Framework Development for Remote Clinical Trials: Assembly Process Design

by

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Abstract

Clinical trials are facing new difficulties after the COVID-19 outbreak, with enrollment decreasing by about half after January 2020. Tufts Clinical and Translational Research Center has partnered with the Massachusetts Institute of Technology to develop a framework for a "clinical-trial-in-a-box" for use in fully remote clinical trials, which would reduce risk of infection due to the lack of physical contact. The goal is to increase enrollment and create a safe system in which to conduct medical research while requiring as little knowledge of technology from the participant as possible, in order to include the most potential participants and eventually expand into rural regions.

This thesis focuses on the assembly process of this framework, detailing the steps from receiving trial materials to shipping out the finished trial box. For more depth into the other aspects of this project, please refer to the other theses from the project group: Imane Ait Mbiriq, Carly Smith, and Joyce Noh.

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Chapter 1

Introduction

1.1 Company Overview

This research originates from Tufts Clinical and Translational Research Center, based in downtown Boston, Massachusetts. It is a center for biomedical research and is the principal teaching hospital for Tufts University School of Medicine. At the time of writing they were pursuing a new form of clinical trial that does not require in-person contact, a remote trial system that could reduce the amount of traffic coming in and out of the medical center.

The research team was based at the Massachusetts Institute of Technology, a private land-grant research university. MIT was heading the project with the support of Tufts Medical Center, with the goal to develop and instate a framework with which any number of clinical trials could be performed remotely, regardless of location, number of participants, and with minimal necessary technological knowledge.

The MIT Lincoln Laboratory, the United States Department of Defense federally funded research and development center, was supporting the project. They were also running fully remote clinical trials and were invested in helping a framework be developed for future use.

1.2 Team Introductions

The working project team consisted of

A. Ryan Lin, Imane Ait Mbiriq, Joyce Noh, and Carly Smith- four graduate students from MIT's Master of Engineering (M.Eng) in Advanced Manufacturing and Design program, responsible for development and delivery of the project.

B. Dorothy Dulko, Manlik Kwong, and Cortney Wieber- three research personnel from Tufts Medical Center who provided background information, project motivation, resources, and much guidance.

C. Brian Anthony, MIT M.Eng thesis advisor, and Xiang Zhang, Postdoctoral Associate at MIT, who helped define project specifications and helped the team through the thesis project process.

1.3 Project Motivation

Tufts Medical Center is using two clinical trials to be case studies for the use of the remote clinical trial framework, one headed by Dorothy Dulko and another by Manlik Kwong. In order to best keep a safe trial environment as well as increase enrollment, the two trials are planned to utilize this framework.

The institute’s motivation is to organize remote studies and change the patient’s experience of participating in a clinical trial, and therefore having access to the traditionally harder-to-reach communities to participate, especially during the current sanitary situation.

The main objective of remote clinical trials is to revolutionize the clinical trial model and increase patient enrollment as well as racial and ethnic diversity in enrolled patients. According to the FDA’s data, only 3% of the country’s physicians and patients take part in clinical trial research that leads to new therapies [1]. COVID-19 has also been reducing enrollment by a large amount, with a 50% reduction seen since January 2020 [2].

Remote clinical trials have high potential in reducing patients' reluctance to participate in clinical trials and dropouts. These can be related to different factors: Occupation: Participants are concerned about losing pay or not getting leave and therefore refuse to participate in trials involving hospitalization as per the protocol requirements [3]. Transportation: In-person trials require participants to be present in the trial facility which can result in transportation difficulties and additional costs. Understanding of trial requirement and consent form: participants with less advanced education background may have difficulties comprehending the trial’s instructions which can lead to wrong expectations and eventually dropouts.

The alarming world health situation and the clear need to conduct trials remotely, is the main incentive to work on the process of the design and implementation of remote clinical trials and apply it to these case study trials.

1.4 Project Timeline

Building from data from a previous remote clinical trial held by Tufts Clinical and Translational Research Center, the team focused on reviewing the foundation of the project itself, including the current methods used to conduct the trial, results from surveys and interviews, and specific components involved in the trial. Based on this knowledge, research was done on specific areas of improvement.

Over the course of February to August 2022, the project team split and focused on different sections of the framework development. Joyce Noh focused on the design of the trial kit box itself, developing a box customized for remote clinical trials to fit user needs [4]. Ryan Lin focused on assembly and verification in which he designed the process from receiving the devices and materials to getting the kits ready to be deployed. Carly Smith focused on the design of the instructions for remote medical device setup using the two Tufts trials as case studies [5]. Finally, Imane Ait Mbiriq focused on designing the inventory management system of the materials and components of the trial box [6].

Initially, the idea was to develop the framework and then subsequently run through the two case study trials to determine the effectivity of the framework and rework if necessary. However, due to the clinical trials taking longer than expected to be approved through the Institutional Review Board (IRB) as well as delays in obtaining funding, the scope of this project changed to developing a generalized framework as a guide for all potential future remote clinical trials.

Chapter 2

Framework Design Process

The concept behind the design of assembly process is to design a system to take the raw delivered materials and devices and efficiently and consistently output sealed, tagged, and verified trial kits. The secondary goal was to make a system that would be as technologically simple as possible for the patients, so as to keep the trial group inclusive and also allow expansion into more rural regions. Because of the lowered clinical trial enrollment rates due to COVID-19, it is more important than ever to exclude as few potential participants as possible from the enrollment process [2].

In this section there will be a closer look into the design process of each step in the framework and specifically more detail about the assembly process design.

2.1 Background Information

The first step in the assembly design was collecting background information about the trial requirements. The materials needed for different trials vary greatly, and thus constant communication between designer and medical personnel is necessary to develop the necessary trial kit material list. This can be broken down into the following parts:

1. Acquiring the list of materials that will go into each box.
    a. This should be done by much communication with the medical personnel in charge of the trial, so that the steps can be prepared to receive, setup, and package each of the materials on the list.
    b. If batteries or other peripheral products will be needed, obtain that information in advance to receiving the shipments of medical devices and materials.
2. Obtain at least a rough estimate of the trial participant count for storage space allotment.
    a. Depending on the size of the study and the amount of materials, storage and assembly space may become an issue that will need to be resolved prior to receiving the trial materials.
    b. Each medical device or package received will have measurements to determine the storage capacity needed. By multiplying the number of trial participants by the each of the items, a rough amount of space can be calculated.
        i. For example, a certain health wristband device has a package dimension of 8.95 x 4.15 x 2.65". If the medical trial involving these wristbands requires 100 wristbands, a rough plan can be drawn up to store these 5 by 10, stacked up by 2. Meaning

someone in charge of storage would need to set aside roughly 4 x 4 x .5’ worth of space. A quick back-of-the-envelope calculation can determine the number of storage racks needed to receive all the materials.

c. The number of trial boxes will also need to be multiplied by the number of trial participants, and a certain amount extra will need to be manufactured as a margin of safety for defects, failed deliveries, replacement packages, and as general extra buffer. These will most likely take up the most space for storage and can be stored separate from the other devices. To order storage racks for just the boxes would be wasteful and costly. Storing them underneath tables, closet floors, and any other space should work perfectly fine.

2.2 Storage Planning

As mentioned briefly in 2.1, allotting storage space is an important step not to be overlooked. If managed properly, when the time comes to assemble the trial kits it should be as easy as wheeling out the inventory from storage and begin assembling, with all materials accounted for.

There are multiple suppliers capable of providing shelving units but for this project, Uline was chosen for their fast delivery and quality [7]. This included two 36 x 18 x 69” mobile storage shelves, rated for 1000 pounds of storage, which would be enough space for the small participant number and short product list required by the first of the two case study trials. To determine how much space is needed prior to accepting trial materials, refer to section 2.1.

Figure 1: Uline stock picker cart model H-2653

The trial is still undergoing the approval process at the time this is written so the storage capabilities was not expanded past this initial step, but sorting containers and labels are also a good future step to keeping the devices and materials organized and easy to access.

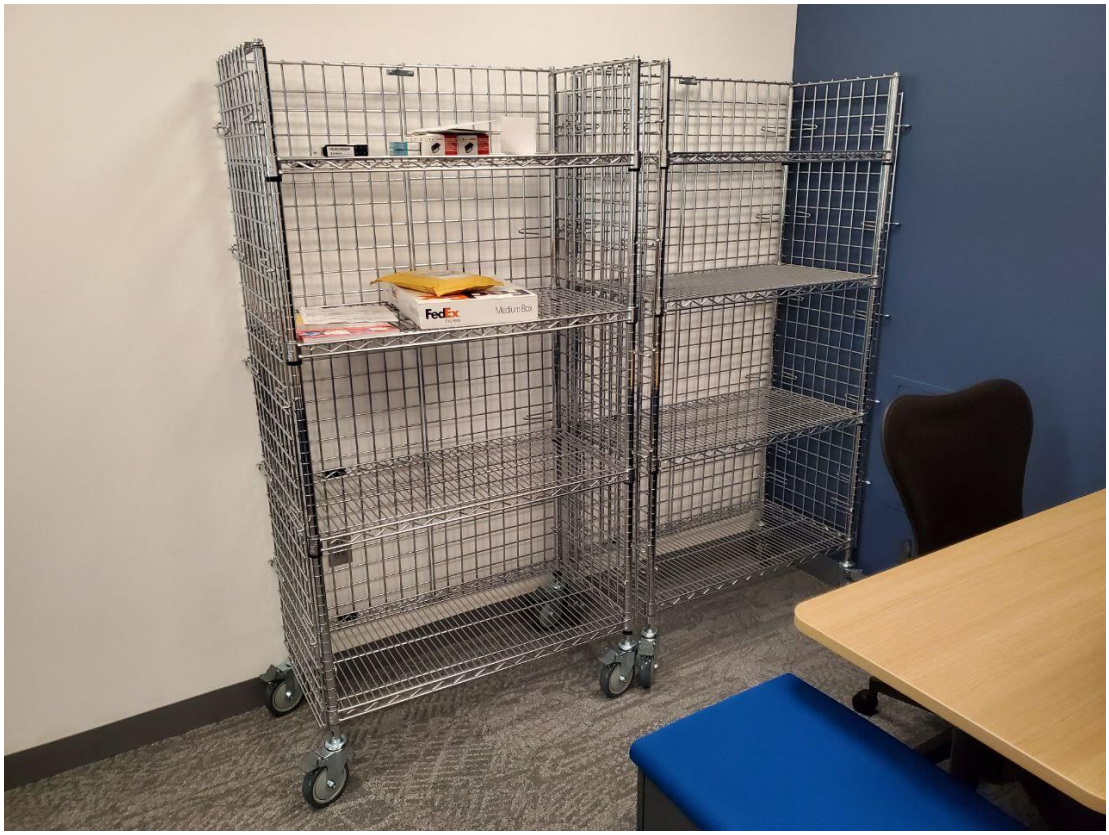


Figure 2: Completed mobile storage shelves in the device storage area

The idea behind the mobile storage units is to create a “factory-on-wheels” design, which allows for swift retrieval of trial kit materials, where the assemblers can wheel all the necessary items to a separate assembly area and put it away safely when not in use.

2.3 Special Case Receiving and Handling

Some devices or materials may need special handling, such as pharmaceutical drugs. One of the two case study trials in this project required handling of drugs and placebo

pills in a double-blind experiment. Because clinical trials are often double-blind, these drugs aren't separated, and must be safe to be stored in the same environment. Be cautious when dealing with these kinds of materials and ask the medical physician in charge of the study about the necessary precautions of the specific drug in question.

Other special cases include peripheral products which will not be provided by the medical center, such as batteries. This involves a review with the instructional pamphlets for each of the products needed for the trial to determine what peripheral products are needed and of what quantity. These will most likely need to be purchased by the point-of-contact in charge of purchases for the project, or by an individual to be reimbursed.

2.4 Wearable Product Sizing and Customization

In cases with customizable products, the participants will need to send the information during enrollment. This information should be entered into an easily accessible database for later retrieval for device ordering or in case the participant needs replacements (see 2.5 for details into data collection). In the case that this information cannot be easily provided by the trial participant, and because the goal

is to create a fully remote clinical trial, measurement kits or a suitable package should be delivered to the participant and should be sent prior to the main trial kit.

For example, for one of the case study clinical trials for this project, one of the necessary medical devices will be a wearable ring device. For accurate measurements among many other reasons, this ring needs to be sized appropriately for each trial participant. This involved talks with the supplying medical device company to send ring sizing kits, which could be as simple as a very small box with several labeled plastic rings to determine ring size. Depending on the agreement with the supplying company, such kits may need to include return packaging and instructions.

Figure 3: Medical ring device sizing kit

2.5 Data Collection Setup

Different devices will require different data collection methods. For devices such as thermometers or pulse oximeters, these can simply be taken down manually by the participant or read aloud during the virtual video chat or call with the clinician. Because of such device's simple data format, there's no need for further setup. However, with many clinical trials, as was the case for one of the trials involved with this project, there are more complex devices involved. Some of the products that had to be dealt with were the ring monitor device and electrocardiogram, both of which measure with constant output. By partnering with the supplying device companies, this project had accounts for the device pre-generated and put aside for the clinical trial specifically. The trial participants only had to log in to their device with their assigned account through their smartphone, and the data would automatically be sent through their home network to the supplier. Then, as agreed upon, the company would send the collected data from those accounts to the medical center to be analyzed.

The requirement for the participant to own a smartphone was a compromise that had to be made with regards to keeping the remote clinical trial framework low-tech. The goal is of course to include as many potential patients as possible to keep enrollment rates high, but with the large amount of data, as well as other

inconveniences with participating in a remote clinical trial without a smartphone, this was an unavoidable sacrifice.

Besides collecting data from partnered suppliers, certain non-private patient information can be kept track of through a database or even a spreadsheet. This is necessary to keep track of customization options in case the patient needs replacements, or to manage package deployment scheduling. A simple example of a patient datasheet for a small trial is shown below.

A	B	C	D	E	F	G
Patient #	**First**	**Last**	**Ring size**	**Oura Ring ID**	**Oura account ID**	**email**
1	Ryan	Lin	9	2ac37ebh33	000041251	mit0369@mit.edu
2	Imane	Mbiriq	Not received	Not sent	000034123	mit0370@mit.edu

H	I	J	K	L
Account connected?	**Box sent?**	**Box received?**	**Requires replacement:**	**First telehealth visit**
Yes	Yes	Yes	Pulse Oximeter - on route	Complete
No	No	No	NA	Not complete

Figure 4: Patient data sheet

2.6 Inventory Management

Inevitably, with inventory constantly being received and delivered out, a rigorous inventory management system will be needed to keep track of all devices and kits. For more information about the development of this system and management strategy, refer to “Framework Development for Remote Clinical Trials: Supply Chain Management” by Imane Ait Mbiriq [6].

2.7 Box Design and Manufacturing

With the importance of keeping the contents of the trial kit box safe and secure, part of this project was the development of a box design that would suit the needs of a remote clinical trial. For details, refer to “Packaging Design for Remote Clinical Trial Operations” by Joyce Noh [4].

2.8 Physical Assembly

When all devices, manuals, drugs, and boxes have been received or manufactured, deployment can begin. There is a large variability in this process, because of the different requirements of each clinical trial. A checklist should be created for each trial to make the assembly process consistent, as well as to make sure all devices are setup and included. See 3.10 for details. Because of the importance of handling the materials, this checklist should be developed through communicating with the physician or the contact who is running the trial.

Device setup is a large part of this process. Each device must be ready to use out-of-the-box with minimal setup for the patient. Sometimes this just means putting batteries in the pulse oximeter or could be much more involved. Some devices, such as the customizable ones, will need to be tagged or otherwise labeled to make sure

it is included in the correct patient's kit. For more information about device setup and instruction manuals, refer to "Remote Clinical Trial Operations: Patient Education for Medical Device Use" by Carly Smith [5].

2.9 Returns

At the end of the trial or if there are drop-outs, packages will need to be sent back to the assembling location or the medical center to reuse the kits and devices. The devices that are returned will need to be cleaned and have their data wiped. This will be a different process for each device, so it is important to keep a consistent set of instructions for each person who will be wiping the devices. The box design for this project also includes a return system, which can be found in more detail in "Packaging Design for Remote Clinical Trial Operations" by Joyce Noh [4].

2.10 Delivery Verification

Last was developing a method of which to keep track of and verify kit delivery. Initially, QR codes or RFID tags were brought up as a solution to this. QR codes were generated to write and send emails automatically to our server, which would confirm that the participant received their specific box.

Figure 5: Example of a functional generated QR code

RFID tags could keep better track of the more expensive medical devices, as well as the specific product IDs and model numbers. Tufts Medical Center ran a private data server that could receive this information through SMS or email, which contained sensitive patient data and will be used as the telehealth platform for the two case study trials. Through this method, the participants would be relieved of any pre-requisite technological knowledge, aside from owning a phone and scanning the code.

This QR code/RFID tag idea was discarded after a few weeks, due to an underwhelming benefit. It was found to be more practical and cost-effective for the clinician to simply verify trial kit delivery and confirm the contents during the first telehealth visit. The patient could then just verbally identify the presence of all items and instructions in the box, as well as that they received the correct box. A simple name tag on the box would be enough to differentiate the box for the patient, as is necessary for multiple family members enrolled in the same clinical trial.

Chapter 3

Generalized Framework for Remote Clinical Trials

This is the generalized framework, intended to be a comprehensive, but general guide for medical researchers to create their own remote clinical trials. This framework was developed in conjunction with all four MIT project members: Ryan Lin, Imane Ait Mbiriq, Carly Smith, and Joyce Noh. For more detailed information as well as each member's development of this model, please refer to their respective theses [4][5][6].

3.1 Process Outline

1. Parameters and Timeline of Trial
2. Participant Tracking System
3. Device Storage and Cleaning
4. Device Setup (prior to packing/shipping)
5. Supplemental Instructions for Device Use (for participant)
6. Current Device Inventory

7. Device Inventory Tracking System

8. Box Design

9. Box Inventory Tracking System

10. Box Assembly Plans

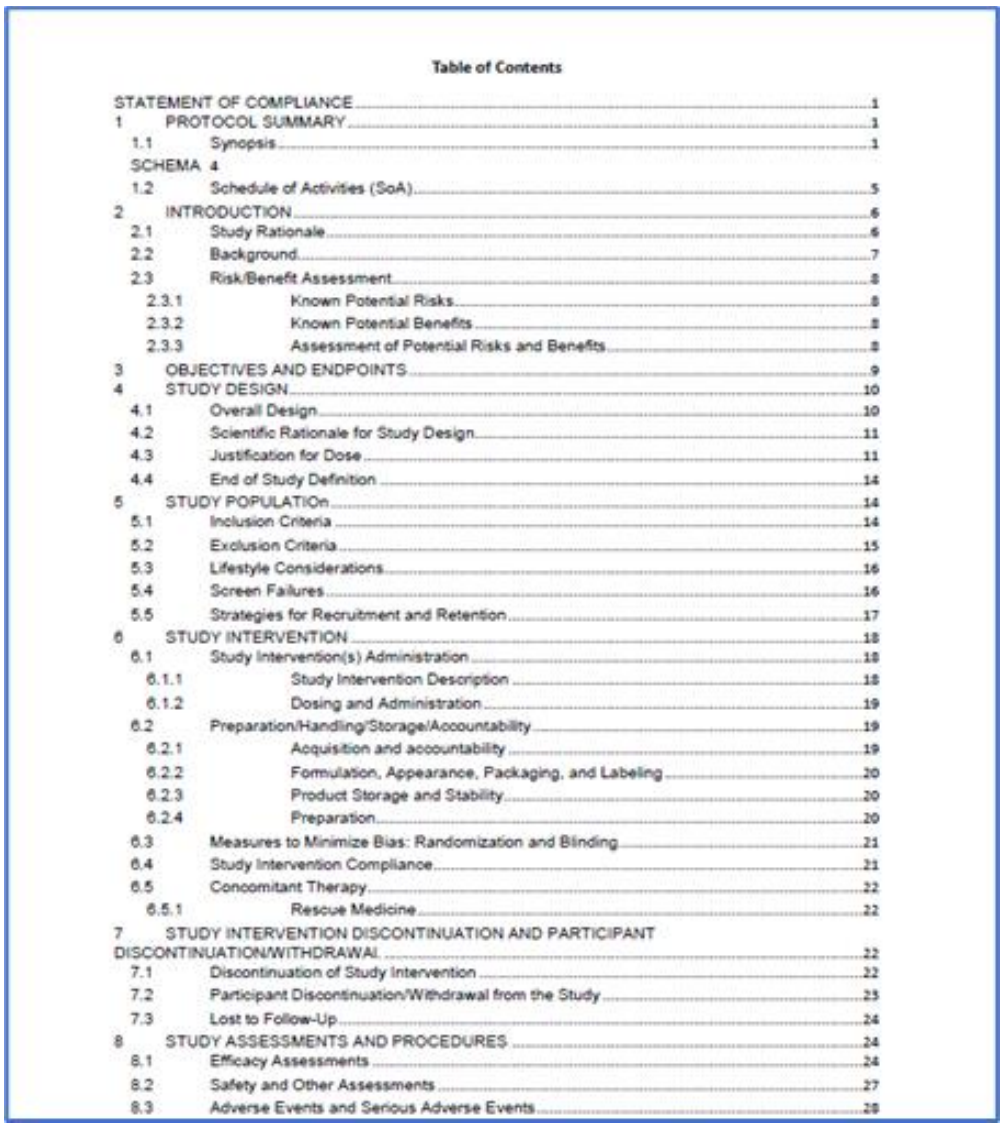
11. Shipping and Delivery Management

12. Returns

3.1 Parameters and Timeline of Trial

An institution's Institutional Review Board (IRB) process and structure holds authority over all clinical testing in the United States. The IRB reviews research requests, either approving, requesting modification, or disapproving of new clinical trials [8]. Minimally, an IRB application must include Risk Anticipated Benefit Analysis, Informed Consent, Assent, Selection of Subjects, Privacy and Confidentiality, Research Plan for Collection, Storage, and Analysis of Data, and Research Design and Methods [9]. One of the most significant documents reviewed by the IRB is known as the IRB Protocol. For any clinical trial this document includes a timeline of activities, background and rationale, risks/benefit analysis, study design details, study population criteria, study preparation, product storage and

stability, safety assessments, statistical considerations, etc. In preparation for a remote clinical trial, one must leverage this existing IRB document to derive parameters which will be used to later establish inventory, handling, assembly, box design, and all other remote system parameters.



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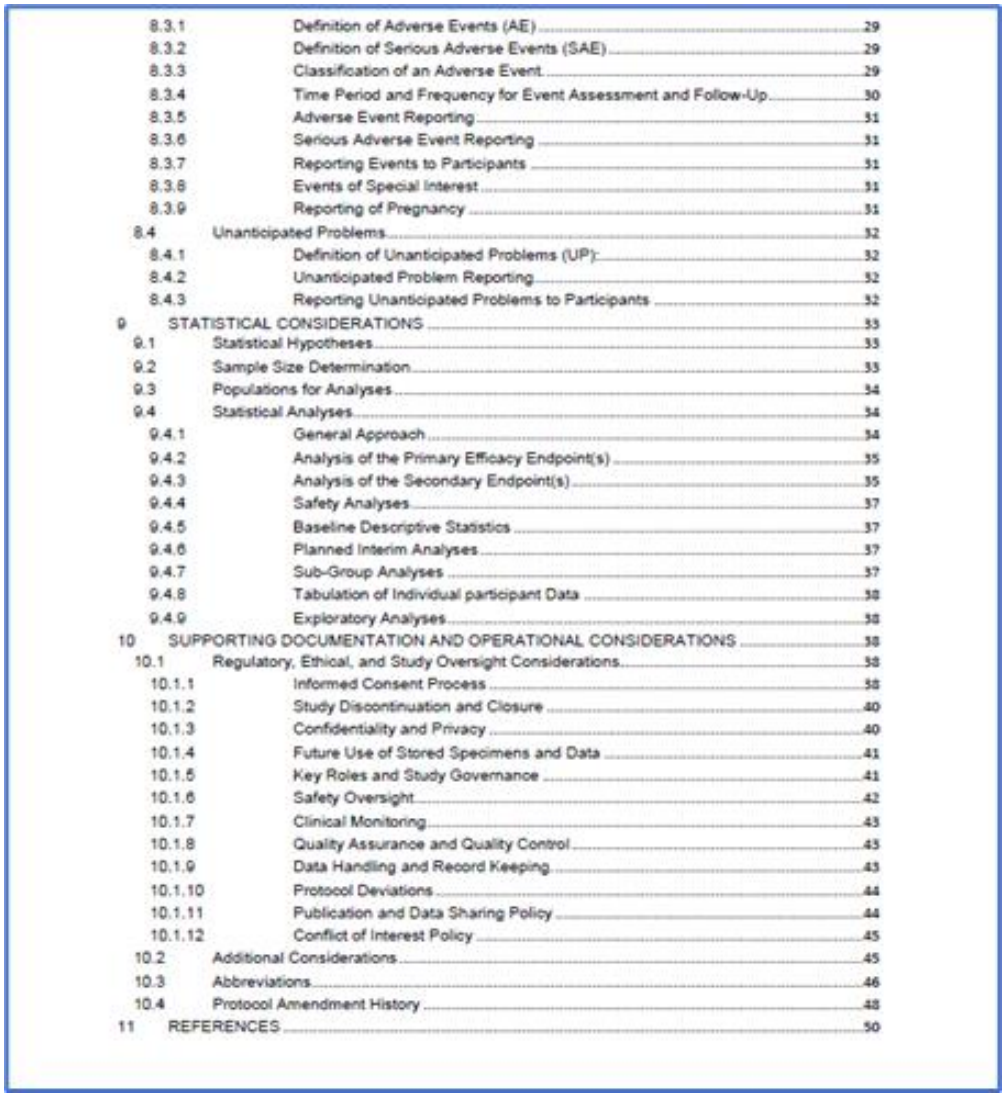


Figure 6: Example Table of Contents from IRB Protocol Documentation

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent (IC) is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. The investigator will explain the research study to the participant and answer any questions that may arise. Utilizing the telehealth platform, an explanation will be provided in terms suited to the participant's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Potential participants will have the opportunity to ask questions. The participants will have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate.

Figure 7: Supporting Documentation and Operational Considerations

As for the timeline, below is a rough procedural timeline from the IRB Protocol Documentation for one of the two case study clinical trials from Tufts

Clinical and Translational Research Center. It serves as a step-by-step guide for a remote clinical trial from start to finish.

The overall study design is a non-invasive observational study – data acquisition using wearable devices and daily/ad hoc self reporting of observations and Long COVID-19 related symptom events. Patients are enrolled from a pool of candidates identified from running a query on the TRDW, followed by initial contact and screening to make eligibility determination before enrolling the patient for a 3-month data collection period. The procedure is as follows:

5. Execute a query on TRDW with the inclusion criteria of previous discharge from Tufts Medical Center with a positive COVID-19 diagnosis between June 1, 2021 through June 1, 2022. The results of the query will include patient name, demographics, medical record number, date of admission/discharge, and contact information – phone and/or E-mail address. This forms the recruitment pool of patients.
6. Working from most recently discharged to oldest, make initial contact with patient to confirm Tufts Medical Center visit information from #1 and gauge interest in participating in the study.
7. For those patients who express interest, conduct a follow-up screening phone interview to assess technical capabilities to participate. If the patient is eligible to participate, review the informed consent document and arrange to send the ICF electronically or by mail for signature.
8. For those patients who qualify to participate, send ICF for signature
9. Once ICF has been sent – initiate building the study participation package – assign wearables and log device serial numbers to the study participant. Study participant study ID is the same as the TRDW de-identified integer person.person_id. This will be used to reference the study participant throughout the study and its data.
10. Once the signed ICF has been received and logged, ship the study package (contains LetsGetStarted20220410.docx) to the participant and E-mail the tracking number to the participant or send a SMS Text message to the participant.
11. Contact the enrolled participant and schedule an "Unboxing" Doximty session to walk through the contents and setup of the wearable devices and mobile phone contact information.
12. Contact the enrolled participant 5-7 days after the "Unboxing" call to answer any questions or review any procedures and processes regarding the wearables and health monitoring devices.
13. For the next 3 months, monitor and collect data from all enrolled participants, using summary and meta data to form weekly monitoring reports.
14. Provide phone, E-mail, and Text messaging (LongCOVIDSMSTextSurvey.xlsx self reporting questions) support to enrolled participants.
15. Any lost or broken study devices will be reported to the study support team for return of broken device or de-activiation of the lost device. Upon confirmation and review of the broken/lost incident, a return shipping label/box for broken devices and replacement device will be shipped to the participant. There will be no cost to the participant if devices are un-intentially broken or lost.
16. At the end of the 3 month data collection period, send the study termination package to the participant that includes closure instructions and return shipping box/envelop to retrieve the wearable devices.
17. Upon receiving returned study materials, log the return devices – checking serial numbers and note the condition of the devices. If all devices are returned, mark the study participant as closed/complete. If device(s) are missing, contact participant to request return of device(s).
18. Upon closure of all enrolled participants – generate final summary report
19. Prepare the collected data into a AI/ML longitudinal dataset for model building in a follow-on study.

Figure 8: Example of procedural timeline taken from the IRB Protocol Documentation

Key parameters to gather from the IRB protocol documentation for the remote clinical trial are the patient sample size (projected enrollment numbers), required medical devices and their suppliers, and timeline.

3.2 Patient Tracking System

As patients sign up for each trial they should be entered along with any relevant information into a database. At its most basic, this can be an excel spreadsheet with columns for the patient information. This should include the patient's first and last name, account information for any medical devices that need to be sent, IDs or product number for each device sent to the patient, individual box deployment status, device replacement status if necessary, and telehealth visit information (as applicable). A very basic example from one of the case study trials is shown in Figure 4.

This data can be obtained by initial patient registration, as well as utilizing the telehealth visits to confirm delivery and account completion. Any special requirements or accommodations should also be taken careful note of and entered into the database. Any sensitive patient data should be handled respectively.

Prior to registration, screening should be done consistently and with a script, so there are no statistical biases when enrolling new participants. Because the aim is to produce a clinical trial that can be done completely remotely, screening should be scripted for both phone call and email recruitment, as well as voicemail. An example of a voicemail script is provided below (obtained from one of the case study trials):

This message is for (name of potential participant). My name is …… I am calling from Tufts Medical Center to provide you with information about a research study being conducted here at Tufts Medical Center. I will try you again later today/tomorrow. If you would like to reach me in the meantime, my number is …. Thank you and have a good day.

For a trial with a small participant size, this data entry is doable. A simple spreadsheet should be able to keep track of all the participants and their data. But in the case of a clinical trial in a later phase with a large participant number, this becomes less feasible. Because of the large number of screenings, there will need to be multiple people entering data at the same time, and a more rigorous data management program is needed.

3.3 Device Storage and Cleaning

Regardless of whether the assembly of the trial kits is done onsite or offsite from the medical center, incoming inventory must be received and stored properly. An estimate of the storage volume can be given by obtaining the number of participants, multiplied by the amount of volume each of their necessary materials will take up (for devices this can be obtained from the product website, and trial box dimensions can be obtained from the designer or manufacturer). For ease of assembly and access,

a “factory on wheels” should be built, or mobile storage racks that can be taken out of storage to an assembly area. These racks should contain all the necessary components for each trial kit, as well as any materials needed to clean or otherwise set up the devices. For example, for one of the case study trials, mobile storage shelves (purchased from Uline and assembled onsite) were required to store the following:

30x Trial box
30x Pulse oximeter
60x AAA Batteries
30x Electronic thermometer
30x Electrocardiogram
30x Health tracking ring device
30x Ring sizing kits
30x Patient instruction pamphlets

A space should also be set aside for returning medical devices, where they are labeled as returned and used, or cleaned and ready to be shipped back out. Devices which are returned and need to have their data cleaned out should undergo a consistent cleaning process. This process may vary from device to device but will likely include using sanitary wipes to wipe down the device and resetting the device back to factory settings. Placing the device into a bag and tagging it with the device ID number can also help improve inventory management.

3.4 Device Setup

The devices should be ready to go out of the box for the participants, to make the trials as technologically inclusive as possible. As each device has a different setup, there should be documentation written for each device and given to each assembler to make sure the devices are all set up in a consistent manner. Some might be as simple as follows:

Pulse oximeter setup:

Unbox the pulse oximeter carefully.

Remove the battery cap by applying gentle pressure and pushing away from the device.

Install two AAA batteries and replace the battery cap.

Return the pulse oximeter to the original package and ensure the instructions remain inside.

If prepared in this way, each participant can take their own measurements out of the box (as instructed) without any difficulty.

This includes tailoring the necessary devices and services to each enrolled participant. If the study includes wearables or garments that require sizing, first acquire accurate sizing information. For example, for a wearable medical ring this step involves sending each participant a ring sizing kit, which will inform the medical center which size ring to send to them. This kit can be sent back and cleaned

for reuse, or disposed of if applicable. The data can then be collected through either a telehealth visit or other means should be recorded with the patient in the database.

3.5 Supplemental Instructions for Device Use

Besides the usual included manufacturer instructions that come with each medical device, there is also a need for supplemental instruction pamphlets to be written for use of the device for each trial. This should include diagrams, the frequency the patient should use the device, simple instructions for operation, and anything else to keep the trial as easy to understand as possible. Any complicated operation left unexplained may lead to inaccurate readings or even participant drop-outs. For more detail on supplemental instruction authorship, refer to "Remote Clinical Trial Operations: Patient Education for Medical Device Use" by Carly Smith [5].

3.6 Current Device Inventory

In order to organize the trial's supply chain, the first step was to collect data about all of the supplies that can be used in future remote trials. This ensures that existing

devices are considered and that no unnecessary purchases are made. This step is also crucial to build and organize an inventory tracker.

Tufts' team has been conducting trials on site in the past years and the supplies used were stored in both Tufts Medical Center and Lincoln Lab.

The first step of getting the current device inventory is obtaining a list of all the existing supplies.

Device	name/brand
Pulse Oximeter	W.B Mason NWLPulsoximeter
Thermometer	Avantik GL4687
Electrocardiogram	Alivecor Kardia mobile 6L
Oura ring	Oure gen 2
Garmin watch	Garmin Venu Sq
FitBit health tracker	Fitbit Inspire 2
Samsung Watch	Samsung Galaxy Watch 3
Covid-19 Testing Kit	CUE health rapid PCR test
Test Sample Box	Cosmos ID sample box

Figure 9: Example of required device list

The second step would be collecting characteristics and parameters of each of the supplies:

Count: Number of units of each item in the different storage locations, including the items currently used in a trial and that will be returned to Tufts.

Description: Concise explanation of the device and its usage.

Storage location: Current placement of the units at the time the inventory audit is done.

Price: The price at which each unit was purchased from the supplier. The price is included to determine which item will be kept by the participant at the end of the remote trial. High-priced items are returned to be used in future trials, while other items with a lower value can be kept by the participants and can be considered as a reward.

Supplier: The company or organization that the items were sourced from.

Dimensions: The exact measurement of each item is needed for the design of the trial's box.

Lead time: The period it takes to receive an order of an item from the suppliers, the lead time is needed for planning orders ahead of the trial's start and avoiding delays of trial's supplies.

Restock level: The minimum reorder stock level is the level of inventory at which a new purchase order should be placed. It is generally higher than the minimum level to cover any emergencies that may arise as a result of unexpected delays. The restock level is most important in the case of items that are often used in every trial or that have a high lead time.

Minimum order quantity: The lowest order level of an item imposed by the supplier.

The third step is then the verification of all information in the inventory log by the trial's staff and the rest of the team in order to validate the information about each item.

3.7 Device Inventory Tracking System

Rigorous management of inventory is a necessity to keep track of devices and other trial materials. There are several inventory management system platform options, but for the case study trials the team opted to use Google's AppSheet program

(which integrates Google Sheets spreadsheet software) [10]. The system helps create an accessible inventory log that includes all the information collected previously for each device and allows quick data input and real time analysis of the stock level of each device.

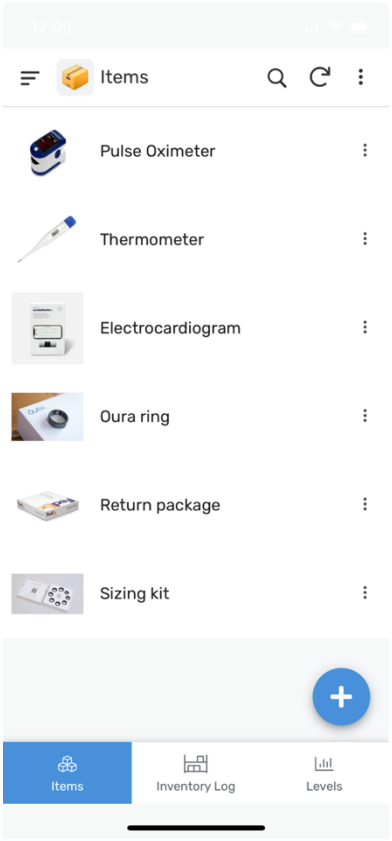


Figure 10: AppSheet inventory management interface for case study trial

For each trial device or material, the inventory levels can be either updated on the Google Sheet or directly on the app. Appsheet can use the camera on the mobile device to capture barcoded data, which can be used to record any movement, whether it is stock in or stock out. For further detail about how to set up and best utilize this

inventory management system, refer to “Framework Development for Remote Clinical Trials: Supply Chain Management” by Imane Ait Mbiriq [6].

3.8 Box Design

After considering the tradeoffs of each of the existing boxes researched and detailed above as well as each trial’s contents and their dimensions, the box was modeled using Autodesk Fusion [11].

There will be one universal box that will have dimensions that fit all the contents of both the case study trials. Within the box will be foam inserts that will have cutouts where the specific devices will be placed. This design was mostly inspired by the Pelican case as shown in Figure 10 for the following reasons [12]:

1. The larger polypropylene hard shell case makes the packaging durable to stand against most damages from external factors experienced during shipping and handling as well as while in the patient’s personal environment.
2. The foam inserts safely secure all components.
3. The cutouts in the foam make it easy for the patient to identify where devices need to be placed.

4. Both the outer hard-shell case and the foam inserts inside can be reused for future trials.

Figure 11: Pelican case example with foam cutouts (~16 x 20 x 8”)

The following shows the assembled models of the box for each trial:

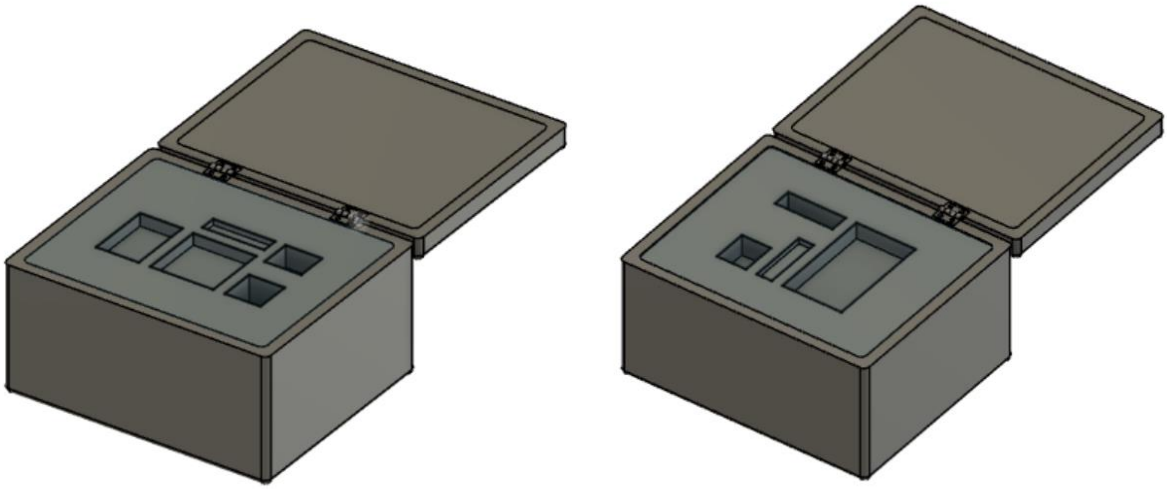
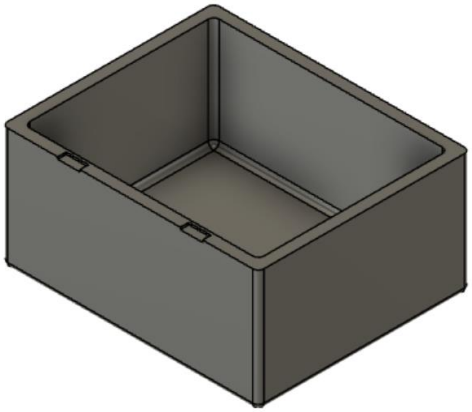


Figure 12: Complete assembled packaging for the two case study trials (~19 x 23 x 11”)

Each of the major components are modeled and shown below along with the dimensions.



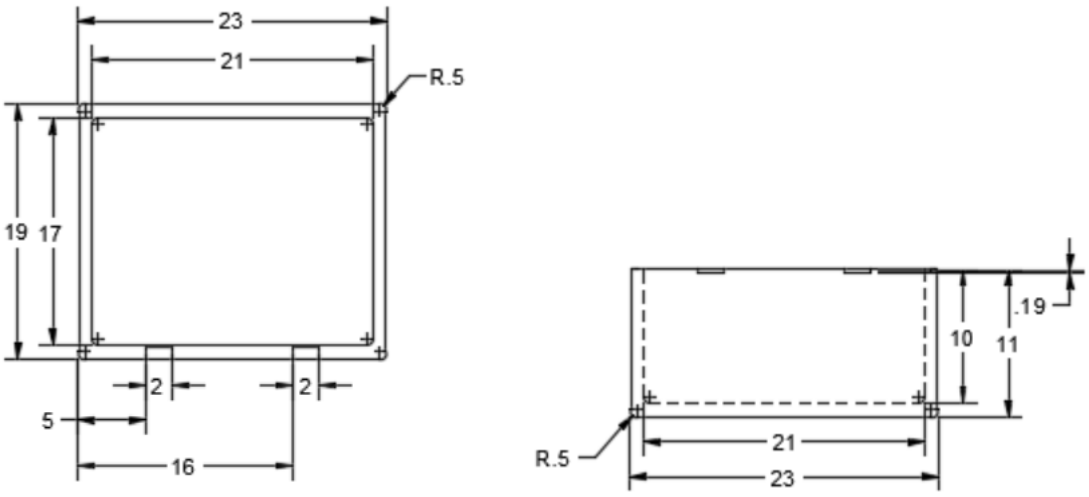
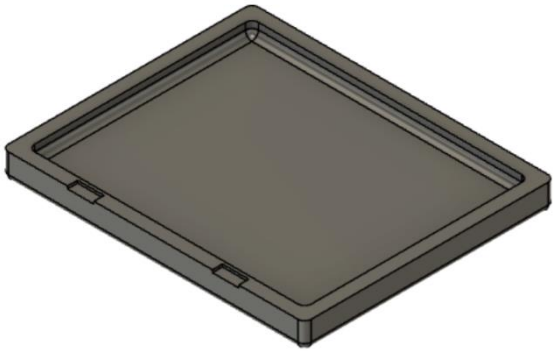


Figure 13: Body of outer casing (top) with drawings (bottom), units in inches



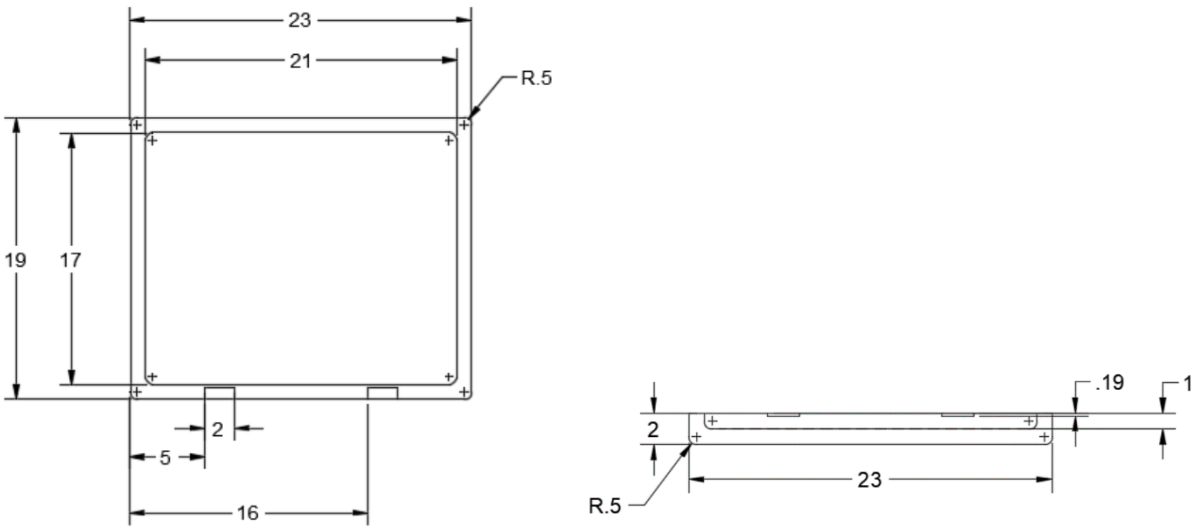


Figure 14: Lid of outer casing (top) with drawings (bottom), units in inches

The following is the assembly of the top lid and body of the outer casing using polypropylene hinges:

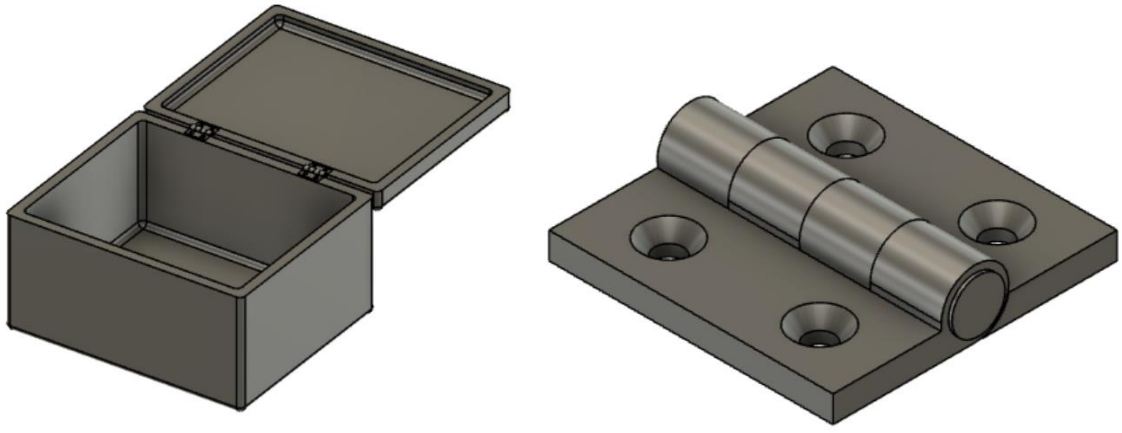


Figure 15: Outer casing assembly of lid and body (left) and hinge (right)

There are many more components in one of the case study trials than there are in the other. Therefore, to design a universal box for both trials while keeping the size as small as possible, two layers of foam were used for one of the boxes.

The following are the two foam layers for the second box:

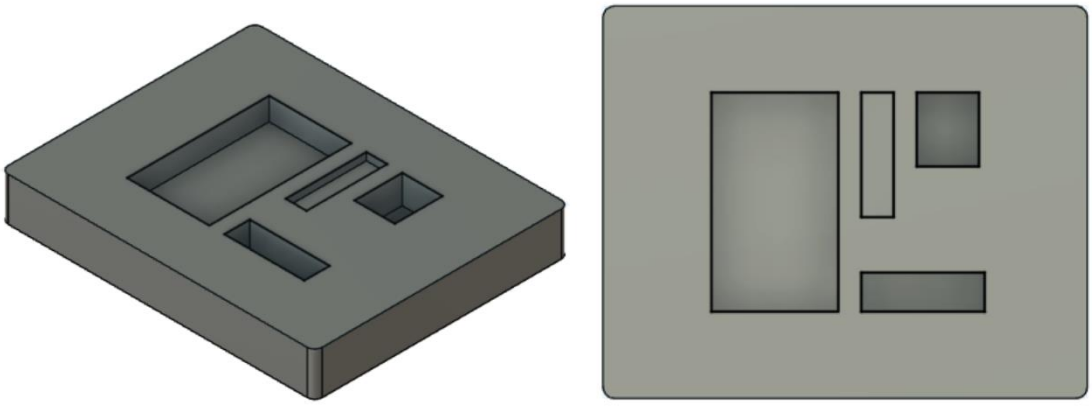


Figure 16: Top foam layer of the second trial box (left) and top view (right) (~17 x 21 x 3”)

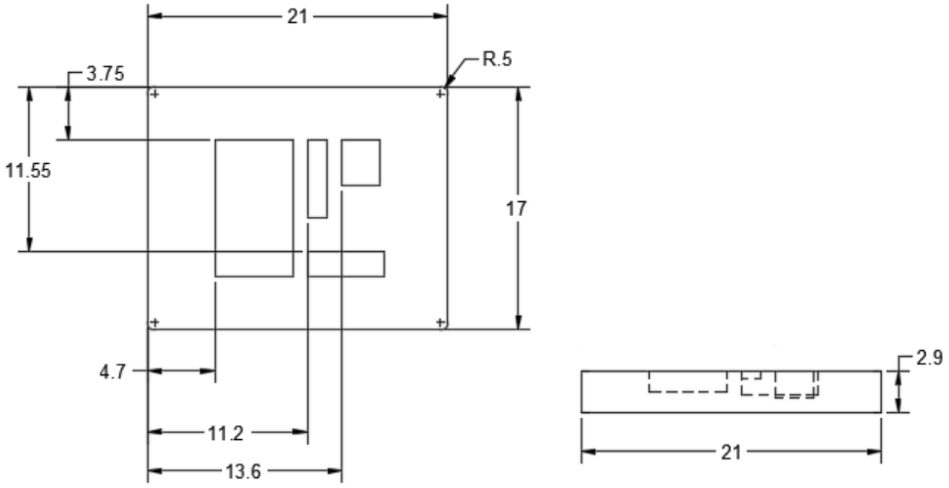


Figure 17: Top foam layer of the second trial box drawings, units in inches

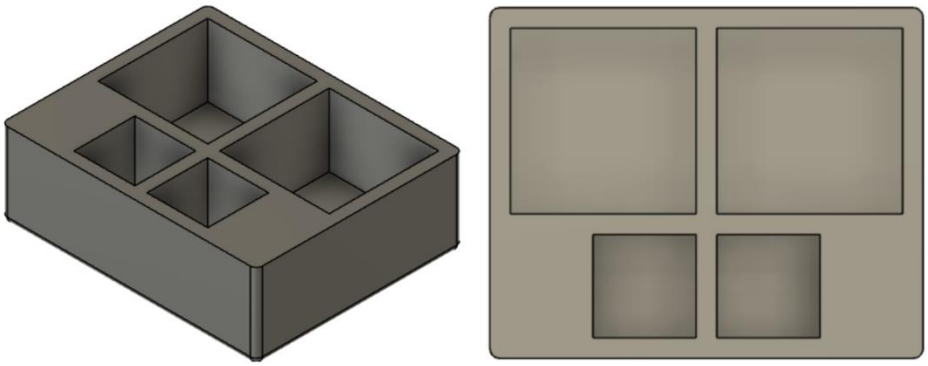


Figure 18: Bottom foam layer of the second trial box (left) and top view (right) (~17 x 21 x 7”)

The first, smaller trial only needs one foam layer as shown:

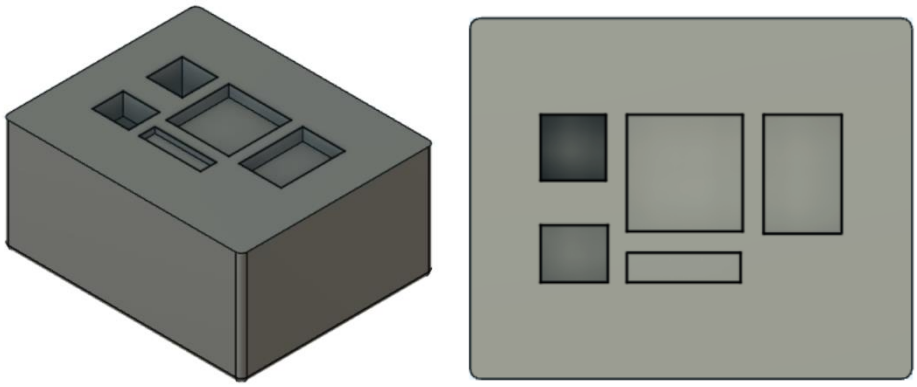


Figure 19: Foam layer of the first trial box (left) and top view (right) (~11 x 21 x 10”)

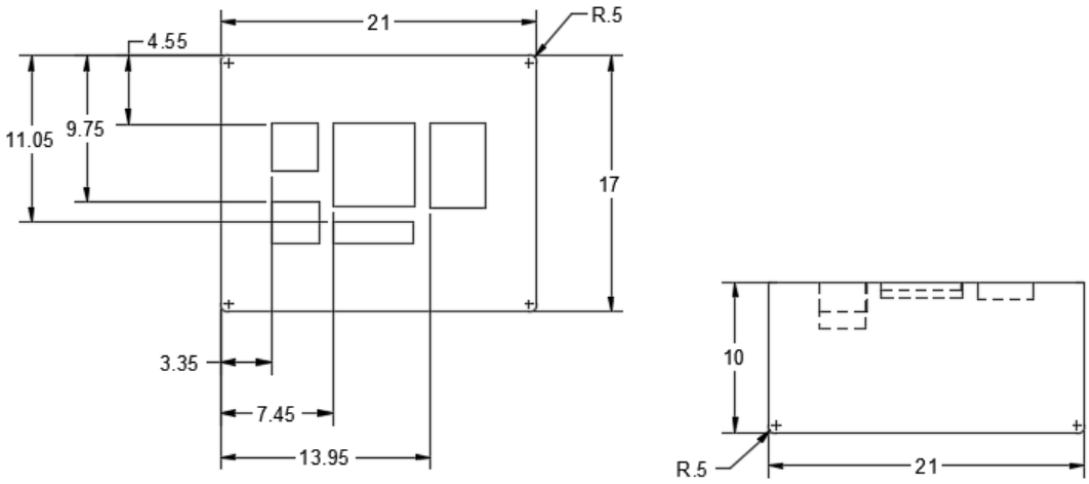


Figure 20: Foam layer of the first trial box drawings, units in inches

The top lid also has a foam layer that is simply fitted into the recess. This is to provide protection for the contents sitting on top in the body of the outer casing.

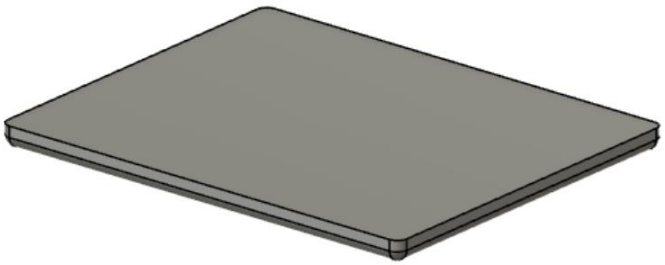


Figure 21: Foam layer in top lid of outer casing (~17 x 21 x 1”)

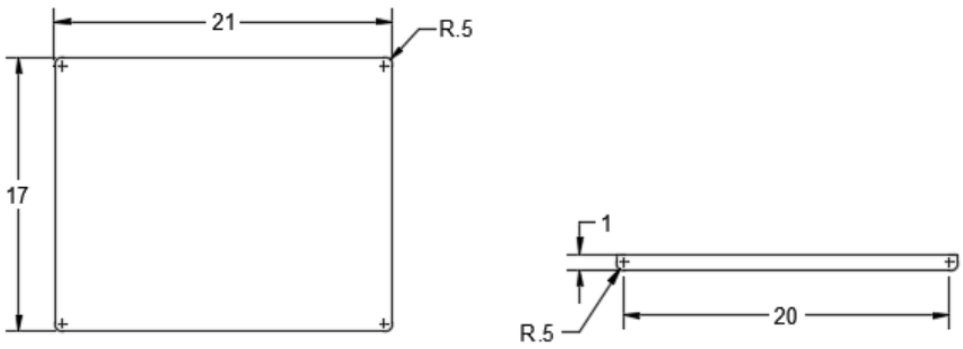


Figure 22: Foam layer in top lid of outer casing drawings, units in inches

The foam inserts and its cutouts are designed to snugly fit each of the devices as well as leave at least one inch of space between any two edges or surfaces. This includes between device cutouts as well as between the cutouts and all sides of the outer casing.

The following table describes how the proposed solution meets the customer needs that were considered throughout this process:

User Needs	**Importance (5 star scale)**	**Solution**
Outer Appearance		
Integrates well into the patient's environment	****	The outer aesthetic of the box can be easily branded and colored to meet these needs. The smooth outer surface of the outer casing allows for adhesives or post-processed lamination to be applied.
Appeals to different age demographics	***	
Is visually associated to the project/organization	*****	

Inner Layout		
Keeps the contents safe	***	The cutouts in the foam inserts safely secure each of the components as they are fitted to their specific dimensions. The outer casing will also feature a latch closure system that secures the box closed.
Is direct	*****	The layout of the devices in the foam inserts clearly shows the front of each device. At the bottom of each cutout will be a label, indicating the name of the device that should be placed there.
Functionality		
Is easy to open and close	*****	The latch closure system (as in a toolbox or standard Pelican case) will allow the patient to easily open and close the box. The hinges also allow it to open and close smoothly.
Materials		
Is sustainable	****	Both the outer casing and the foam inserts can be reused. When the patient returns specific items, they may place it back into the box and return them.
Is durable	****	The polypropylene outer casing and the secure latch closure and hinge system makes the box safe, keeping it safe from external damages.

Table 1: Solution features that meet customer needs

An additional design feature considered was a handle that would be attached to the top of the outer casing's lid. This would allow for anyone to easily carry and move the box.

The following is the material breakdown of each of the major parts of the box with additional detail as to their advantages:

Part	Material	Advantage
Outer Casing (Lid + Body)	Polypropylene	- Durable: resistant to external damages - Can be reused for future trials - Allows for easy return shipping
Foam Inserts	Polyethylene (Kaizen Foam)	- Known to be shock absorbent, vibration dampening, insulating, and cushioning in packaging applications - Multi-layered foam: easy to cut out the placement holes for the devices
Hinge	Polypropylene	- Durable - Smooth open and close
Latch Closure	Acrylonitrile butadiene styrene (ABS)	- Durable: withstands heavy use and adverse environmental conditions - Easy injection molding
Handle	Acrylonitrile butadiene styrene (ABS)	- Durable: withstands heavy use and adverse environmental conditions - Easy injection molding

Table 2: Materials List

3.9 Box Inventory Tracking System

Much like the device inventory tracking system detailed in section 3.7, individual boxes can be kept track of with an inventory management platform such as AppSheet or even just a basic database. This will keep track of which participants have yet to receive their boxes, which boxes still need to be shipped out, and which have been delivered successfully.

There should be enough boxes delivered from the manufacturer to satisfy all patients, including the need to send replacement boxes in case they are lost or damaged en route, or otherwise need extras. For this reason, there should be a healthy buffer of extra cases to be used in case issues arise. Because the box design is a reusable one, the boxes which are sent back from the participants after the trial is completed should be kept track of through this management system as well and prepared to be sent back out by replacing the foam and wiping down the box.

3.10 Box Assembly Plans

The boxes will need an assembly checklist for each individual clinical trial. The list of tasks will vary from trial to trial, and should be tailored to the specific needs of the current trial. This most likely includes making sure all the necessary materials and devices have been received, device setup to make data gathering as easy for the patient as possible, verifying all materials are in the box, marking the box with a nametag or writing the participants name on it, and sealing it. A simple example is shown below:

42.9%

#	Activities / Tasks / Items	Priority	Completed
1	~~Obtain all materials on the material list~~	High	✓
2	~~Setup pulse oximeter~~	High	✓
3	~~Setup electrocardiogram~~	High	✓
4	Setup Oura ring	High	
5	Add each item carefully to the box	High	
6	Take the specific QR code for this box and apply it to the lid	High	
7	Take nametag for this box and apply it to the lid	High	
8			
9			
10			

Figure 23: Assembly Checklist

A second checklist should keep track of which boxes have been completed, and thus will let the assembler know which box they are currently working on, and which ones will still need to be done.

24.0%

#	Activities / Tasks / Items	Priority	Completed
1	~~Box 01~~	High	✓
2	~~Box 02~~	High	✓
3	~~Box 03~~	High	✓
4	~~Box 04~~	High	✓
5	~~Box 05~~	High	✓
6	~~Box 06~~	High	✓
7	Box 07	High	
8	Box 08	High	
9	Box 09	High	
10	Box 10	High	
11	Box 11	High	
12	Box 12	High	
13	Box 13	High	
14	Box 14	High	

Figure 24: Completed box checklist

The details of each trial will differ from case to case, so an accurate checklist is pivotal to be obtained by working with the trial project owners.

3.11 Shipping and Delivery Management

Every participant ID will be connected to a shipping ID and the shipping will be done through FEDEX [13]. The package tracking available through FEDEX allows the researchers to determine which participants have received their packages, and which participants are still waiting. Further verification can be done through the initial telehealth video chat/phone call where the clinician can confirm that all devices were received and are accounted for, and that the patient has received the correct trial kit.

As mentioned in section 3.9, the data for shipping information and delivery management can be recorded in the inventory management software or a separate database for use by the clinicians. Because of the clinical trials with personalized trial kits such as custom-sized wearables or trials with placebo pills, it is important to have rigorous management of each shipped trial kit.

3.12 Returns

For both trials, some parts must be returned. The cutouts in the foam inserts for the specific devices that need to be returned will be colored and labeled. This will allow the patient to easily determine not only which items need to be returned but how to place them back into the box. The box will come with a set of instructions for how to proceed with the trial as well as instructions on how to return the package and a return shipping label.

Devices that are returned and received will need to be cleaned consistently and thoroughly. A set of instructions or checklist should also be created for this purpose for each device so that the data is wiped off the device consistently. Some devices may not need to be reset and can just be cleaned and put away.

In the case of partnership with a supplying medical device company, further communication for how to handle returned devices will need to be addressed, such as returning the devices back to the original packaging, or bagged and tagged, or however the company wishes to handle getting its materials back.

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