Preliminary Product Design Specifications

Biomedical Engineering 300/200: Biomedical Engineering Design

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Title: VETMED: Conversion of Human COBE
Plateletpheresis Machine for Large Animal Use

Clients: Professor Sabrina Brounts, Dr. Harpeet Singh, and Dr. Andrea Pennati
Advisor: Dr. Melissa Kinney

Team Members: Aditya Ailiani - Team Leader (300), Cate Flynn - Communicator (200), Nesya Graupe - BSAC (200), Lokesh Kumaravel - BPAG (200), and Trevor Silber - BWIG (300)

Function: Plateletpheresis uses centrifugal technology to separate platelets from other donor blood components, returning other components to the donor. Our clients, Professor Sabrina Brounts and Dr. Andrea Pennati, have developed a new equine platelet therapy and would like to use plateletpheresis rather than whole blood extraction to extract platelets for further research [1]. The COBE© Spectra Apheresis System they are using costs $2000 - $2600 per use, mainly due to the expensive tubing sets that can't be reused. Our goal is to develop a system to decrease cost per use, allowing the client to reuse tubing sets or use cheaper tubing.

Client requirements:

- Replace all of the tubing in the COBE© Spectra Apheresis System by Terumo
- The operating cost should go down from $2300 a use to about $100 a use
- As a final deliverable, the client would like either a cheap set of tubing, a new tubing fabrication technique, or a new sterilization process

Design requirements:

1. Physical and Operational Characteristics

a. *Performance requirements:*

- Single Use Condition: If the tubing can be produced at a low cost, the client has specified that a single use tubing system could be adequate. In this situation, the tubing would be disposed of after every use. This approach would remove durability concerns from use to use, but there are no cost estimates at this time to decide if this is a viable approach.
- Multi Use Condition: If the tubing can be produced from a more durable material, the client has outlined that they would be satisfied with 20 to 25 uses with sterilization between uses.
- Sterilization Condition: If the original tubing is kept, the client has stated that they would be satisfied with the development and documentation of a comprehensive sterilization of the existing tubing (most likely by gas or steam). If this approach is pursued, there will need to be testing to determine the durability of the existing tubing, as it has only been used once in the past.

b. *Safety:* The product involves the transportation of animal blood, therefore standard biochemical safety regulations apply as outlined in the Laboratory Safety Guide by OSHA [2]. The original tubing is medical grade and follows regulations in place for human consumers, but animals tend to have fewer regulations, since bloodborne pathogens are less common. In order to protect the handlers of the product, the tubing must be non-permeable to restrict leakage of the blood. Biohazardous contamination is the main safety concern when working with the tubing. We may want to consider adding a biohazard indication after every use of the product until sterilization is complete.

c. *Accuracy and Reliability:* The tubing should withstand being washed and reused 40-50 times. Any malfunctions will likely put the horse in danger and therefore the tubing must

successfully collect blood from horse, transfer to apheresis machine, and return to horse every time used with no clotting, breakage, stoppage, or other difficulty.

d. *Life in Service:* The client requested tubing that can be reused at least 20 times (more reusable would be better), so the material would need to withstand either repeated steam or EtO sterilization without degrading or accumulating EtO residuals. Equine plateletpheresis has a run time of approximately 160 min, so the tubing should withstand working pressure at least that long [3].

e. *Shelf Life:* The tubing, bought or fabricated, will be created in a sterile environment and placed into a pathogen free sealed container. Nothing from the outside environment will be able to get in, meaning the tubing will stay sterilized. The tubing should be kept out of direct heat to prevent any possible deformation. Theoretically, the tubing should be able to be stored for an indefinite amount of time.

f. *Operating Environment*:

- The tubing and machine cannot be exposed to temperatures above 81° F.
- The inlet flow rate cannot be 25 mL/min or less.
- The tubing cannot be occluded or bent before use, this will damage the machine.
- Any stretching of the tubing will result in damage to the tubing itself or the machine if it has already been connected.
- Tubing must be stored in a sterile environment: outside contaminants such as hair or dirt will damage the machine or contaminate the extracted platelets.
- The tubing must be dry upon use: any excess fluid can cause an unwanted electrical response.
- The tubing should only be handled by this team in testing or the client and their approved partners when finished. [4]

g. *Ergonomics:* The plateletpheresis device will have set limits on the rate of blood draw and transfusion. Although larger animals can handle a faster draw rate, the client has asked us to keep the limits preset on the machine. The inlet pump rate will have a maximum restriction of 65 mL/min for the Dual-Needle procedure [4]. Tubing will interact with the larger animal's blood, specifically a horse. Equine blood is on average 100° F, therefore the tubing must be able to handle such temperatures [5].

h. *Size:* Tubing should be portable and, when gathered together, not larger than 2ft x 2ft. Tubing should contain a 1L bag to hold collected platelets [3]. The length of tubing required will be determined once we see the setup of the apheresis machine and proposed area where the horse will stand. The tubing should be very accessible for cleaning. The tubing itself should have a diameter of approximately 0.115 inches and hold 150 mL of blood [4].

i. *Weight:* Tubing weight is not a major concern, as the diameter and length of the tubing are fixed. Once we see the tubing, we will be able to record specifications for weight of the plastic they use; any tubing we buy or make should be similarly lightweight for the user's convenience.

j. *Materials:*

- According to a Terumo representative, their apheresis tubing is made of PVC plasticized with DEHP (di(2-ethylhexyl) phthalate). However, DEHP has been shown to leach into the blood in this tubing, resulting in accumulation of toxic metabolites [6]. For a new tubing system, we will consider DEHP-free PVC tubing.
- In addition to plasticizer toxicity, the material must be shown to retain ethylene oxide residuals below acceptable limits after sterilization, resist degradation by high-pressure steam, or be significantly cheaper than currently available apheresis tubing. Plasticized PVC would be ideal due to its flexibility and resistance to kinking, but other clear, flexible plastic alternatives include liquid crystalline polyesters, thermoplastic elastomers, or PTFE (mainly for collection bags) [7, 8].

k. *Aesthetics, Appearance, and Finish:*

- Since the final product is a component of an existing machine, it will need to conform to the existing shape of the current tubing system. The inner diameter is 0.113 in and the total volume is 131 mL (more specifications can be added when current tubing is acquired from the client) [4].
- The tubing will be clear as the appearance of the inside of the tube will be one parameter in judging the cleanliness of the tubing after sterilization if a multi use tubing system fabrication is pursued.

2. Production Characteristics

a. *Quantity:* The quantity of the product depends on the frequency of use. The product cannot be used indefinitely and the tubing will need to be replaced after x amount of uses. The goal is to improve the current tubing so that it is cheaper and is more durable for more uses after sterilization. Ideally, the quantity of tubes being used will be kept to a relative minimum throughout the life of the COBE Spectra Apheresis System.

b. *Target Product Cost:* The target cost is less than $100 per use of tubing. Terumo Blood and Cell Technologies currently sells disposable tubing for the COBE Spectra Apheresis system for $2,600 a use.

3. Miscellaneous

a. *Standards and Specifications:*

- *Specific to device:* The COBE Spectra Apheresis System that the client is using is Type B medical electrical equipment according to IEC Standard 60601-1 [4]. This means that the parts that come in contact with the patient are non-conductive [9]. Because we are not making changes to the electrical components of the Apheresis System, the precautions taken by the manufacturers for insulation and protective earthing will be sufficient [9]. The device itself was unclassified by the FDA but was subject to 510(k) premarket notification [10].

- *Sterilization:* Under IEC 60601-1, multi-use equipment that contacts patient bodily fluids must include detailed instructions for sterilization including parameters such as allowable temperature, pressure, humidity, and exposure time [9]. These parameters will depend on the tubing material and must follow validation requirements in ISO 11134 (autoclaving) or ISO 11135 (ethylene oxide) [9]. Current COBE disposable tubing sets are sterilized with ethylene oxide before use once and cannot be used again, likely due to retention of biohazardous EtO residuals [4, 11]. A modified sterilization technique or alternative tubing system would have to effectively kill resistant microbes (as described in ISO 11134,11135) and retain EtO residuals below the maximum safe levels outlined in ISO 10993-7 (Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals) [11].

- *Tubing:* The FDA classifies blood collection devices, including tubing, as Class II medical devices, making them subject to premarket notification [12]. The tubing should be flexible enough to avoid kinking, which can result in clotting in the line [4]. The tubing should withstand pressures at least from -250 to +400 mmHg, have about 0.113 in. inner diameter, and be made of a clear plastic similar to PVC based on the COBE Spectra device's standards [8, 12].

b. *Customer:* Currently, the product will not be sold on the market, just used in our clients laboratory space. However, Terumo has been phasing out many of the products for the COBE© Spectra Apheresis System, as there are newer machines on the market. A new tubing could be sold to others who also have this machine. If a new sterilization technique is created, this can be applied to any range of products that need to be sterilized after coming into contact with blood.

c. *Patient-related concerns:*

- The intended use of this product is on horses. This indicates a lower concern for protection of patient data, it is likely that any horses used in testing or final intended use will be assigned subject numbers.

- There is a lower concern for bloodborne pathogens in horses, but sterilization between uses will still be required. Ethylene oxide is currently used as a sterilization agent. [4]

d*. Competition:* We are tasked with finding a more affordable and easy to clean tube that is already on the market. The tube must fit our clients needs. The likelihood that we create a new type of tubing is slim, therefore, we do not have to be wary of patents. As far as competition, there are hundreds of medical and non-medical grade tubing options and we are not necessarily competing with any of them.

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