240 N force will ever be exerted completely perpendicular to the plunger; there will likely always be a parallel component, reducing the bending moment. The deduced hoop stress; 376.2 kPa is well below the yield strength of 33 MPa (with a safety factor of 88), so the reservoir will not fail. The resulting maximum deflection was determined to be 3.6", which means that the valve will open under a pressure of 1psi, and will therefore open with much larger applied forces on the plunger. The area for the two dowel pins is calculated to be 35.63 mm². Therefore, the force required to shear the dowel pins is 6600 N which greatly exceeds the forces that will be applied on the plunger.	The position at which the plunger has the largest bending moment is when it is fully extended from the reservoir, supported only by the O-ring at the end. If a perpendicular force is applied to the end of the plunger and it is modelled as beam which is rigidly attached at one end, the bending stress is calculated assuming a 95th percentile strength in the arm of a man. Because the reservoir tube and the plunger are composed of the same material, it is only necessary to analyze the failure of one of these. <u>Hoop Stress Test</u> Operation of the device. That stress was modelled using the following assumptions: 1) grip force of 622 N (95th percentile of adult males); 2) uniform pressure around the reservoir. The hoop stress is then deduced after measuring the wall thickness and external diameter of the reservoir barrel. <u>Check Valve</u> Operation of the device. That stress was modelled using the following assumptions: 1) grip force of 622 N (95th percentile of adult males); 2) uniform pressure around the reservoir. The hoop stress is then deduced after measuring the wall thickness and external diameter of the reservoir barrel. The disc is simplified as a square of uniform cross section (1.5" x 1.5") for the calculation of beam deflection. The corresponding a value was 0.75" and the I value was 1.5". The moment of inertia (I) of the beam is calculated. <u>Dowel Pins</u> The plunger will apply a shear force (F) on contact to the two dowel pins, this force is determined from the force exerted by the user. The shear strength of material from which the pins is known. The Area of the two pins is calculated and the force required to shear the pins is calculated.
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13.9 Environmental impact analysis

Statement of Requirement Purpose of Test	Part of device under test	Type of test
To ensure that disposal of device does not have adverse effects on the environment. In our final design, we will require a mass of 0.5 kg of polypropylene and 0.5 kg of PMMA for a disposable device. These are the mass values that were used in our environmental performance calculations.	Whole Device materials	Material Analysis
Test Pass Fail Criteria	Test Entry / Exit Criteria	Test Deliverables

The test will be failed if our chosen material has more than two of EI99 damage classifications.		The test will end after device has been fully analysed by all CES environment modules.	graph of total emissions Relative Impacts in Disaggregated Damage Categories Normalized score in Human Health, Eco-Toxicity, and Resource Categories Single Score Comparison in "Points" See appendix.
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
N/A		Total Emissions in air, and water. Relative impacts	CES Edu Pack Software Tools
Number of units under test	N/A	Detailed Procedure	
Length of Test	N/A	Deduce the planned materials to use in manufacturing	
References	CES	Analyse materials with Cambridge Engineering Selector - CES	
Results			
The PMMA (equivalent to the COC polymer) has a bigger impact on the environment within all four of the EI99 damage classifications. This material also has the highest EI99 point value and is likely to have a bigger impact when the life cycle of the whole product is considered. The main resource that is used in substantial quantities during the manufacturing of PMMA is water. The lifecycle of this device in use would be at most 1 procedure as a disposable medical device. Therefore, the impacts of the PMMA polymer in the device lifecycle would have a substantially greater impact than the COC polymer. However, these two plastics fit within the environmental impact range of all plastics. Therefore, we would not need to select a different material based on this analysis.			

13.10 Device reliability tests

Statement of Requirement Purpose of Test		Part of device under test	Type of test
As a measure of reliability of the device, we carried out tests to deduce the device's failure matrix. We deduced the MTBF, MTTR, MTTF, MTBB, MTBR		Whole Device	Mathematical Modelling
Test Pass Fail Criteria		Test Entry / Exit Criteria	Test Deliverables
The aim was ensure a decreasing MTBF with increased use of the device else, the test was failed.		All groups where started off with a brief description of the device is and how it works or just what the device does. Testing was stopped when the processing time curves where asymptotic	1. MTTF 2. MTTR 3. MTBB 4. MTBR
Test Suspension Resumption Criteria		Parameters to be recorded	Test Environmental / Staffing / Training Needs
Test will be abandoned if device gets damage beyond repair		Occurrence of failure Time in between specified events	Field Test
Number of units under test	1	Detailed Procedure 1. Record number of cycles device has operated and the number of failures that occurred in those cycles. Failure is defined as clogging of the filter, or the plunger being stuck requiring the user to reset the device. 2. Record the time required to "reset" the device 3. Calculate MTBF from $\frac{\text{Total operational cycles}}{\text{Total number of failures}}$ 4. Calculate MTTR from $\frac{\text{Total time taken for repair}}{\text{Total number of failures}}$ 5. Calculate MTTF from $\frac{\text{Total operational cycles for all units}}{\text{Total number of failures for all units}}$ 6. Calculate the MTBB from the time taken to repair device.	
Length of Test	48 hours		
References	(Paul H. King & Fries, 2015)		
Results			
In total, the device run for 75 cycles. Considering a sequence of 11 tests, we calculated our MTBF. During this time, the device failed 5times. The failures occurred at the beginning of the user interaction sessions and declined to zero after the first use. Failure was due to a large airspace trapped in the reservoir barrel which required a reset. The total time taken by the respondents to reset the device during the entire running process was a mean of 312 seconds. Thus Total Cycles = 75 MTBF = (11/1) = 11cycles MTTR =(312/5) = 62.4s MTTF = (75/5) = 15 MTBB = (312/5) =62.4s Reliability is key because the device is lifesaving. These reliability parameters are key in acceptability and usability of the device. There's a need to reduce the MTBF In order to improve the reliability of the device. Since in this testing we did not use the actual filter setup as designed, we may not fully regard the results deduced herein.			

Section IV

14 Re-design

“Testing leads to failure, and failure leads to understanding,” - Burt Rutan. In order to perform a redesign of our current product version of haemoSAVE, we analysed the results from tests we had carried out.

14.1 Results analysis

14.1.1 Functional Tests

Functional tests were performed by two separate groups. In the first, a sub group of 3 trained users processed 2L of water through the device 10 times, while the other members of the subgroup where given up to only 3 tries. The time to process was recorded, and the procedure was repeated ten times for each user. The processing time significantly decreased over the first 4-5 trials, but reached a stable point of 60 ± 15 s over trials 6-10. This indicates that the device has a maximum potential comfortable flow rate during operation which is acceptable based upon the relevant specification (≥ 0.5 L/min).

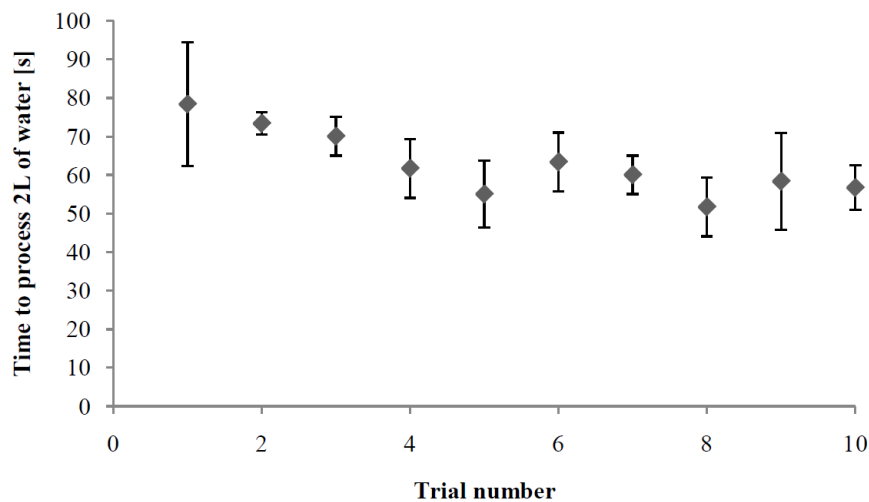


Figure 18 Graph (time to process 2L of water over multiple trials $N = 3$)

The second group processed 2L of water thrice without any training Time to process significantly decreased after only one use, even without any formal training.

Table 8 Time Distribution for two litres of water

	Mean time [s]	Mean flow rate[l/min]
First Use (N= 9)	50 ± 20	1.6 ± 1.0
Second use (N=9)	30 ± 10	2.0 ± 0.8
Third use (N=9)	25 ± 10	2.1 ± 1.0

For both groups, the time needed to process 2L of water and the average flow rates meet our specifications of ≥ 0.5 L. Furthermore, the device has been shown to be capable of processing 2L of liquid, can be operated by a single user, and requires less than 30 minutes of training time (since users unfamiliar with the device were able to operate it after only a brief, 5 minute conceptual description of the concept).

A force gauge was used to measure the force needed to draw the plunger back when the device was fully submerged in water. The measured force was 10 ± 10 N, which meets our specification of ≤ 48 N.

However this value is not final since the prototype was just a representative of the actual product. Additional testing was performed, in which the tip of the device was fully clogged, and the force needed to pull back the plunger was measured. This resulted in a force of 15 ± 10 N, which is significantly higher than the unclogged pulling force, and is noticeable to the users.

14.1.2 Human factors

The human factors associated with the device operation were tested through the use of a short survey. Subjects were asked to operate the device by processing 1-2L of water and then completing a survey regarding the comfort and ease of use. Subjects performed the operation thrice; once to gain familiarity with the device (as novice users), and a second and third time as experienced users. The results of the survey are shown below. A score of 5 indicates that users strongly agree and a score of 1 indicates that they strongly disagree.

Table 9 Results from Human Factor Tests

Human Factors Survey Results	Mean Rank out of 5
Device was easy to use	4.2 ± 0.8
Device was comfortable to hold	3.7 ± 0.8
Handle was comfortable to hold	3.9 ± 0.5
Was fatigued after completing the task	1.7 ± 0.9

Shown in the table above, users found the device easy to use, with a strongly positive ranking of 4.2 ± 1.0 . On comfort of both the device as a whole, and more specifically the handle, users had neutral to positive rankings of 3.7 ± 0.8 and 3.9 ± 0.5 , respectively. This would indicate that a redesign of the device, and especially the handle, which weighs the human factors more heavily should be considered. Regarding the ease of operation, users ranked their fatigue after use as low to very low, with a score of 1.7 ± 0.9 .

Additionally, more open questions were included in the survey. Specifically, we asked the users how long they thought they could operate the device without becoming fatigued; what would make the device easier to use; what would make the device more comfortable to use; what was the least comfortable part of using the device; and whether they would prefer an alternate handle design. For the last question, we fabricated two additional handles, a T-grip and a knob.

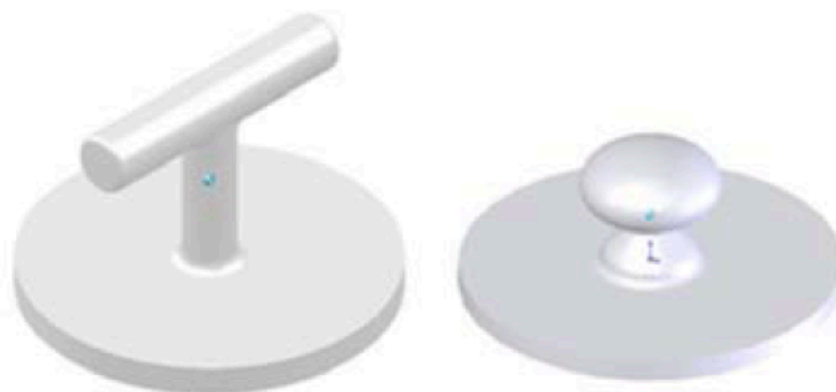


Figure 19 T-grip and knob alternate handle designs

Users reported a wide range of projected times for operating the device without fatigue, ranging from 30 seconds to 2 hours. The average time was 20 minutes, which is significantly longer than we would expect the device to be in operation.

Common comments regarding the ease and comfort of the device included the need for a grip on the barrel; a splash guard to prevent liquid from exiting through the back of the barrel (this happened frequently when the plunger was jerked, breaking the seal between the O-ring and the barrel); and a more ergonomic design of the existing handle. Specifically, users preferred the T-grip handle design over the knob and the current square handle, although many commented that a more ergonomically designed version of the current handle would be ideal (a curved rather than square fit, rounded edges).

14.1.3 Design critique

During the testing of our device, several design critiques were determined. We divided these critiques into two categories: user critiques and functional critiques. User critiques were provided to us by survey respondents and functional critiques were determined based on our engineering judgment during the use of the device.

14.1.3.1 User Critiques

The two user critiques that were consistently mentioned in the surveys were the comfort of the plunger handle and the lack of a grip on the reservoir. The current plunger handle is a rectangular grip that forces a user into a certain hand orientation that may not be the most ideal position for reducing fatigue. Furthermore, the plunger handle had several sharp edges which reduced the comfort in holding the device.

The lack of a grip on the reservoir was the second user critique. During our tests with water, some residual water would frequently splash on the barrel of the device, making it very slippery during operation. Users would often grip the blood bag connector or the tip of the device to get an adequate hold on the device during operation.

14.1.3.2 Functional Critiques

Three functional critiques were determined during our testing: poor fitting of the duckbill valves, custom fit of the fine filter, and residual fluid left in the suction tip after use. The duckbill valves were attached to the device using superglue adhesive that bonds to rubber surfaces. However, after a few uses of the device both duckbill valves (at the suction tip and blood bag connector) became loose and fell out of the seats.

The fine filters (170 μ m) that we obtained from a free sample of an arterial blood filter at CORSU did not fit to the dimensions of our filter compartment. The filter mesh was also very thin and could not be adequately secured to the housing. Since the filtering capacity was severely diminished due to the poor fitting, we removed the fine filter during operation and testing and fit it at the suction tip of the device.

Residual fluid in the suction tip between the duckbill valve and the swing check valve amounted to 150mL after 2L of water was removed from the reservoir. This is a substantial amount of fluid that was left within the suction tip that did not pass through the filtering chamber. If this residual fluid had been blood, it would need to be discarded as it would not have been filtered.

14.1.4 Recommendations

14.1.4.1 Plunger Handle Design

We propose that the two alternate handle designs discussed previously be further evaluated, in addition to the rectangular grip. The knob and t-grip are two grips that we believe may be more ergonomic by allowing the user greater flexibility in selecting a grip orientation.

14.1.4.2 Reservoir Grip

A rubber grip can be placed over half the circumference of the reservoir barrel that will give the users a better hold on the device during operation. The rubber grip should have indentations that allow fingers to fit comfortably without slipping. Additionally, it might be possible to reshape the barrel itself to create a better fit.

14.1.4.3 Mechanical Fitting of Duckbill Valves

We contacted the manufacturer of the duckbill valves and obtained additional information on attaching duckbill valves to a medical device. The manufacturer provided us with specifications for a mechanical fitting of duckbill valves. The mechanical fitting consists of a seat where the lip of the valve will sit and a mate that fits into the seat to compress the lip of the valve. Once the lip of the valve is compressed, the duckbill valve will not fall out of place unless the mate and seat become loose.

14.1.4.4 Reduction/Removal of Volume in Filtering Chamber

The 150mL residual fluid that is left within the filtering chamber can be reduced by decreasing the volume in the chamber. The volume of the chamber is primarily determined by the size of the filters, so reducing both their overall size (not pore size) and the space between the coarse and the fine filters is key.

14.2 Manufacturability

There is a major difference between prototyping using 3D printer or assembling a single prototype unit from parts. Even though 3D printing that can easily create complex inner components it cannot be used for a vast manufacturing project. There are other standard manufacturing methods to manufacture multiple parts of the device assembly like CNC or injection moulding. There are many incongruities between rapid prototyping and high-volume manufacturing.

The problem arises from the fact that while 3D printers are excellent at making one piece without any fixturing, regardless of complexity, manufacturing is completely different. Therefore, it is impossible to notice any irregularities with our 3D printed prototype. The goal of a manufacturing facility is exactly the opposite - it is designed to put forth effort and expense initially in order to mass-produce a product as quickly and cheaply as possible over the long run. So, a production facility will invest in the necessary fixturing or purchase the moulding machines and presses and lathes because time and cost are the most precious resources in large-scale production. Unfortunately, that will impact the design.

3D printing services can create infinitely complex internal pieces because they are simply extruding minuscule filaments of plastic layer by layer. A production facility will not run that way; they use an injection mould to force the material into a certain shape, and the plastic won't flow well into the tiny crevices or crannies. The created mould itself should be tested because it's the negative image of the part we intend to manufacture.

14.2.1 Design for Manufacturability Paradigm

14.2.1.1 The Manufacturing Process

To examine the manufacturing process, we looked at every aspect and interaction this product will encounter in the facility i.e. the shipping and receiving of the goods, storage, transportation and movement and analyse the machinery used and their capabilities. An injection mould can't handle some of the delicate structures a 3D printer can create, and the individual parts we will purchase for some of the components may not be the exact same configuration we had drawn up for the initial prototype.

14.2.1.2 Examine the Product's Design

The product's design and tolerances are what will drastically impact its manufacturability. Keen attention has to be given to the following parameters;

- Wall thickness – If you're moulding something, you'll need to have a gauge on how thick the walls of your product will be. The thickness will impact the cooling, the stress in the mould, and the possibility for deformation after completion.
- Transitions – Does the part transition between drastically different sizes or elements? With a CNC, this can create serious problems as brittle points will occur and stress will build up around the junctions, and the same will happen with a mould.
- Directionality – It is important with plastic moulds. When injecting, a moulded piece should have everything in the direction of pressure, because you are unlikely to get even pressure in ancillary directions.

14.2.1.3 Material Analysis

We need to ensure that our material of choice is easily machine-able as per our specified production process.

14.2.2 Manufacturing Process

The manufacturing process that we selected for the production of our housing (polypropylene) and plunger (COC) is injection moulding. Injection moulding is a quick manufacturing process that can yield the 100,000 units per year needed to meet demand. It can meet a production rate of 60 to 3000 units per hour. Although the capital cost is high initially (~ \$10,000 for the initial mould), we can expect to distribute this cost amongst the large volume of units manufactured. Injection moulding is also an ideal process considering the tight manufacturing tolerances needed in the barrel of the syringe—to

create the seal necessary with the O-ring, the inside diameter in the barrel must be consistent to within 0.001". Therefore, extrusion processes will not work to create tolerances needed. Both parts (housing and plunger) are symmetrical around one axis and can be easily injection moulded.

The barrel will need to be injection moulded in two parts: reservoir and suction tip. The blood bag connector can be attached in the mould of the reservoir. However, the suction tip and the reservoir will need to be separate pieces, as the filters and check valves will need to be inserted into the device prior to sealing it. Once the suction tip is moulded, the fine and coarse filters will be inserted into the respective cavities and affixed using an adhesive. The large one way check valve and duckbill valves for the blood bag connector and suction tip will then be attached using a silicone adhesive. Once the filters and valves have been attached, the suction tip and reservoir can be connected together using a solvent adhesive.

The plunger can be injection moulded in a single part. The O-ring will then be placed into the slot in the plunger and silicone lubricant applied to allow for smooth operation. The final step for assembly will be placing the c-clip on the top of the reservoir to ensure that the plunger cannot be accidentally removed during operation.

14.2.3 Shape Optimisation

Shape optimisation and the proceeding Mould flow design and analysis were iterative until we got the best possible results. At the end of the process, we had arrived at our best design of the HaemoSAVE.

Below are the engineering changes to better fit the manufacturing process:

Component	Parameter	Units	Old Value	New Value	Reason for Adjustment
All holes from extrusions and surface finishing e.g. barrel walls	Tapper Angle	degrees	0	2	To allow flow of plastic during injection moulding – inspect design for in Draft analysis to ensure all walls are green.
All vertical walls i.e. from extrusions and surface finishing e.g. barrel walls	Draft	degrees	0	1	To allow flow of plastic during injection moulding. Inspect the draft with Inspect > Draft Analysis. Set the draft angle values from -1.5 to positive 1.5 to ensure all vertical faces now are green or red depending on their pull direction.
Adding Ribs & plastic supports on inner walls of barrel, and suction tip.					This part is intended to be injection moulded and needs a few extra features to accommodate the process.
Split the face of the plunger					To improve the flow of molten plastic during injection moulding. Modify> Split Face. For the control panel's Faces to Split selection, on top faces via the XZ plane.
Barrel, Blood bag Connector, & suction tip Wall thickness	Thickness	mm	1.5	2.00	To fit into minimum recommended thicknesses of bodies for injection moulding
Sharp shape transitions on suction tip	Inclination angle	degrees	45	50	To allow for shape accessibility during finishing of injected moulded part. Inspected with tool accessibility in fusion 360.

14.2.4 Mould Design

We created a negative of the shape optimised 3D CAD model of the barrel, plunger, suction tip and blood bag connector in order to deduce the mould designs. For each component, we created a box encompassing it. We then used the combine tool (set to cut) in Autodesk fusion 360 to subtract the component from the box before splitting the remainder of the box via mid line construction plane to create a two part mould.

14.2.5 Mould Flow Analysis

We used Autodesk Mould Flow Analyser a simulation software for high end injection moulding computer aided engineering. We imported each component into the software and carried our proceeding analysis. The results in this process were re-iterated to produce an even more efficient design. The flow analysis helped us to further deduce the best location for entry of the molten plastic.

We juxtaposed the flow of the deposit using one and two injection points whilst monitoring the cooling time variance, fill time, confidence of fill, quality prediction, injection pressure, presence of air traps, and the presence of weld lines. The analysis was done for every haemoSAVE component for which we intend to be injection moulded. The raw data from these tests and analysis is available in the appendix section.

15 Market size and Opportunity

15.1 Market Description

The blood market accounted for \$7,201 million in 2020 and is expected to reach \$10,253 million by 2027, registering a Compound Annual Growth Rate – CAGR of 4.5% in that period (Mordor Intelligence, 2020). The global market of autotransfusion devices stood at about \$250 million in 2018 and is projected to reach \$320.5 million by 2026 (Pharmiweb, 2020).

The factors driving market growth are the increasing number of invasive surgical procedures that boost the adoption of autotransfusion devices, increasing accidents and trauma cases, the rise in a number of blood disorders and technological development (Fortune Business Insights, 2020). For the case of HaemoSAVE, blood disorders are out of scope for the market application but the product line has a strong business case in the domain of autologous blood transfusion and whole blood collection in trauma cases. The scarcity of blood is the biggest driver of auto transfusion devices.

Autotransfusion devices are widely used for collection and reinfusion of patient's own blood. These systems play a major role in cell salvage techniques, enabling autologous blood transfusion with an aim to reduce the risk of infection associated to allogenic blood transfusions. These devices are widely used in cardiovascular, orthopaedic, neurological, obstetrics and gynaecological, other invasive surgeries and trauma & accident injuries. As per usability of systems, auto transfusion systems can be characterised into intraoperative systems, postoperative systems and dual mode systems.

The pathogen and other unwanted particles reduction system segment of the blood transfusion market is believed to witness a healthy growth over the forecast period. The demand for pathogen reduction system is growing with the emergence of numerous cost-effective and innovative solutions to inactivate or reduce the risk of infection. It is for this reason that the filtration system in HaemoSAVE is a key component in the device.

North America is a high volume and high value market, it currently dominates the market for blood transfusion devices and is expected to remain strong in the future due to an increasing number of trauma cases and surgical procedures, which are driving the demand for blood transfusion (Mordor Intelligence, 2020). The United States holds the majority of the market in North America (Pharmiweb, 2020). These statistics indicate the high requirement for blood transfusion products in that region but they also indicate the difficulty to penetrate such tightly competitive market. In addition, a low cost blood transfusion contraption using somewhat traditional technology will not be sufficient to catapult any market transitional behaviours.

Countries with developing economies especially in Africa and some parts of Asia have not considered surgical care to be a public health priority (World Health Organization, 2016) and thus access to enough safe blood is almost impossible and not to mention, costly. Africa, is a grey area for significant market data. However we can rely on the prevalence of surgical care and trauma related problems to estimate the business case therein. Patients receiving surgery in Africa are younger than the global average, with a lower risk profile and complication rates and yet are as twice as likely to die (Krishnamurthy, Ishwaraprasad, Rajanna, Samudyatha, & Pruthvik, 2016). 20% of deaths in these surgeries are due to loss of blood. Thus, an innovative low cost solution to this scourge is vital, ensuring its consistent supply is crucial to support the healthcare gap. These low income regions are therefore easy to penetrate and could easily be profitable as high volume low value markets. Our product line fits perfectly into this puzzle.

In Uganda – our proposed pilot market, only 10% of the health centre IVs can provide blood transfusion (UBTS, 2018). Even though the factors driving market growth globally may not perfectly resonate with those in Uganda, there are still significant levels invasive surgical procedures, and increasing accidents and trauma cases that can be used as basis for a strong needs and business case. There is still a reported gap due to high deaths succumbed due to blood loss and particularly failure to receive blood for transfusion due to financial and logistical issues. Financial constraints affect both the affected patients and the blood processing organisation; Uganda Blood Transfusion Services has a funding gap of UGX 8.4 billion and faces even further budget cuts. Health facilities do not have the sufficient instrumentation to store blood packets for transfusion and there is a scarcity of

some blood types. The functional scope of HaemoSAVE fits perfectly into the country as it presents a cheap sustainable solution.

15.2 Market Segments

Our blood market is segmented into product, end user, and region. On the basis of product, it is classified according to the method of whole blood collection and processing. More definitely, the method of whole blood collection here refers to whether the device is manually powered, mechanically/pneumatically powered, or electronic. This product segment is further bifurcated into the sub-segments whole blood collection system and whole blood collection consumables. HaemoSAVE has both consumables and components acquired once.

On the basis of end user, the HaemoSAVE market is classified into blood and blood component bank, ambulatory centres, surgical centres, and hospitals. Region wise, it is analysed across low income countries in Asia-Pacific (Nepal, Pakistan Tajikistan, Yemen, Kyrgyzstan, Cambodia, Myanmar Syria, Brunei etc.), and sub Saharan Africa.

On the basis of the secondary consumer, we have identified two market segments; the governmental and non-governmental agencies. Since blood is an essential medical supply, we are confident that we will secure market attention from these segments since the need is one of high prioritisation from funders like the UN, WHO and the World Bank.

15.2.1 Segment Review

The market is heavily segmented to provide the end users with a power of selection according to their financial capability and resources available in the environment they intend to use the product.

On the basis of product, the whole blood collection and processing segment acquired the major share of the market in 2019. Rise in demand for whole blood across the globe and surge in number of whole blood collection centres propel the growth of this segment. In order to tap into this market segment, we have decided to extend the purpose the HaemoSAVE beyond just blood transfusion, but also whole blood collection. Contrary to the usual blood collection methods, our device would be able to collect blood from a patient's injury site and pre-process it before it is taken to a blood processing entity and eventually returned to the patient. We were swayed to take this direction by factors such as the predicted rise in number of blood banks and the surge in demand for light weight blood.

By end user, the blood and blood component bank acquired the major share in the market, owing to the surge in number of blood banks across the globe. This however, is only valid for the auto transfusion market. Health facilities are the biggest market share holders for autologous blood transfusion. Due to the wide range of use of the haemoSAVE product line, we will tap into both market segments.

On the basis of region, Asia-Pacific and Africa are expected to register fastest growth during the forecast period, owing to surge in healthcare expenditure, and increase in awareness and government prioritisation.

The global blood market is highly competitive and the prominent players in the market have adopted various strategies to garner maximum blood market share. These include collaboration, product launch, partnership, and acquisition. Major players operating in the market include Abbott Laboratories, Bio-Rad Laboratories, Inc., CSL Limited (CSL Behring), F. Hoffmann-La Roche Ltd., Grifols International SA, Haemonetics Corporation, Merck & Co., Inc., Novo Nordisk A/S, Ortho Clinical Diagnostics, and Terumo Corporation (Terumo BCT, Inc.). We plan to ignite partnerships with some of these global leaders.

15.3 Market Competition

The blood transfusion market is moderately competitive and consists of several major players. However, with technological advancements and product innovation, mid-size to smaller companies are increasing their market presence by introducing new products with cost-effective pricing. Companies like Immucor Inc., Becton Dickinson, B. Braun, Terumo Corporation, and Grifols SA., hold a significant share in the blood transfusion market.

Intraoperative blood salvage first became widely used in the mid-1970s with the introduction of two different systems: the centrifuge-based cell salvage system and the passive canister collection system. A centrifuge-based cell salvage system was first marketed by Haemonetics in 1974. The company's "Cell Saver" brand has become so widely accepted that centrifuge-based cell salvage systems are commonly referred to as cell savers. Sorin, Fresenius Kabi, Davol, Medtronic, and many other companies produce their own versions of a cell-saver. These devices are widely used throughout the United States, Western Europe, and other developed nations (Association for Surgical Technologists, 2018).

15.3.1 SWOT Analysis on Competitors

15.3.1.1 Strengths

All current market competitors have highly reputable global brand names. It is therefore hard to compete with such an absorbed market place.

15.3.1.2 Weaknesses

The biggest market competitors lack of a portfolio sales force in Uganda and other LMICs i.e. there are no licensed distributors in these markets. They tend to concentrate their after sale services in markets regarded as high value low volume rather than the low value markets.

The devices on the market are far too expensive per unit of blood processed. Therefore they do not provide a viable solution to the shortage of blood in LMICs.

Almost all marketed interventions provide light weight blood transfusion for trauma patients. The advantages of whole blood transfusion for such criteria of patients have already been rigorously expounded on in this text.

15.3.1.3 Opportunities

The opportunity therefore is to provide a unique autologous blood salvage, processing and transfusion system that is cheaper than current solutions and exhibits a higher efficacy for trauma patients.

15.3.1.4 Threats

It is already difficult to convince and earn the trust the stakeholders in the blood market about the safety and efficacy of this technology. It is a big threat to the development and launching of our whole blood transfusion line.

Additionally, there are no dedicated approval pathways for autologous whole blood transfusion devices. This implies a long approval process for some markets.

15.3.2 Competitive Comparison based on user requirements

We used the following table to assess the performance of our product line against other market competitors as per the factors of the environment in the low and middle income countries which are our major market segment.

(A) = Weight (how important) The weights for all criteria added together must be 100 (B) = Raw Score (how well does the Machine Option fulfil the criteria (1-10)) (AxB) = Weighted Score									
	HaemoSAVE (syringe Pump)	HaemoSAVE (Mechanical/Electrical)	Cell Saver	Hemosep Cell Salvage					
Criteria	(A)	(B)	(AxB)	(B)	(AxB)	(B)	(AxB)	(B)	(AxB)
Ease of Setup & operation	20	10	200	5	100	3	60	6	120
Speed of Processing	10	6	60	8	80	8	80	6	60
QC of Final Product for trauma patients	30	10	300	10	300	6	180	8	240
Company Support	20	10	200	10	200	2	40	1	20
Price of Buying and Operation	20	10	200	7	140	4	80	5	100
Total	100		960		820		440		540

Clearly, the HaemoSAVE product line has huge competitive advantage against other products on the market.

15.4 Distribution Channels

We adopted a sales decision tree from Stanford Biodesign 2010s to guide us on which is the best distribution channel for us.

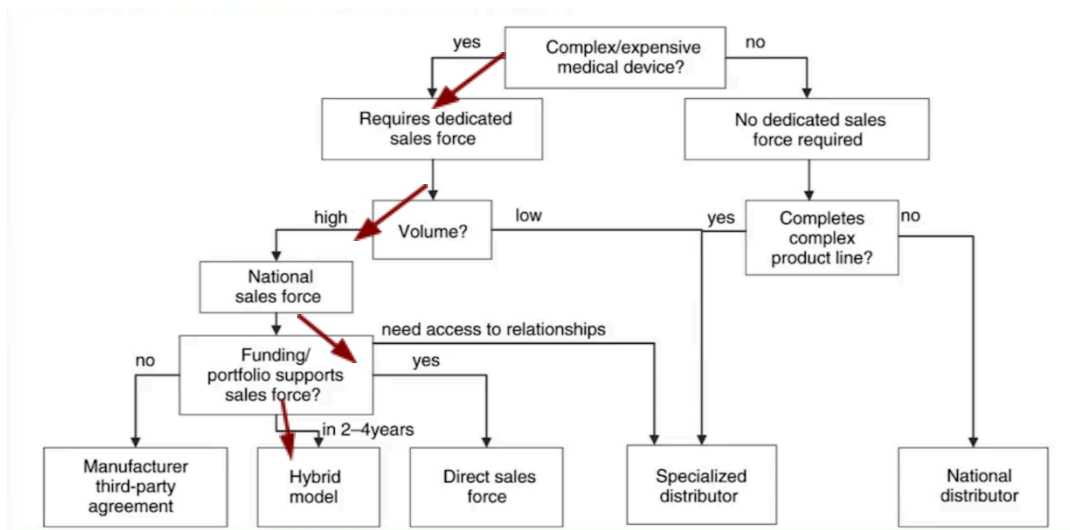


Figure 20 Sales model decision tree, HaemoSAVE pathway shown in red

HaemoSAVE is a low value medical contraption. We intend to have a high volume of users across all our market segments. Therefore, it's natural for us to choose a distribution strategy that reaches the most number of users. One of the most intricate concerning the device is its use; the wrong use of the device could potentially cause death. We need to incorporate feedback channels and user training in our distribution model.

We will deploy a specialised distributor & national distributor amalgamate distribution channel. This will be implemented by way of forming strategic partnerships with existing medical device/ pharmaceutical distributors. We will push for product specialist units to be trained within national distributors.

15.5 Market Strategy

We are aware of the influence that educational institutions can have on the market. Furthermore, since our technology has been met with a lot of prejudice and doubt, the only way of dissolving this challenge is by working with Universities to further endorse the product and use it as part and parcel of their medical and clinical training. We have therefore decided that they will be our entry point into any market we decide to penetrate. This point of entry inevitably calls for free products being donated to education centres like universities and teaching hospitals but we are confident that this will have great returns in the long run.

An alternative point of entry into the market is through the government – ministry/department of health. Obtaining endorsement from such a national government body and also securing them as our first customer is crucial. If successful, all government/public health facilities would have at least one of our products for use in their facilities.

As mentioned the preceding chapter, we shall use a hybrid distribution strategy combining both a dedicated sales force and exploitation of already existing distribution networks. Therefore, we shall have to make partnerships with these distributor companies as specified earlier. Our hybrid distribution strategy will target private health entities like hospitals and ambulatory centres. The biggest advantage of partnering with already existing distribution companies is the inheritance of customers.

15.6 Product Lines

We have diversified our product lines to engulf a bigger market share, and fit in into the requirements of the diverse market segments within the LMICs. The product lines are segmented based on the

'engine' powering the Cell Salvage and Depletion Filter Components. The syringe pump can work alone, but it can be assembled onto other accessories to simplify the cell salvage.

- Syringe Pump
- Hand Crank Pump
- Mechanical /Pneumatic Foot Pedal Pump
- Electronic Pump

15.7 Uniqueness & Value Added Proposition

Intraoperative Cell Salvage and Whole Blood Transfusion can be used routinely in some areas of surgical practice.

15.7.1 Advantages:

- Associated with recognised benefits for patients:
 - Reduces exposure to allogeneic blood and therefore reduces exposure to the risks associated with allogeneic blood transfusions (e.g. Incorrect Blood Component Transfused)
 - Lower infection rates and shorter hospital stays when compared to patients who receive allogeneic blood.
- Has minimal risks (providing the manufacturer's guidelines are followed)
- Provided the minimum volume of blood has been collected, processing is quick and blood can be reinfused within minutes
- Disposable kits cost less than a unit of allogeneic red blood cells and can process very large volumes of blood. ICS is therefore a cost effective alternative to allogeneic blood (especially for large blood loss cases).

15.7.2 Disadvantages:

- May be contraindicated in certain surgical procedures

15.8 Pricing Strategy

In order to deduce the final price of the haemoSAVE product line, we will first aggregate the total cost of device development (i.e. regulatory processes, IPRs, clinical trials), initial production/manufacturing costs, and market deployment/market launching costs. From our user requirement survey and needs assessment studies, we have already established that the total cost of the product should not be greater than about \$25, \$200 and \$300 for the syringe blood connector, mechanically powered version and the electronic version consecutively. We are confident that we will be able to achieve these market prices. However, it may require a much longer time to break even of the initial costs.

15.9 Cost Analysis: Reusable vs. Disposable Materials

We completed a preliminary cost analysis comparing the cost per unit to produce a reusable and a disposable device with the same geometry. Additionally, it is worth noting that the design for a reusable device would be slightly different from that for a disposable device; in the reusable version, the filters would need to be removable. This factor has the potential to further complicate the manufacturing process.

The recorded cost of our targeted disposable polypropylene material from Techapro MD | Ensinger was around \$10 per kilo. The cost of Topas' autoclavable COC resin material was quoted at \$15 per kilo; if this material was used, the device could be autoclaved up to four times (validated by manufacturer specifications). Materials such as glass, which can have extensive life spans in the autoclave, were originally considered, but rejected due to its tendency to shatter when dropped in addition to the manufacturing complexity of the design.

With Topas having a density of 0.037 lb/in³ and the medical grade polypropylene having a similar density of 0.0308 lb/in³, the resulting plastic material cost per unit was \$6.97 for the Topas and \$3.31 for the polypropylene. Other costs of the device included the \$12 filter from Terumo Cardiovascular and small accessories such as the valves from Vernay and the O-ring from McMaster.

After consulting an industry professional, we concluded that the injection mould for manufacturing would cost in the range of \$10,000. We then assumed production and distribution of enough units for one million uses, which would result in sales of 1 million units of the disposable polypropylene and 250,000 units of the reusable Topas. The resulting cost of the mould per unit was \$0.1 cents for the disposable unit and \$0.4 for the re-usable device.

The price of filters for the reusable device was set 25% higher than those in the disposable because of the additional manufacturing complexity that a removable cartridge and packaging would entail, as well as the additional distribution costs. A cost of 4 units was first directly calculated, since the reusable design must to be used four times to be fully utilized. We were then able to calculate a flat unit cost as shown in the table below. These calculations, assumptions, and conversations with industry professionals validated our decision to move forward with the disposable design.

Cost of material	Disposable (# of parts) (USD)	Reusable(# of parts) (USD)
Plastic Material	3.31(4)	6.97(1)
Filter	12.00(4)	15.00(4)
Mould	0.10(4)	0.40(1)
Accessories (valve & o ring)	2.00(4)	2.50(4)
Cost of 4 units	65.64	77.37
Cost per unit	16.41	19.34

16 Clinical & Regulatory Process

The autologous transfusion device that we designed is classified as a Class II medical device by the FDA (21CFR868.5830). Class II medical devices present a unique set of challenges in regards to the design of the device. These devices must include specific labelling requirements and mandatory performance standards to ensure patient and operator safety, which will drive the design of our device. Additionally, medical device export laws and international medical device regulations for countries that our device may be applicable in. On the international stage, the device requires to follow the manufacturing, performance and safety standards specified in ISO/DTR 23128 – Medical Devices Transfusion Set and Blood bag compatibility methods and ISO/DC76 Transfusion/Infusion and blood processing equipment for medical and pharmaceutical use.

To help us with our challenges specific to medical device design, we required assistance from experts that have worked with medical devices in the past and have had experience working with the FDA/ISO/EU -preferably international medical device regulations. We will re-design our device considering the impact of these regulations on our specifications and revising our user requirements and engineering specifications as needed. We have sited consultancy companies such as MDI Consultants, and the Weuinburg group who have a good reputation for products at the base of the pyramid in emerging markets.

16.1 Required Approvals

The regulatory process of medical contraptions such as HaemoSAVE in LMICs is very ambiguous. It is difficult to know what process to follow to be legally accepted to market medical devices in such countries. The apparent impression is that EU/FDA/ISO certified stickers qualify a medical device for the market in LMICs such as Uganda. However, in Uganda there is national bureau of standards (UNBS) and the national drug authority (NDA) which jointly offer market approval for medical devices.

17 Intellectual Property

Intellectual property (IP) refers to creations of the mind: inventions; literary and artistic works; and symbols, names and images used in commerce. Intellectual property is divided into two categories:

- (i) Industrial Property includes patents for inventions, trademarks, industrial designs and geographical indications.
- (ii) Copyright covers literary works (such as novels, poems and plays), films, music, artistic works (e.g., drawings, paintings, photographs and sculptures) and architectural design.

They allow creators, or owners, of patents, trademarks or copyrighted works to benefit from their own work or investment in a creation. Intellectual Property (IP) Policy/protocol refers to a set of measures formulated and implemented by government/institution/organization, to encourage and facilitate effective creation, development and management of IP assets. An efficient and equitable intellectual property system can help all countries to realize intellectual property's potential as a catalyst for economic development and social and cultural well-being. The intellectual property system helps strike a balance between the interests of innovators and the public interest, providing an environment in which creativity and invention can flourish, for the benefit of all. The promotion and protection of intellectual property spurs economic growth, creates jobs and enhances the quality and enjoyment of life.

Globally, The World Intellectual Property Organization (WIPO) is responsible for IP. WIPO is one of the specialized agencies of the United Nations (UN) system of organizations whose mission is to promote through international cooperation the creation, dissemination, use and protection of works of the human mind for the economic, cultural and social progress of all mankind. Its effect is to contribute to a balance between the stimulation of creativity worldwide, by sufficiently protecting the moral and material interests of creators on the one hand, and providing access to the socio-economic and cultural benefits of such creativity worldwide on the other. WIPO uses international treaties, agreements and protocols to grow registration activities for patents, trademarks and industrial designs for states/countries subject to those treaties.

In Africa, The African Regional Intellectual Property Organization (ARIPO), an intergovernmental organization is responsible for IP. ARIPO was established on 9 December, 1976 under the Lusaka Agreement signed in Lusaka, Zambia and its mandate is to develop, harmonize and promote intellectual property in the Member States of the Organization and in Africa. Membership of the Organization is open to all the States members of the United Nations Economic Commission for Africa (UNECA) or the African Union (AU). Currently there are nineteen Member States, namely; Botswana, The Gambia, Ghana, Kenya, Lesotho, Liberia, Malawi, Mozambique, Namibia, Rwanda, São Tomé and Príncipe, Sierra Leone, Somalia, Sudan, Swaziland, United Republic of Tanzania, Uganda, Zambia and Zimbabwe. ARIPO can be designated under the Patent Cooperation Treaty (PCT) and therefore its members are also Contracting Parties to the PCT, with exception of Eswatini. ARIPO is also a member of the Paris Convention for the Protection of Industrial Property. The substantive activities of the Organization are implemented through three treaties each focusing on a specific field of intellectual property.

17.1 Patentable Technology

The HaemoSAVE product line is made up of an assembly of components i.e. the whole blood collection system, the filtration system, the pump, blood infusion system. The blood infusion system is sold separately. We assessed these three components to deduce if they qualified as intellectual property. There are a number of registration bureaus that we could consider since we aim for the global market but, we decided to assess haemoSAVE against the requirements for a utility model in Uganda since it's our pilot market. The following are the requirements for utility model protection in Uganda:

1. Novelty: The innovation or invention should not be disclosed in any publication anywhere.
2. Inventive step: The new product or process should not be obvious to a person skilled in the art.
3. Industrial application: The invention can be made or used in some kind of industry.

In order to determine the novelty of any component of the device, we had to carry out a patent search for each component of the device in both the global and national gazette and the World Wide Web as pour public domain. We confirmed that there is no whole blood collection system that is registered in any gazette. However, the other components had been patented before or been published into the public domain of the World Wide Web as public property. Fortunately, there was no device with similar technology HaemoSAVE.

Component	Novelty	Inventive Step	Industrial Application
Whole Blood Collection System	YES	YES	YES
Filtration System	YES	YES	YES
Pumping System	NO	YES	YES

It is evident that our whole blood collection system is legible for intellectual property protection. We therefore consulted an agent from URSB to give us the process that we will have to follow in order to be awarded a patent/utility model certificate in Uganda. We found that we have to submit a filled patent application form and attach a patent document having a title, abstract, description, claims and drawings. We would then pay a processing fee and submit the proof of payment. URSB – Uganda Registration Services Bureau would then acknowledge receipt of our file and provide us with a patent application number. The amount of time to process the document was not given. However, it was made clear to us that if the application was found to be in order it is then subjected to substantive examination to determine if the claimed invention fulfils all requirements for patentability. We would be notified on grant/refusal of a patent. If successful, we the applicants will then be requested to pay the grant fees and thereafter issued a Certificate of Grant of a patent. The application document for a utility model in Uganda is available in the [appendix below](#).

17.2 Claims

What we claim as new and desire to secure by the Patent Office is:

1. Whole Blood salvage and handling apparatus comprising a suction mechanism selectively positioned for insertion into an uncontaminated wound cavity to withdraw blood by pumping it, leucodepleting it and sending it through a standard blood connector into an infusion bag, (catheter and infusion bag not part of invention herein.)
2. Cell salvage apparatus as defined in claim 1 consists of the tip which includes a rigidly attached internal filter with a maximum pore size of 200 μm . This coarse filter will be used to remove larger clots before they reach the fine internal filter. The filter will be glued onto an internal lip (0.25" width) and has a diameter of 2.25". The tip also includes a hollow space beneath the filter, which is meant to store clots that are caught by that filter and reduce clogging. The second filter has a maximum pore size of 10 μm and is attached in a rigid housing element with a height of 0.5" inside the main reservoir housing. The height of the housing element can be varied as needed to accommodate the filter, but is currently set to 1.5". The next element the blood will encounter is a rubber swing check valve with a 2.25" diameter, which will be glued to a 0.125" lip in the housing of the main syringe. The valve will function like a torsional spring, opening on the up stroke of the plunger and closing on the down stroke. The handle on the plunger allows the user to fully grasp the plunger when pulling upwards. When the plunger is extended in the open position, dowels pins prevent it from being pulled out of the barrel completely. The internal walls of all the components are coated with silicon to avoid coagulation and adsorption of blood.
3. The filtration system and leucodepletion system in claim 2 consists of two filtration systems in series with the latter coming first. The coarse filter is made from a perforated polypropylene plastic sheet. The filter includes a filter housing having an open space within. The housing has a filter inlet for conducting a body fluid into the open space and a filter outlet for conducting filtered body fluids out of the open space. A plurality of glass fibre filter pads are sealed within the open space of the filter housing. Preferably, the glass fibres have a mean diameter of from about 0.1 to about 5.0 micrometres. A plurality of non-woven polyester film filter pads is also sealed within the open space of the filter housing. The non-woven polyester fibres have a mean diameter of from about 0.1 to about 5.0 micrometres. In one embodiment, the glass fibre filter pads and the polyester fibre filter pads are sealed within the open space such that the body fluid which is conducted into the open space first contacts and passes through the glass fibre filter pads before contacting and passing through the polyester fibre filter pads.

17.3 Licensing Agreements & Royalties

In lieu that we are not granted a patent certificate, we would need to contact the holder of the patent for a licencing or royalties agreement.

The agreement will highlight that; whereas, the inventor owns all right, title and interest in and to the Invention and the Licensed Patent application, which Invention is in the field of medical contraptions,

we ugHealth desires to have the Invention perfected and marketed at the earliest possible time in order that products resulting therefrom may be available for public use and benefit.

The agreement will further state that we desire a license under the said Invention and/or Licensed Patent(s) to develop, manufacture, use, and sell the Licensed Products and Related Services in the Licensed Field of Use. The patent holder or licensor should be willing to grant a license under the License Patent in accordance with the terms and conditions set forth in this Agreement. We ugHealth the licensee are willing to pay the licensor a Patent Royalty as a commission on each unit sold over the preceding years in which the patent stands or a single bulk fee.

We plan to hire a legal hand to help through the patent application process and this royalty agreement in case we do not get the patent at the time of application.

18 Milestone Based Design & Development Plan and Budgets

In the event that we- UgHealth secure seed funding, the following would be our implementation strategy. Many of the stages herein are repeated from the ones described in the previous sections, but this is only because there is a need to re verify the business case and the feasibility of the solution with a team that has a wider repertoire than before. In addition, since we intend to put the product on the global market, the regulatory process requires specific documentation especially during the testing phase which we were unable to do due to lack of appropriate financing, laboratory facilities and lack of technical knowhow.

18.1 Initiation

The verification of the formerly detected clinical needs. This will include discussions with surgeons, doctors, end-users, and other stake holders. Furthermore, we will review of the existing methodologies and procedures. Verification activities will also extend to the initial market analysis, financial review, and competitive product evaluation. A comprehensive review of the existing IP landscape and technology risk evaluation will be performed.

18.2 Concept Verification

The second stage of consists of the review of the design and development plan; the product specification; its functions, size, material, packaging, and production concept; schedule and implementation team.

A cross-functional team will be set up to audit the concept, assess device feasibility, and implement the design plan. The team will consist of the principal experts in R&D, quality assurance, production, marketing, regulatory, clinical, and legal entities.

In terms of specific activities, the design requirements plan, product requirement specification, production concept, project plan, risk management plan, clinical evaluation concept and post-marketing clinical follow up (PMCF), business registration plan requirements, and personnel assurance requirements will be reviewed.

At this stage, a Cost Benefit Analysis - CBA method will be elaborated so that it is clear what costs and especially the benefits, which can often be of a qualitative nature, can be expected with each decision and how they will be translated into financial statements.

18.3 Design and Development

After the activities performed in Phase 2, the product will be ready for the conversion—from concept to development.

During this stage, a prototype will be developed and the verification & validation tests before and after the design freeze Phases III and IV of our device will be performed. The verification and validation studies including their methods of documentation will be checked. The proper documentation is a must from a regulatory perspective because all scientific studies must be reproducible. The patent review process will also persists in this stage.

The reimbursement policy of our product will be set in this phase, because reimbursement codes and part numbers are assigned to the new device.

In terms of specific activities during this phase:

- Product design, design verification, and validation (determination of the tests to be carried out before and after the design freeze).
- Regulatory—verification of the protection of the technology, and possibly specifications of accompanying documentation.

The activities connected with the development are as follows:

- Purchase and validation strategy (technical solutions to fulfil customer requirements, specification of all key parameters' specifications, design of production technologies, materials design, supplier decisions).

- Regulatory (post market clinical follow up (PMCF) plan, post-performance qualification, clinical evaluation plan).
- Risk management design failure mode and effects analysis (dFMEA), update advanced failure modes and effects analysis (aFMEA).
- Technical specifications, block diagram, electric diagram, detailed design hardware (HW), software (SW), mechanical design, and prototype.
- Testing – conformity assessment with market standards
- 3rd party Test for independent device verification and validation

18.4 Verification and Validation

Phase IV will be characterized by the creation of formal design prints, final product verification and validation, sales launch preparation, and regulatory approval. Most of the steps from Phase III will continue till completion. Material specifications, packaging drawings, and marking and labelling specifications are finalized, and several sales and marketing activities occur prior to the launch of the new device. In addition, all of the electrical safety and Electromagnetic Compatibility (EMC) tests are to be finalised here.

The conformity assessment procedures will be divisible to modules related to the product design phase and the manufacturing phase, and the product will be generally assessed in both of these phases. The assessment subtly starts in Phase II.

18.5 Production

In the production phase of the device, it will be essential to verify the status of all the activities carried out so far. These will be most important for areas of risk; the dFMEA update, the aFMEA update, a design verification report, and a design validation report. Furthermore, in the regulatory field, a review of accompanying documentation, acceptance of accompanying documentation, and application for the CE and FDA marking will be carried out.

At the end of this phase, it will be verified that the product fulfils the customer requirements, regulators, and Intellectual Property Rights - IPR and is ready for the release on the market. Additionally, the application for the CE and FDA marking will be filed. Once awarded, the mark will be sent to the national authorities and the national administration bodies that register these types of MDs. The application for the conformity assessment will also be submitted.

An iterative economic evaluation alongside phase I and II clinical research will be implemented to provide information about market trial design, market access, and pricing.

18.6 Market Device Deployment

As part of the last step of the product deployment, the marketing objectives set out in the business plans will be monitored with market launches. The post-market surveillance (PMS) and post-market clinical follow-up (PMCF) studies will be made available. Terrain and production data will be collected and evaluated. Feedback from physicians and a vigilance system will be already set, that is, follow-up and reporting of adverse events and the post-marketing follow-up process, which should regulate clinical evaluation and risk analysis and improve and optimize the product.

19 Economic Evaluation of Development of heamoSAVE

19.1 Cost Overview:

Phase	Type of Costs
Initiation	Wages
Concept Review	Wages
Design and development	Registration Costs Wages Leasing Work Space Material for prototypes Procurement - In-house Fabrication Equipment Software Licences (Autodesk, Webex, etc.) IRB process Research participant Recruitment Electrical safety (test costs in the accredited testing facility) Biological evaluation Setting Up in house laboratory for Verification and Validation Technical Auditor – 3 rd Party testing Data Analysis Filing Patents Publishing Data
Verification and validation	Wages Conformity assessment for FDA, EU, ISO
Production	Wages Material Output control (electrical MD—production of own tester, for mechanical MD—preparation and production of own test system)
Market device deployment	Wage per hour Fee for patent filing (patent application—national, African, European, worldwide)
TOTAL ESTIMATED COST USD 350,000	

19.2 Breakeven Analysis

Required Seed Fund: \$150, 000 USD (est. for Phase I – III)

Required Series A Fund: \$200, 000 USD (est. for Phase III - V)

Break Even Strategy: Distribute the total cost of device development and launching costs over the first fifty thousand Units. The price cap from the initial user requirements screening is \$25.

Sales Target to break even: 50, 000 Units sold over four years. Therefore for each unit sold, we would use \$7 to recover funder's investment and plough back \$18 for company operations.

20 Business Canvas

Key Partners ● Patent holders ● Manufacturing Companies ● Venture Capitalists ● Health Government Agencies ● Educational Institutions ● National/ Regional Medical & pharmaceutical Distributors	Key Activities ● Initiation ● Concept Verification ● Design & Development ● IPRs attainment ● Verification & Validation ● Production ● Market Launch into pilot market	Value Proposition The heamoSAVE is a self-contained, dual pump mechanically/electrically powered system for intraoperative whole blood salvage device. ● WBT is associated with recognised benefits for patients: Trauma patients gain faster haemostasis, reduces exposure to allogeneic blood and therefore reduces exposure to the risks associated with allogeneic blood transfusions (e.g. Incorrect Blood Component Transfused, Lower infection rates and shorter hospital stays when compared to patients who receive allogeneic blood. ● Disposable kits cost less than a unit of allogeneic red blood cells and can process very large volumes of blood.	Customer Relationships ● Business to Customer through direct sale forces ● Business to Business via distributor partnerships	Customer Segments Segmentation by: ● Product ● End User ● Geographical Region
	Key Resources ● Seed & Series A funding ● Regulatory Consultants ● Market Consultants ● Clinical Consultants ● Engineering Consultants ● Manufacturing Consultants		Channels ● Health Education Centres ● Teaching Hospitals ● Existing distributor network for pharmaceuticals and MDs ● Governmental Agencies	
Cost Structure (per unit) PROFIT, OPERATIONS, MARKETING, COST OF PRODUCTION 6.00% 16.0% 12.0% 66%			Revenue Streams ● Direct Sales ● Crowd Source Funding	

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22 Appendices

22.1 Appendix 1 - User Requirement Survey

Occupation/position: _____

Please circle one number for each requirement and circle your top 5 requirements and cross-out your 5 least important

1 = Very important (a critical requirement; required for operation)

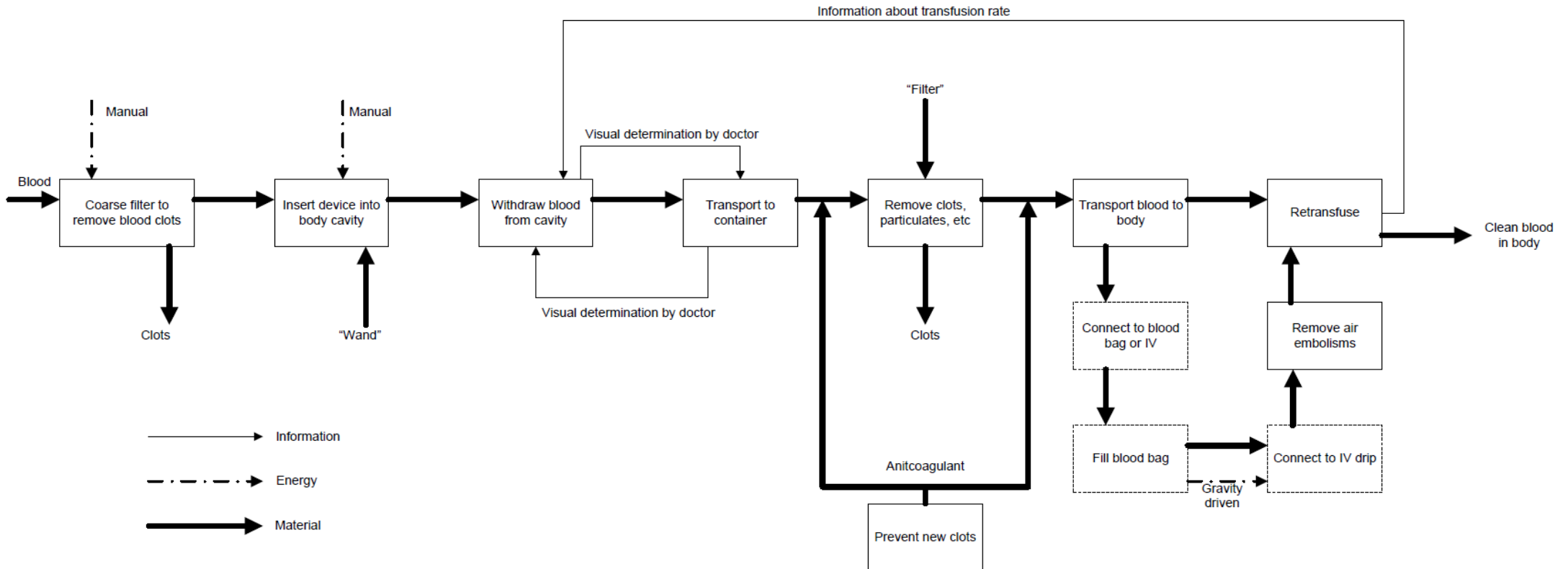
3 = Important (required eventually but could wait until a later release if necessary)

9 = somewhat important (would be nice to have someday if resources permit)

Device Requirement	Very Important	Important	Somewhat Important
Removes particulates and blood clots	1	3	9
Minimizes contamination from environment	1	3	9
Minimizes risk of cross contamination between patients	1	3	9
Can be used in any clean abdominal surgery	1	3	9
Prevents air embolisms	1	3	9
Device is low maintenance	1	3	9
Doesn't require user to use their hands during suction	1	3	9
Alerts user when malfunctioning	1	3	9
Durable and long lasting	1	3	9
Easy to operate by any staff in surgical setting	1	3	9
Device is low cost	1	3	9
Connects to existing blood transfusion kit	1	3	9
Can contain large amounts of blood loss	1	3	9
Measures amount transfused to patient	1	3	9
Quick transition to backup power	1	3	9
Main power source is electrical	1	3	9
Device can be operated quickly	1	3	9
Device is portable	1	3	9
Device is small	1	3	9
Can change transfusion rate	1	3	9
Measures amount of blood lost by patient	1	3	9
Backup power source is mechanical	1	3	9
Device is quiet	1	3	9

Do you have any additional requirements? (Please rank them)

22.2 Appendix 2 - Functional Deposition Diagram



22.3 Appendix 3 - Concept Generation

22.3.1 Siphon powered system

Pros	Cons
Portable	Small Scale
Doesn't require External Energy	Air Embolisms
Wide Scope	Must be fully submerged
	Need flexible material/not autoclave-able
	Squirt back out

22.3.2 Large syringe

Pros	Cons
Low maintenance/ Less removable parts	Heavy to hold when filled with blood
Autoclavable	Force to pull plunger
Small/portable/durable	May require more than one person
Doesn't require pump	Manufacturing Tolerance
Scope of location	Potential smaller SA on filter
Cost	Speed of removal

22.3.3 Foot pedal powered system

Pros	Cons
Modular (two modes)	High Maintenance
Handle Large Volumes	Lots of parts
Generate High Flow Rate	Expensive/manufacturing
Control Each Component with wheels	
Electrical pump can be added	

22.4 Appendix 4 - Analysis with MATLAB

22.4.1 Bernoulli Analysis

% Bernoulli Analysis

d = 1060; % density of blood (kg/m³)

g = 9.81; % gravity (m/s²)

% ----- Barrel -----

l2=linspace(0.08,0.27); %height of barrel

v2=linspace(0,0.5); %possible velocities

for i=1:length(l2)

for j=1:length(v2)

p2(i,j)= -0.00750061683*(-0.5*(d*(v2(j)^2))-(d*g*l2(i))); % mm Hg

end

end

surf(l2,v2,p2)

xlabel('Height of Barrel (m)')

ylabel('Fluid velocity in Barrel (m/s)')

zlabel('Pressure in Barrel (mmHg)')

title('Pressure Array in Barrel')

%----- Suction Tube -----

% Point in reservoir to top of suction tube:

% l1 = heights of suction tube

% v1 = velocities in the first tube

l1=linspace(0.03,.07);

v1=linspace(0,3.125);

for i=1:length(l1)

```

for j=1:length(v1)
p1(i,j)= -0.00750061683*(-0.5*(d*(v1(j)^2))-(d*g*l1(i))); % mm Hg
end
end
surf(l1,v1,p1)
xlabel('Height of Suction Tube (m)')
ylabel('Fluid velocity in Suction Tube(m/s)')
zlabel('Pressure in Suction Tube (Pa)')
title('Pressure Array in Suction Tube')

%----- IV Tubing -----
v3=linspace(0,122);
for i=1:length(v3)
for j=1:length(v2)
p3(i,j) = -0.00750061683*( p2(i,j) + 0.5*d*((v2(j)^2)-(v3(i)^2))); %mmHg
end
end
surf(v2,v3,p3)
xlabel('Fluid Velocity in Barrel (m/s)')
ylabel('Fluid velocity in IV Tube (m/s)')
zlabel('Pressure in IV Tube (mmHg)')
title('Pressure Array in IV Tube')
p21 = linspace(0,6000);
p31 = 0.00750061683*(p21+(0.5*d*((v2.^2)-1.49))); %mmHg
plot(v2,p31)
xlabel('Velocity in Barrel (m/s)')
ylabel('Pressure in IV Tubing (mmHg)')
title('Pressure in IV Tubing')

```

22.4.2 Force on Plunger Analysis

```

%----- Force Analysis -----
density=1060; %density of blood (kg/m^3)
r11=.005; h11=.03;
r21=.02; h21=.05;
r12=.0125; h12=.05;
r22=.035; h22=.125;92
r13=.02; h13=.07;
r23=.05; h23=.2;
F=10;
%----- First Phase -----
t=linspace(0,5);
V1 = sqrt((((2*F)/(density*pi*(r21^2))).*log(t))+ ...
(4.605*F/(density*pi*(r21.^2))));
V2 = sqrt((((2*F)/(density*pi*(r22^2))).*log(t))+ ...
(4.605*F/(density*pi*(r22.^2))));
V3 = sqrt((((2*F)/(density*pi*(r23^2))).*log(t))+ ...
(4.605*F/(density*pi*(r23.^2))));
plot(t,V1,t,V2,t,V3)
xlabel('Time (s)')
ylabel('Velocity of Plunger (m/s)')
title('Velocity in First Phase of Filling')
legend('Value1','Value2','Value3')
%----- Second Phase -----
dV1=@(t,V) F/((density*pi*(r11^2)*h11)+(density*pi*(r21^2).*V.*t));
[t,V4]=ode45(dV1,[0,60],2);
subplot(2,2,1)
plot(t,V4)
xlabel('Time (s)')

```

```

ylabel('Velocity of Plunger (m/s)')
title('Velocity in Second Phase of Filling- Value1')
dV2=@(t,V) F/((density*pi*(r12^2)*h12)+(density*pi*(r22^2).*V.*t));
[t,V5]=ode45(dV2,[0,60],2);
subplot(2,2,2)
plot(t,V5)
xlabel('Time (s)')
ylabel('Velocity of Plunger (m/s)')
title('Velocity in Second Phase of Filling- Value2')
dV3=@(t,V) F/((density*pi*(r13^2)*h13)+(density*pi*(r23^2).*V.*t));
[t,V6]=ode45(dV3,[0,60],2);
subplot(2,2,3)
plot(t,V6)
xlabel('Time (s)')
ylabel('Velocity of Plunger (m/s)')
title('Velocity in Second Phase of Filling- Value3')

```

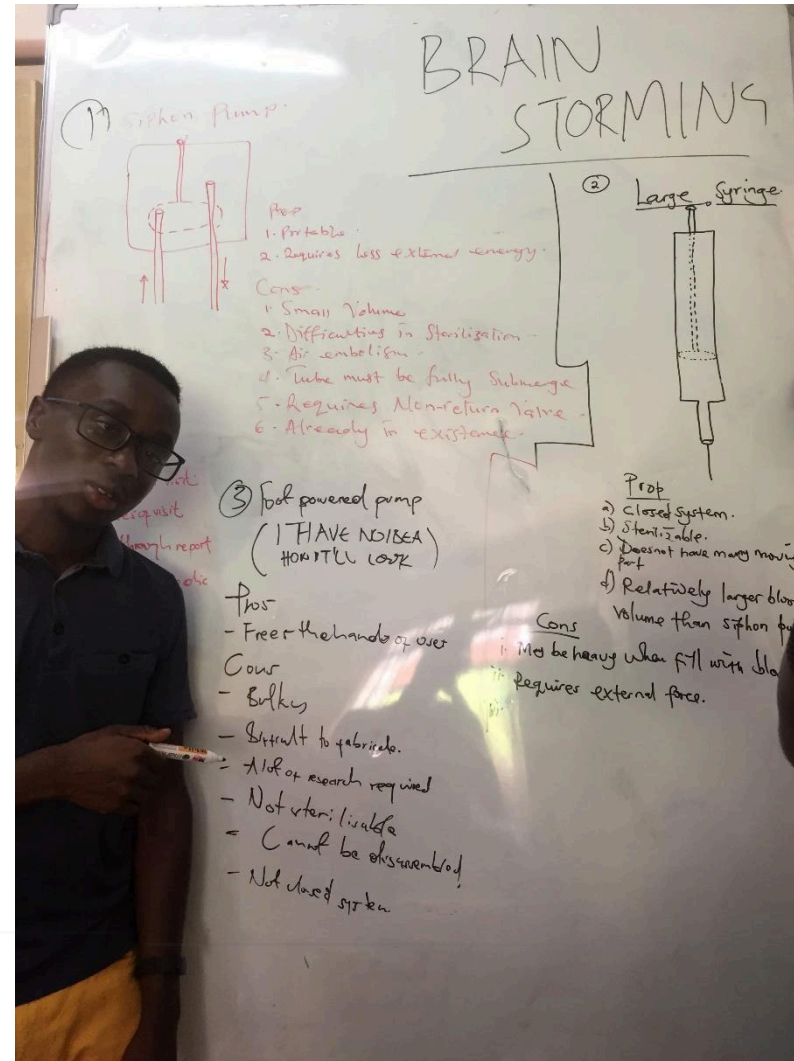
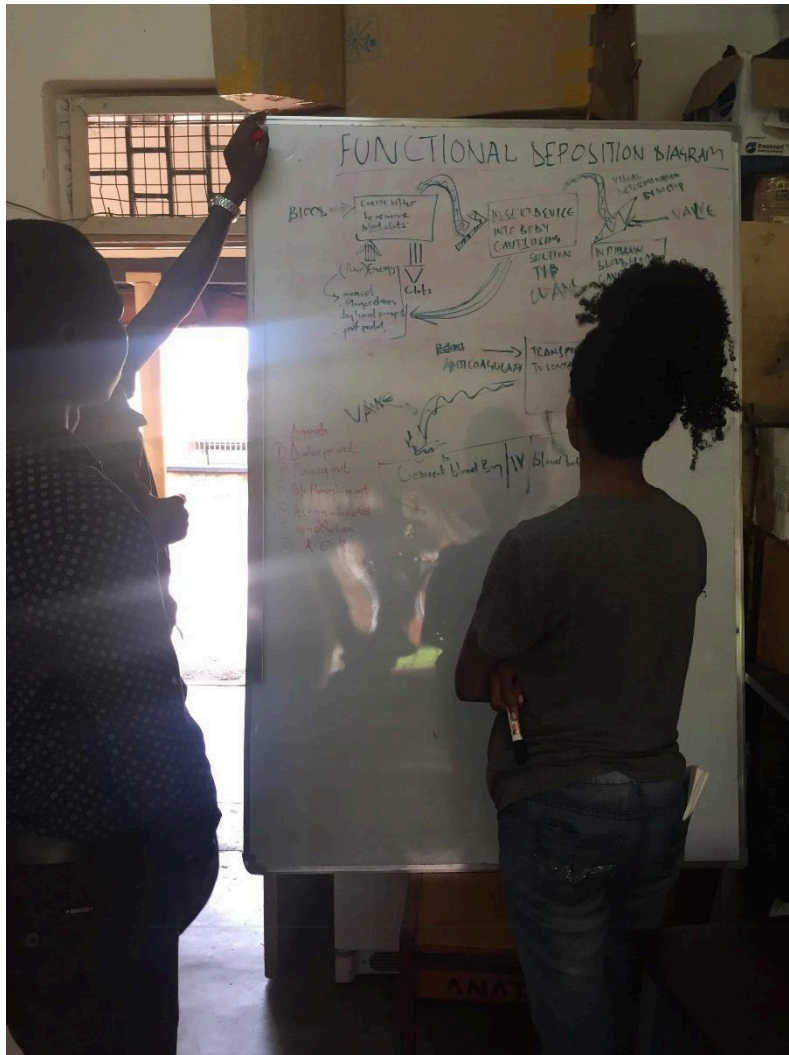
22.4.3 Design Dimension Analysis

```

%----- Specific Dimensions Analysis -----
d=1060;
F=10;
r1=0.007493;
r2=0.028575;
r3=0.006604;
h1=0.05588;
h2=0.18542;
g=9.81;
%----- Barrel Pressure -----
v2=linspace(0,0.5);
p2 = -0.00750061683*((-0.5*d*(v2.^2))-(d*g*h2));
plot(v2,p2)
xlabel('Velocity in Barrel')
ylabel('Pressure in Barrel (mmHg)')
title('Pressures in Barrel')
%----- Suction Tip Pressure -----
a1 = pi*(r1^2);
a2 = pi*(r2^2);
v1 =(a2/a1).*v2;
p1 = -0.0075006168*(-0.5*d*(v1.^2)-(d*g*h1));
plot(v1,p1)
xlabel('Velocity in Suction Tip')
ylabel('Pressure in Suction Tip (mmHg)')
title('Pressures in Suction Tip')
%----- IV Tubing Pressure -----
a3=pi*(r3^2);
p21=133.322368.*p2;
v3=(a2/a3).*v2;
p3 = -0.0075006168*(p21+0.5*d*((v2.^2)-(v3.^2)));
plot(v3,p3)
xlabel('Velocity in IV Tubing')
ylabel('Pressure in IV Tubing(mmHg)')
title('Pressures in IV Tubing')

```

22.5 Appendix 5 - Brainstorming Pictorial



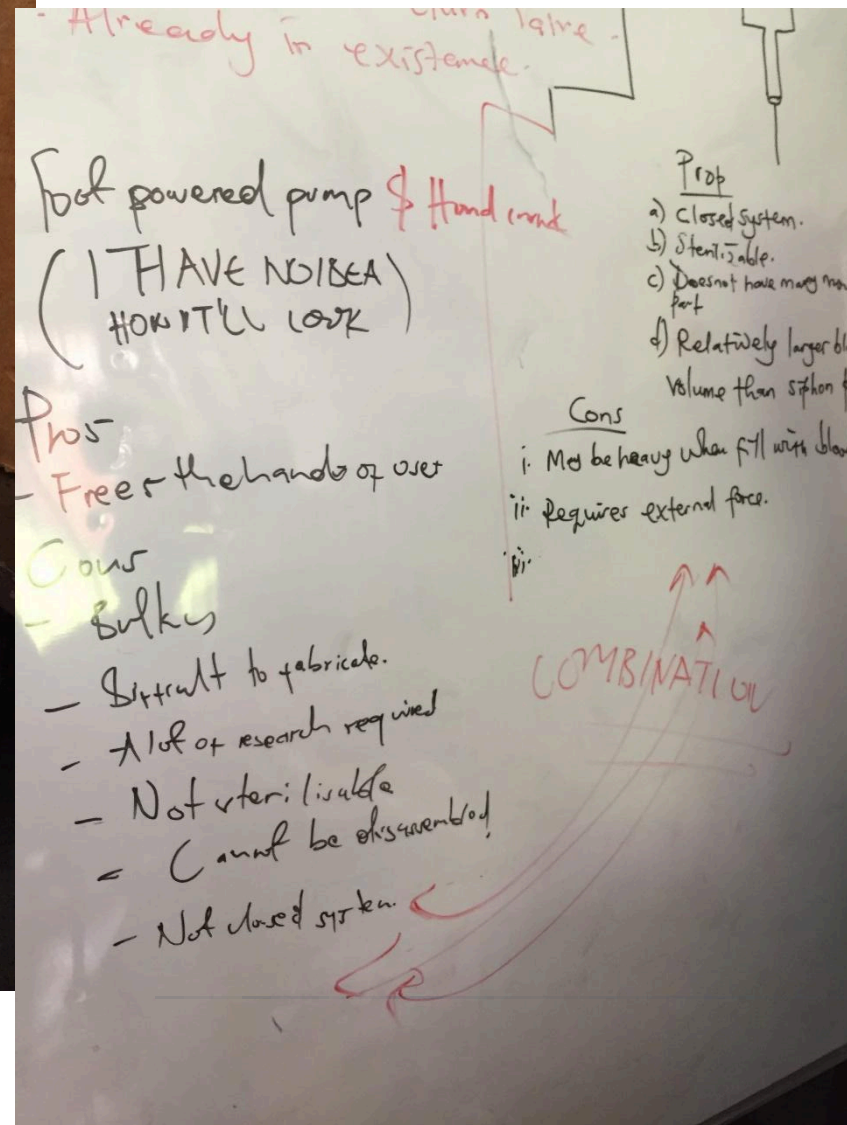
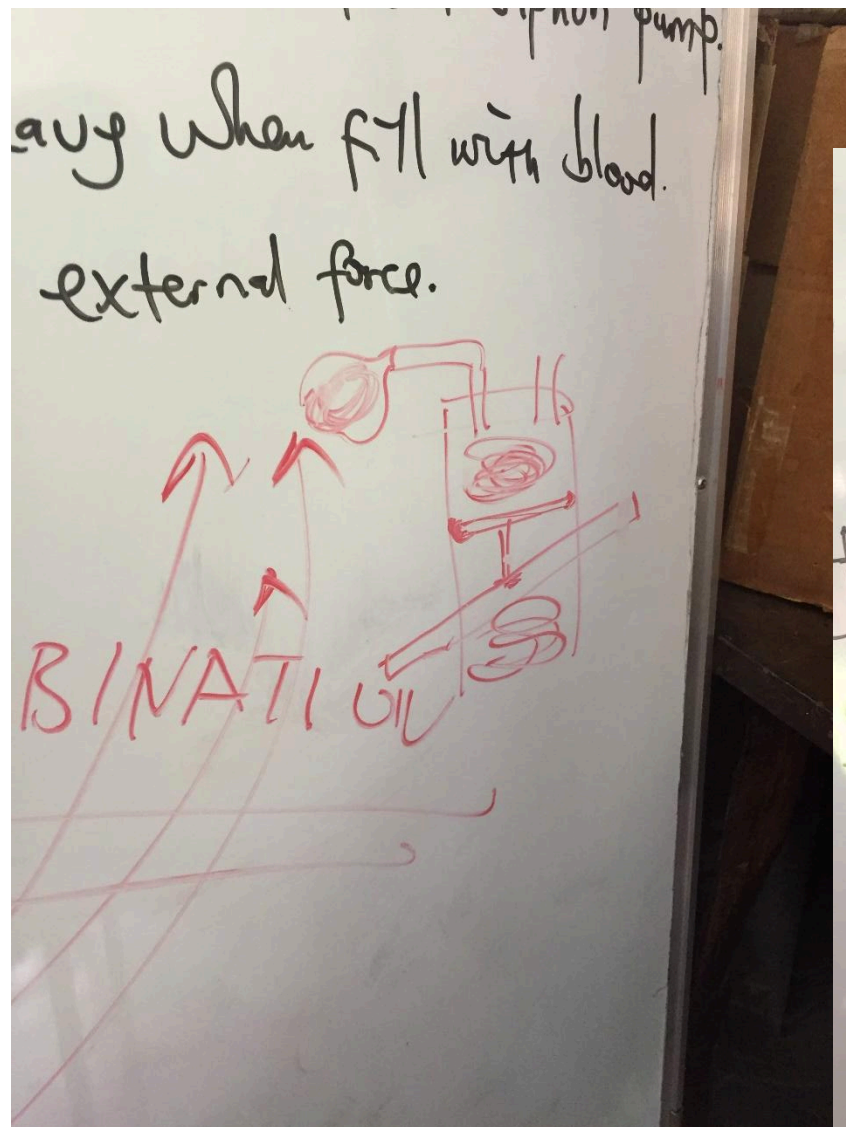
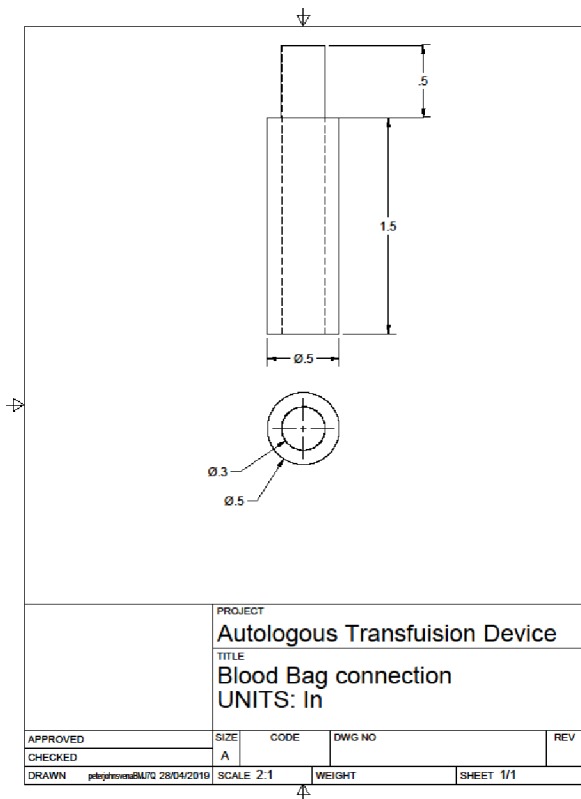
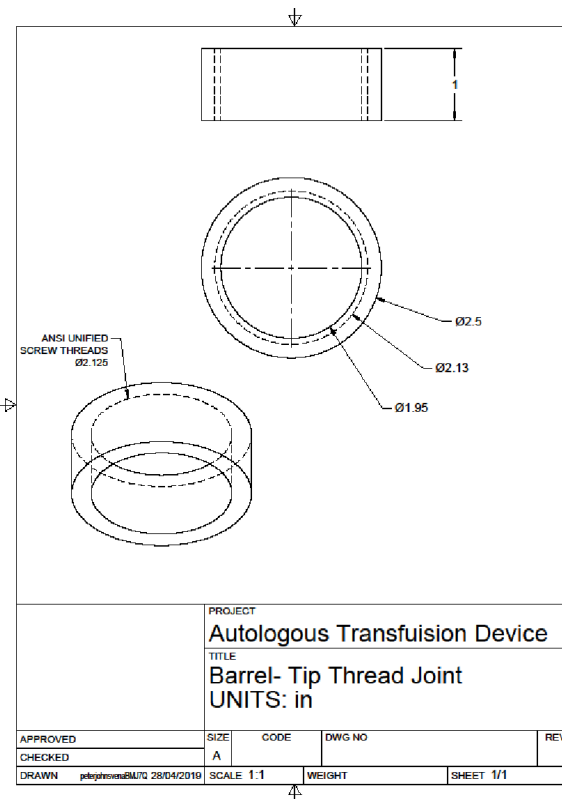
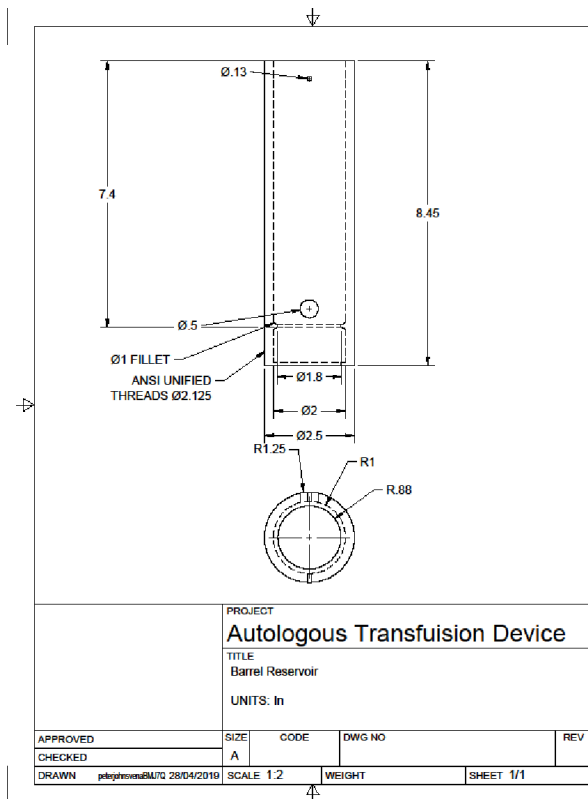
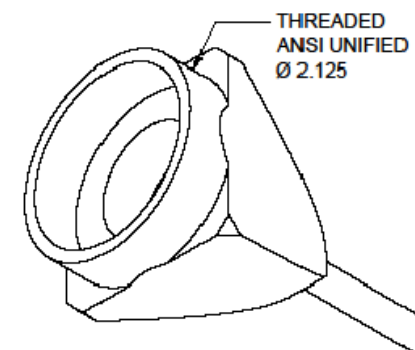
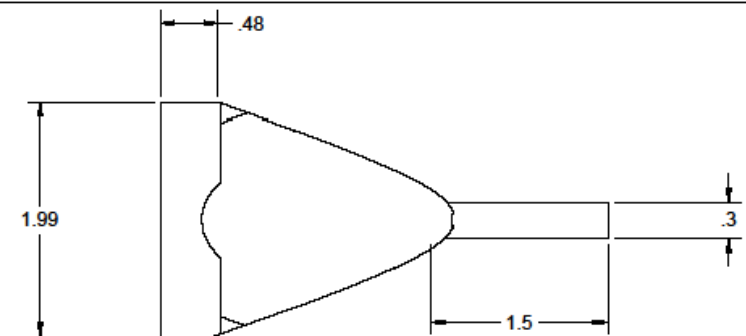
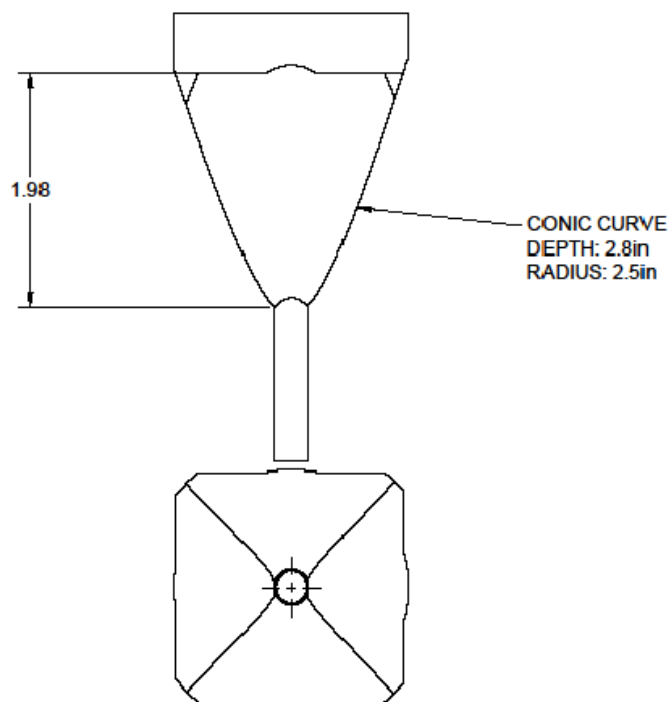
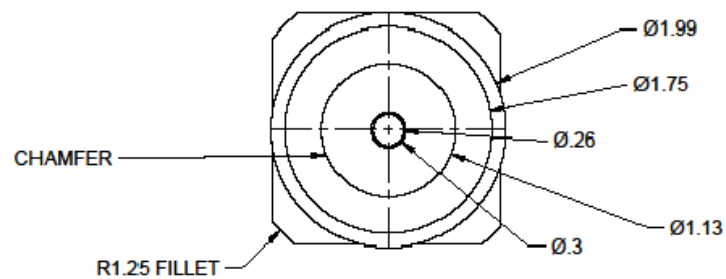


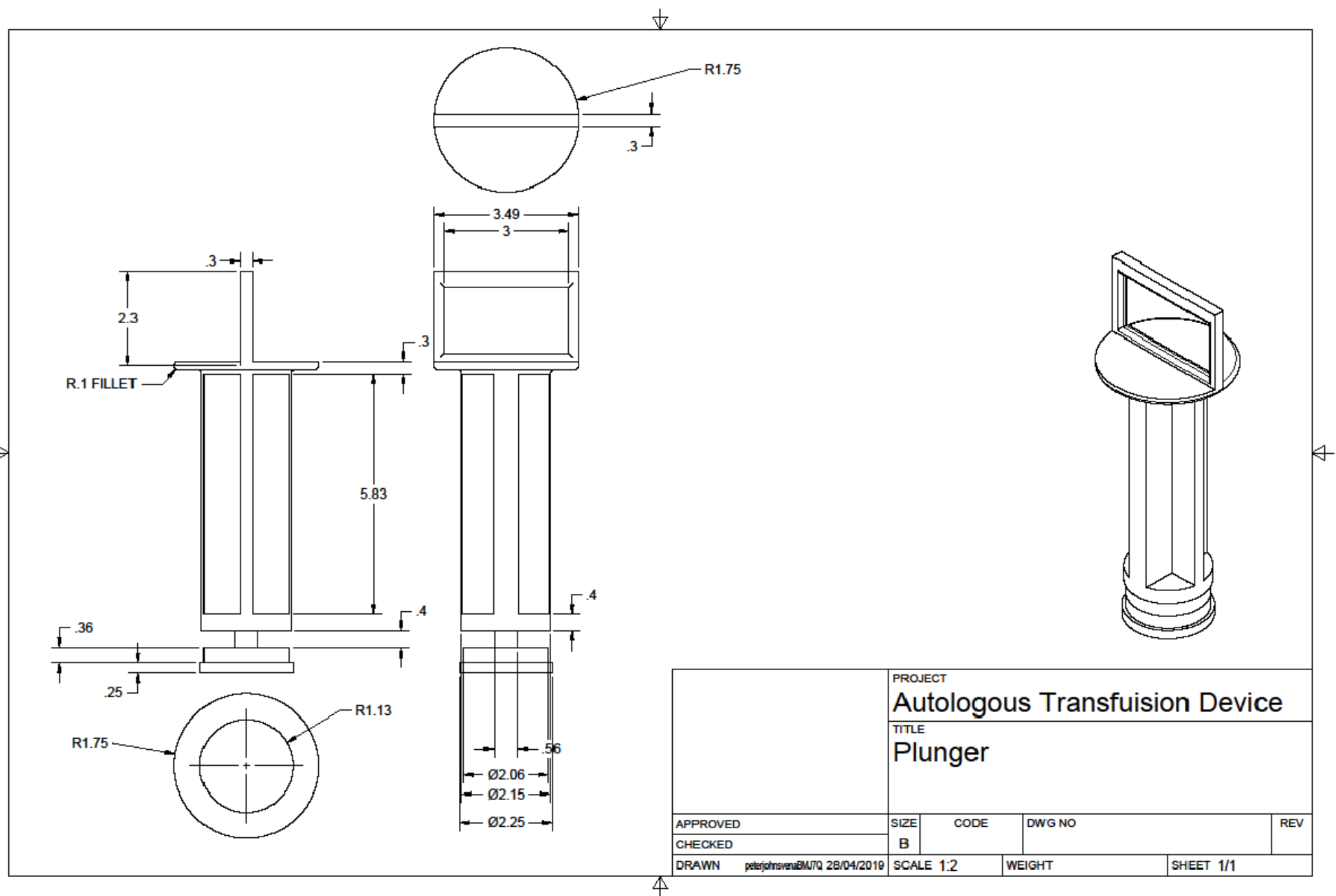
Figure 24 Brain storming about a fluid powered foot pedal

22.6 Appendix 6 - Engineering Drawings

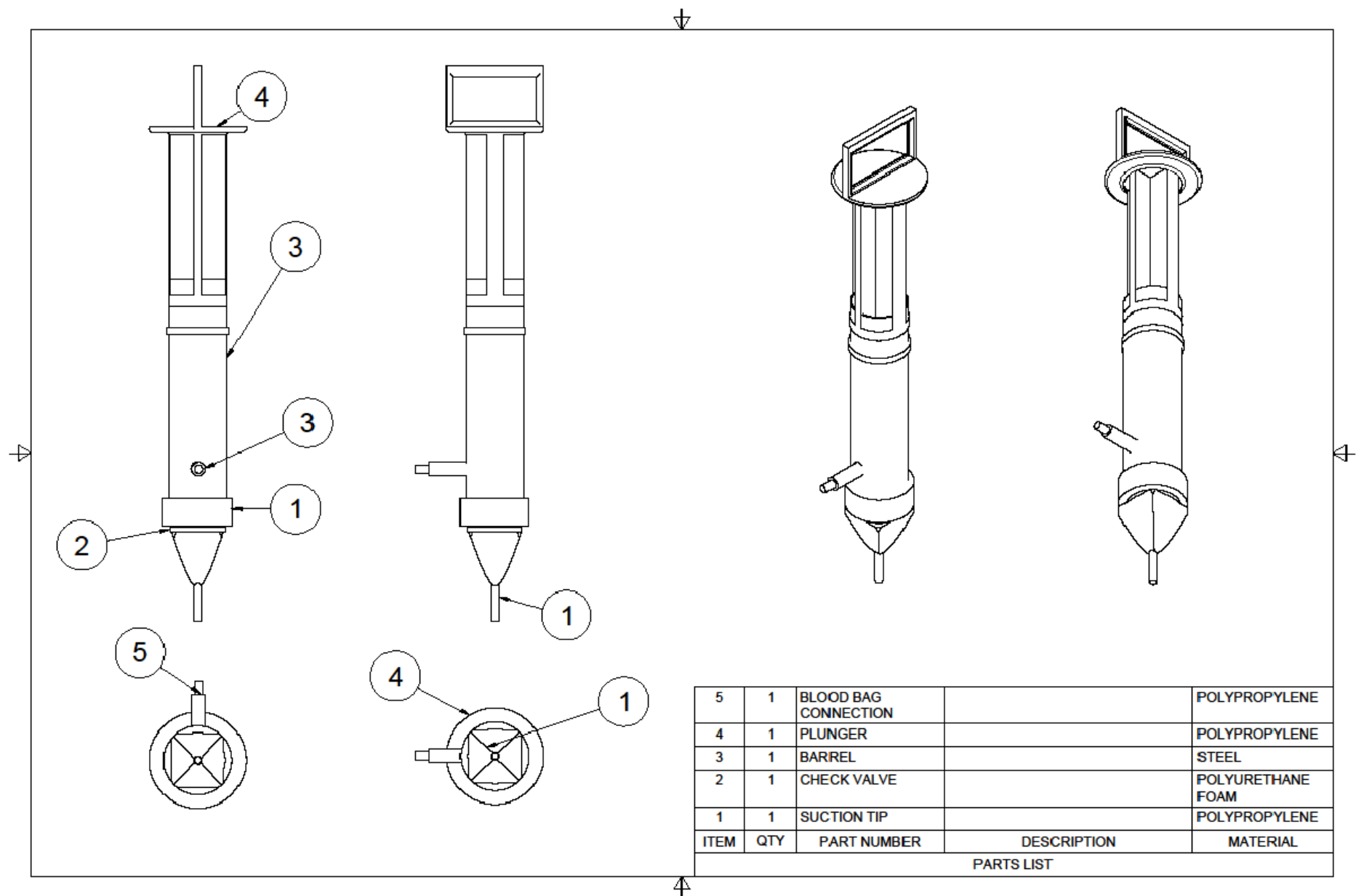


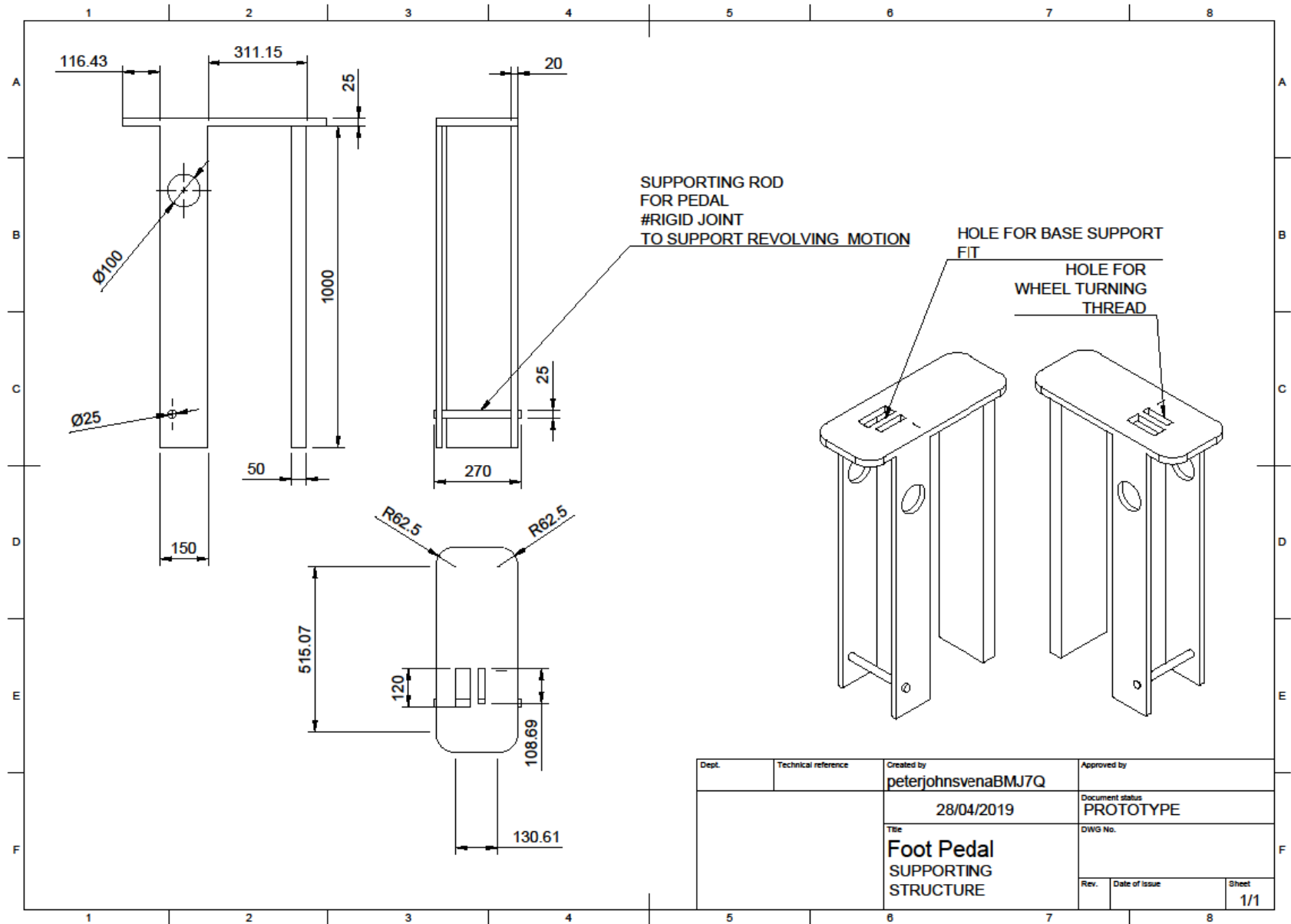


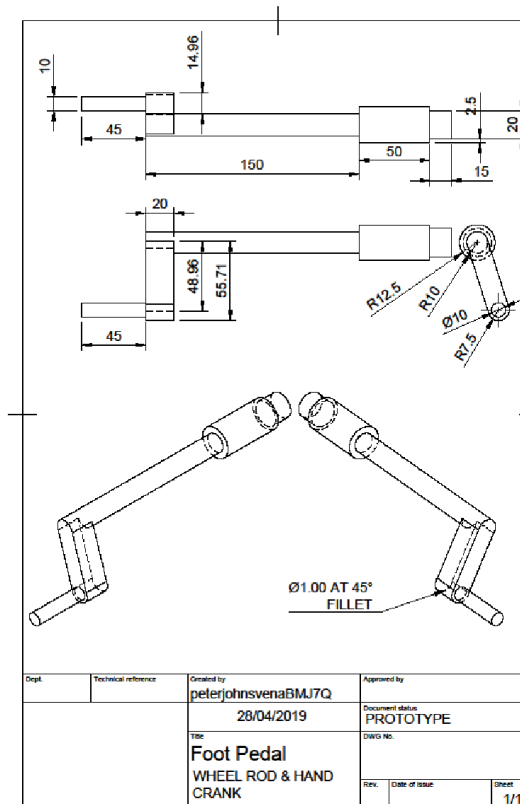
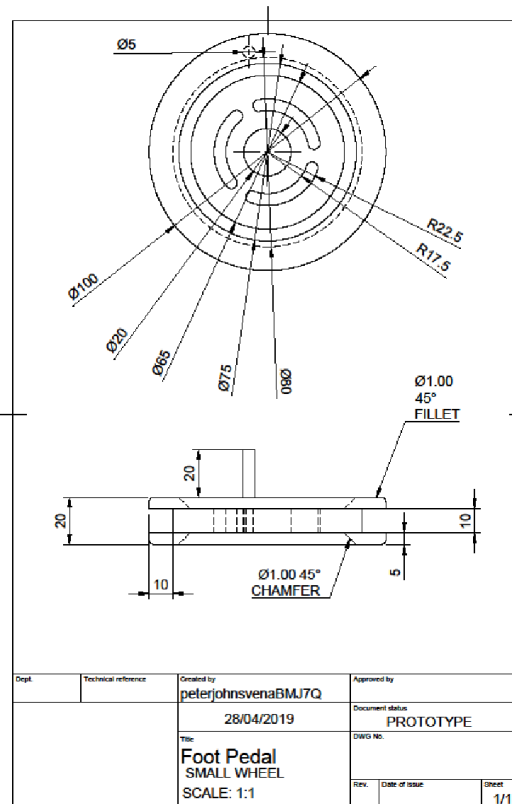
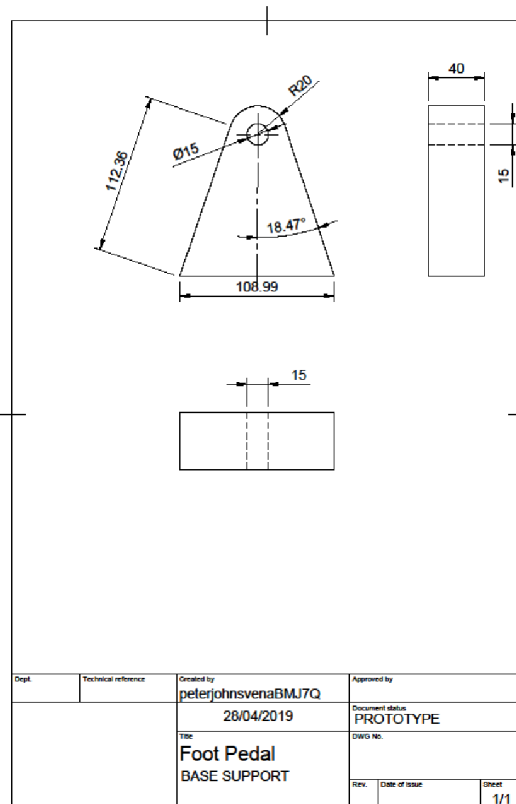
		PROJECT		
		Autologous Transfusion Device		
		TITLE		
		Suction Tip		
APPROVED	SIZE	CODE	DWG NO	REV
CHECKED	B			
DRAWN	peterjohnsenaBM/7Q 28/04/2019	SCALE 1:1	WEIGHT	SHEET 1/1

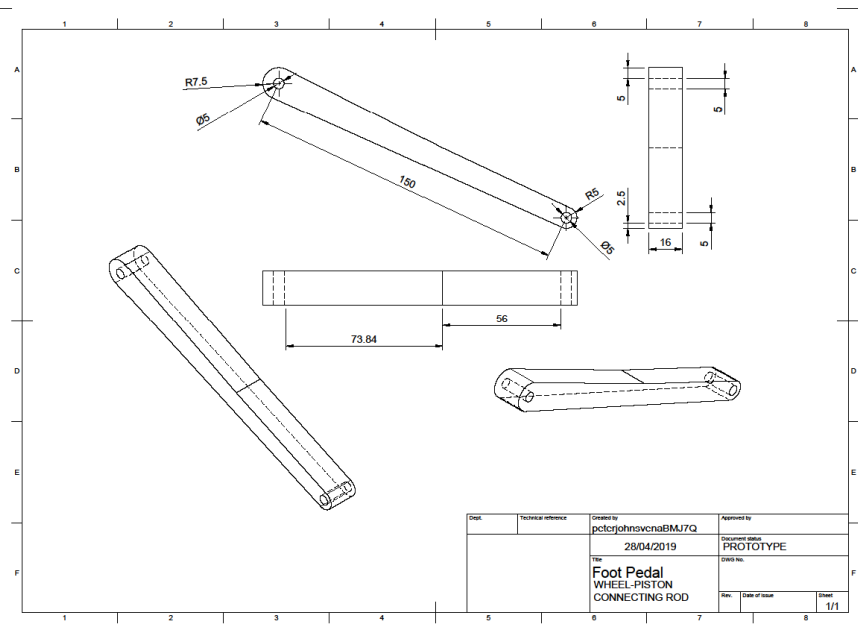
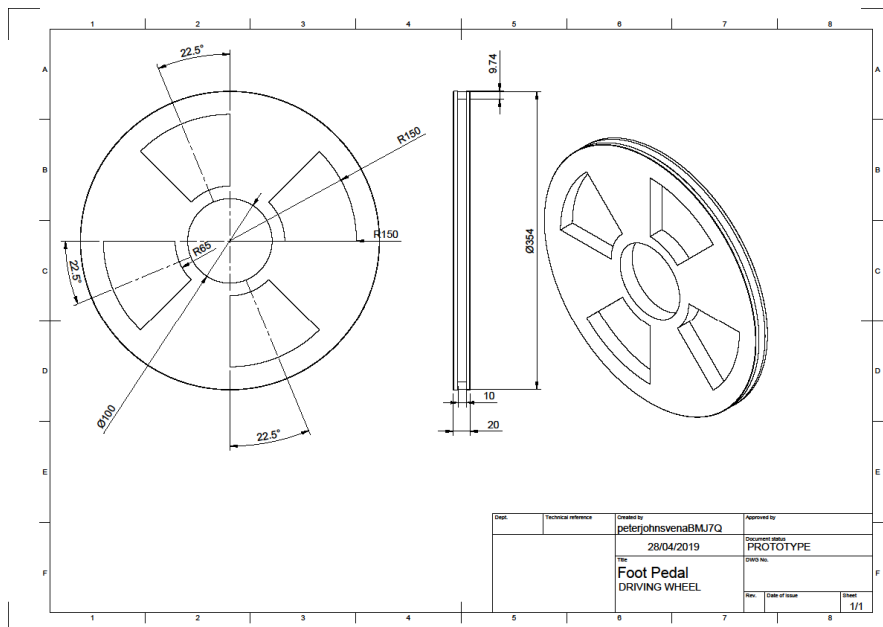


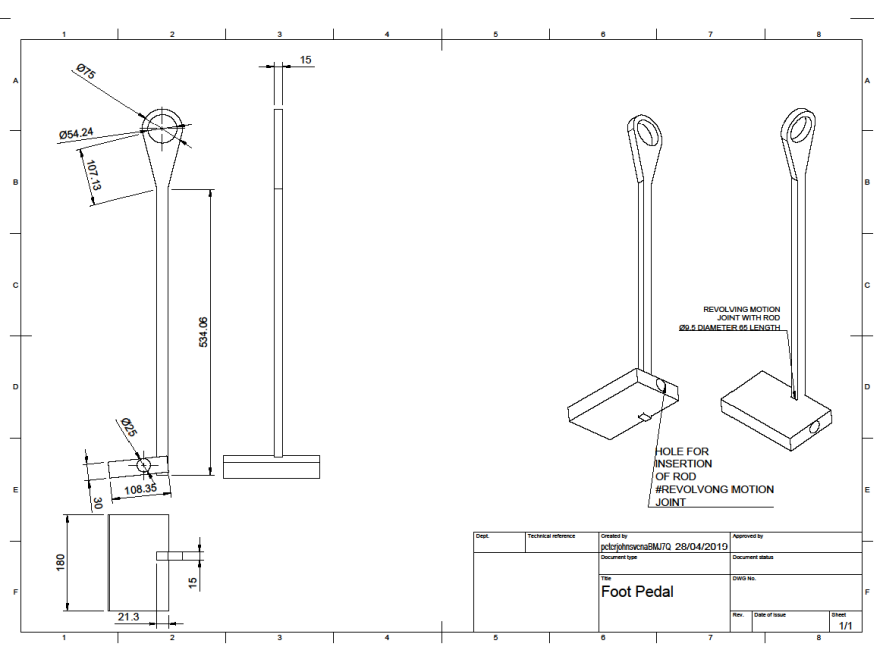
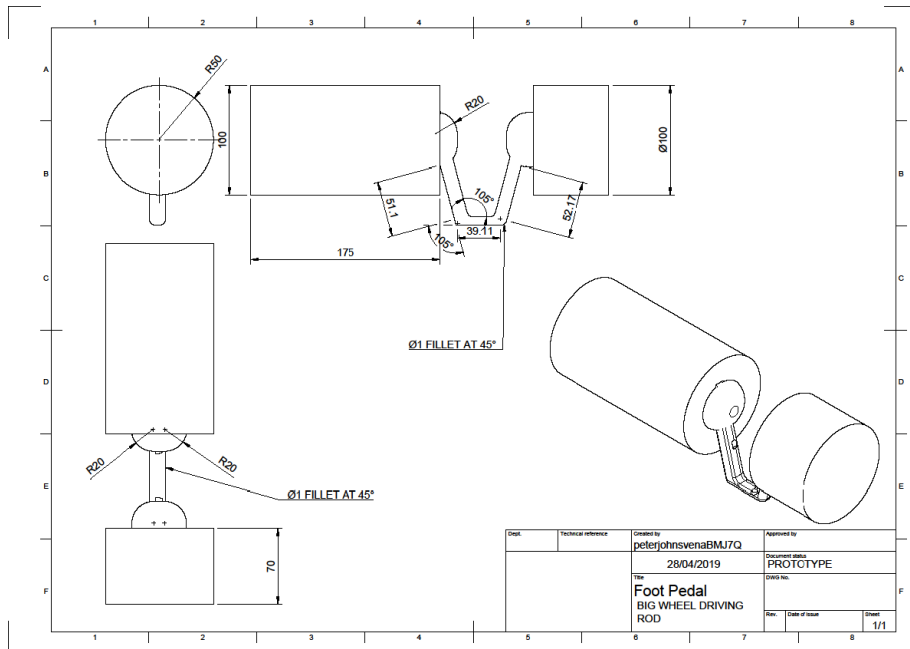
		PROJECT			
		Autologous Transfusion Device			
		TITLE			
		Plunger			
APPROVED	SIZE	CODE	DWG NO	REV	
CHECKED	B				
DRAWN	peterjohnsenaBM/7Q 28/04/2019	SCALE 1:2	WEIGHT	SHEET 1/1	











22.7 Appendix 7– Environmental Toxicity Analysis

Environmental Toxicity analysis was carried out since device was meant to be disposable.

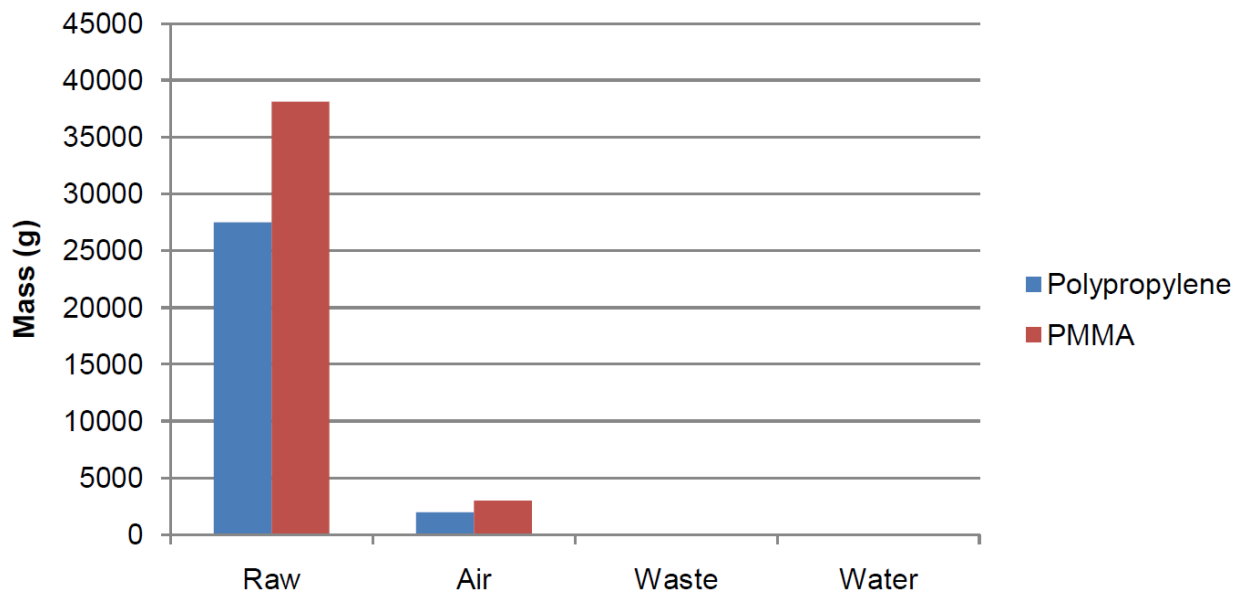


Figure 25 Excel graph of total emissions of intended material

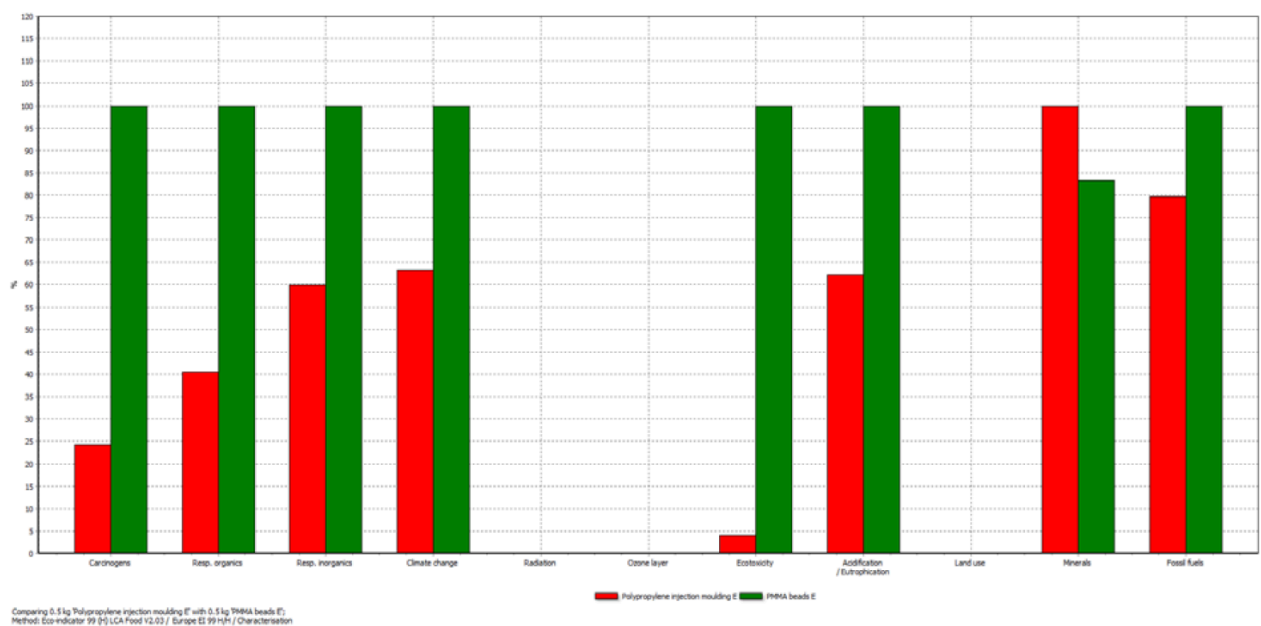


Figure 26 Relative Impacts in Disaggregated Damage Categories

Red = polypropylene, Green = PMMA.

Categories from the right are: Fossil Fuels, Minerals, Land use, eutrophication, ecotoxicity, Ozone layer, radiation, radiation, climate change, respiration inorganics, respiration organics, and carcinogens.

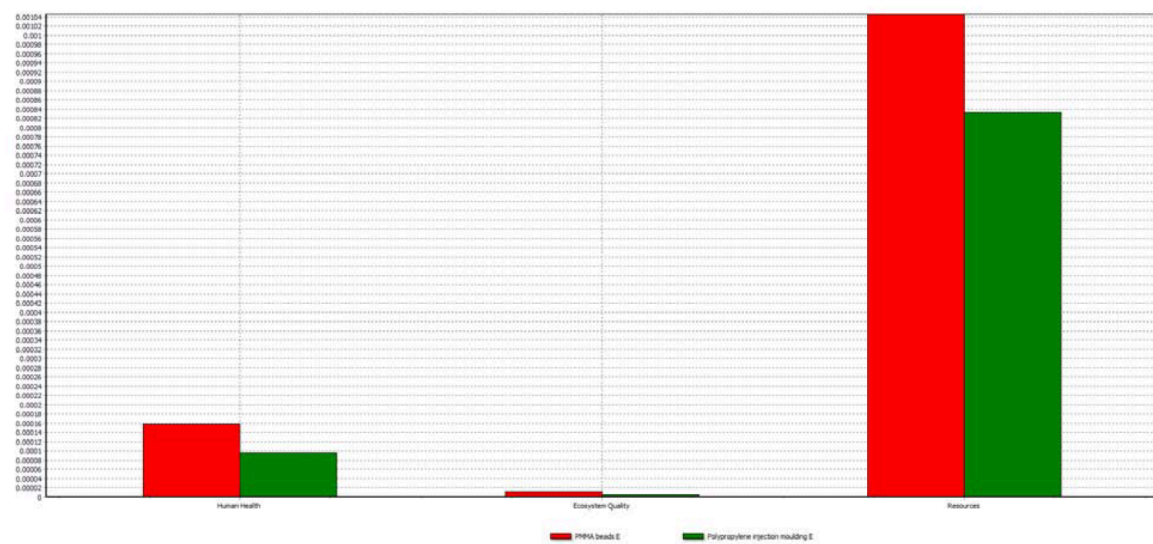


Figure 27 Normalized score in Human Health, Eco-Toxicity, and Resource Categories

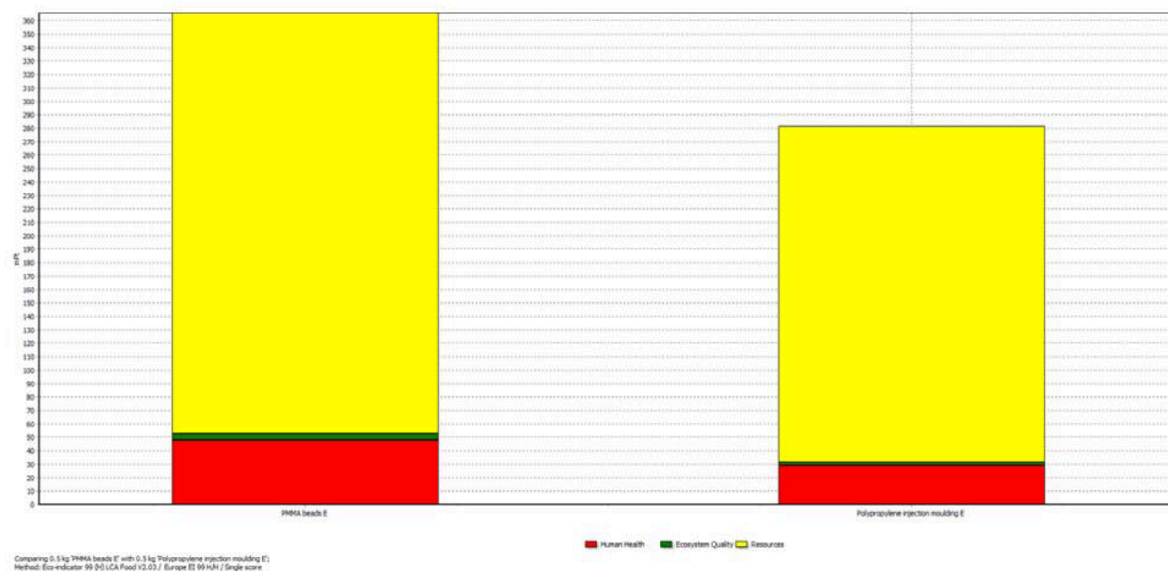


Figure 28 Single Score Comparison in "Points"

22.8 Appendix 8 – Human Factors Testing

	DESIRABILITY												
ID#	better option	operation & handling	require training	new procedures	comfort of design	size and weight	avg	MIN	Q1	MEDIAN	Q3	MAX	WHISKER TOP
R001	3	4	3	3	5	5	3.83	3	3	3.5	5	5	0
R002	4	4	2	3	4	3	3.33	2	2.75	3.5	4	4	0
R003	5	4	2	4	3	3	3.50	2	2.75	3.5	4.25	5	0.75
R004	3	3	1	4	4	4	3.17	1	2.5	3.5	4	4	0
R005	4	3	2	5	4	4	3.67	2	2.75	4	4.25	5	0.75
R006	5	5	3	3	5	5	4.33	3	3	5	5	5	0
R007	2	4	1	3	3	4	2.83	1	1.75	3	4	4	0
R008	4	3	2	4	4	3	3.33	2	2.75	3.5	4	4	0
R009	2	4	2	2	5	4	3.17	2	2	3	4.25	5	0.75
R010	4	4	0	1	5	5	3.17	0	0.75	4	5	5	0
R011	3	3	0	5	1	3	2.50	0	0.75	3	3.5	5	
R012	4	4	1	2	4	3	3.00	1	1.75	3.5	4	4	
R013	3	5	1	4	3	4	3.33	1	2.5	3.5	4.25	5	
R014	3	3	0	2	1	2	1.83	0	0.75	2	3	3	
R015	3	4	0	4	2	1	2.33	0	0.75	2.5	4	4	
R016	5	5	3	3	2	5	3.83	2	2.75	4	5	5	
R017	5	2	2	4	3	2	3.00	2	2	2.5	4.25	5	
R018	5	4	1	3	3	4	3.33	1	2.5	3.5	4.25	5	

22.9 Appendix 9 - Filter Tests

Aliquot Number	Total Volume Filtered mL	Amount of Residue, Test 1	Amount of Residue, Test 2	% of water recovered , Test 1	% of water recovered , Test 2	Max pressure recorded, after test B (mmHg)
1	30	2	1	99	98	0.13455
2	30	1	0	95	90	0.134591
3	30	0	0	90	85	0.136435

22.10 Appendix 10 – Reliability Tests

Occurrence of Failure									Processing Time (s)				
	Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3	Trial 4	Trial 5	Trial 6	Trial 7	Trial 8	Trial 9	Trial 10
Trained Group													
R1	Pass	Pass	Pass	65	59	40	35	34	35	31	30	29	23
R2	Pass	Pass	Pass	55	50	43	33	33	33	27	33	25	25
R3	Pass	Pass	Pass	54	48	46	34	28	31	34	28	28	24
R4	Failure	Pass	Pass	80	58	53							
R5	Pass	Pass	Pass	62	55	48							
R6	Pass	Pass	Pass	67	57	49							
R7	Pass	Pass	Pass	70	50	50							
R8	Pass	Pass	Pass	74	53	42							
R9	Pass	Failure	Pass	65	75	44							

Figure 29 Reliability Tests Results for Trained Group

Untrained Group						
	Trial 1	Trial 2	Trial 3	Trial 1	Trial 2	Trial 3
R10	Pass	Pass	Pass	69	35	29
R11	Pass	Pass	Pass	68	33	25
R12	Pass	Pass	Failure	70	38	40
R13	Pass	Pass	Pass	75	40	31
R14	Pass	Pass	Pass	75	29	29
R15	Failure	Pass	Pass	91	31	34
R16	Failure	Pass	Pass	86	33	30
R17	Pass	Pass	Pass	73	34	33
R18	Pass	Pass	Pass	72	26	65

Figure 30 Reliability Tests Results for Untrained Group

22.11 Appendix 11 – Utility Model Application URSB

FORM 2

s 21, Reg 6(1)

THE INDUSTRIAL PROPERTY ACT 2014.

Application for a Utility Model

I/We the applicant(s) request(s) the grant of a Utility Model in respect of the following particulars—

A. PARTICULARS OF THE APPLICANT(S)¹

(a) Name _____

(b) Address _____

(c) Nationality _____

(d) Country of residence or principal place of business _____

AGENT/REPRESENTATIVE

(a) Name _____

(b) Address _____

INVENTION

Title of the invention _____

INVENTOR

The inventor is the applicant— Yes/No

If not—

¹ Data concerning each applicant must appear in this space. If this space is not sufficient put additional information on separate sheet.

Name of applicant _____

Address _____

DIVISIONAL APPLICATION²

(a) Initial Application No. _____

(b) Date of filing initial application _____

(c) International non-propriety name (INN) in case of
Pharmaceuticals _____

PRIORITY DECLARATION³

(a) Country⁴ _____

(b) Filing date _____

(c) Application No. _____

(d) IPC symbol _____

CHECK LIST

(a) This application contains the following—

- (i) request _____ sheet(s)
- (ii) description _____ sheets
- (iii) claim(s) _____ sheets
- (iv) abstract _____ sheets
- (v) drawings _____ sheets

This form is accompanied by the items checked below—

- (i) _____ power of attorney
- (ii) _____ statement specifying the basis of applicant's right to the patent
- (iii) _____ statement that certain disclosures be disregarded
- (iv) _____ priority documents (certified)
- (v) _____ English translation of earlier applications on which priority declaration is based (vi) _____ other documents (*specify*)

Drawing No. _____ is suggested to accompany the abstract for publication.

Date at _____ this _____ day of _____ 20 _____

Signed _____ applicant (s) agent) paper.

² If divisional application supply reference to the initial application and indicate whether benefit from any priority claimed for initial application is sought.

³ If priority of more than one earlier application is claimed, the data should be indicated on an additional sheet of

⁴ If earlier application is a regional or international application, indicate here the office in which and the countries for which it was filed.