CLINICAL RESEARCH PROTOCOL

PROTOCOL TITLE:	**Aerosol BioContainment Device (ABCD) with Aerosol Clearance for Aerosol Generating Procedures**
IRB PROTOCOL #	**843373**
	NCT#: NCT04532112
INVESTIGATIONAL PRODUCT:	Aerosol BioContainment Device for containment of COVID-19-laden droplets and evacuation of COVID-19-laden aerosol during aerosol generating procedures
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PRINCIPAL INVESTIGATOR SIGNATURE

STUDY SPONSOR:	Dept. of Otorhinolaryngology: Head & Neck Surgery
STUDY TITLE:	Aerosol Biocontainment Device with Aerosol Clearance for Aerosol Generating Procedures
IRB PROTOCOL NUMBER:	843373
PROTOCOL VERSION	1.4

I have read the referenced protocol. I agree to conduct the study in accordance to this protocol, in compliance with the Declaration of Helsinki, Good Clinical Practices (GCP), and all applicable regulatory requirements and guidelines.

Principal Investigator Name		Signature	
Affiliation:	University of Pennsylvania	Date	

Abbreviations

ACH	Air changes per hour
ADE	Adverse Device Effects
AE	Adverse Event
ASA	American Society of Anesthesiologists
BiPAP	Bilevel Positive Airway Pressure
BMI	Body Mass Index
CDC	Centers for Disease Control and Prevention
CFR	Code of Federal Regulations
COVID-19	Coronavirus disease 2019
CPAP	Continuous Positive Airway Pressure
CPR	Cardiopulmonary Resuscitation
CRF	Case Report Form
CRNA	Certified Registered Nurse Anesthetist
CT	Computed Tomography
CTCAE	Common Terminology Criteria for Adverse Events
DCC	Data Coordinating Center
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practices
GMP	Good Manufacturing Practices
HIPAA	Health Insurance Portability and Accountability Act
HUP	Hospital of the University of Pennsylvania
ICH	International Conference on Harmonization
ICU	Intensive Care Unit
IDE	Investigational Device Exemption
IRB	Institutional Review Board
MedDRA	Medical Dictionary for Regulatory Activities
MERS	Middle Eastern Respiratory Syndrome
OHRP	Office for Human Research Protections
PAPRs	Powered Air Purifying Respirators
PHI	Protected Health Information

PI	Principal Investigator
PPE	Personal Protective Equipment
QC	Quality Control
SAE	Serious Adverse Event
SADE	Serious Adverse Device Effect
SARS	Severe Acute Respiratory Syndrome
SARS-CoV2	Severe Acute Respiratory Syndrome Coronavirus 2
SoA	Schedule of Activities
UADE	Unanticipated Adverse Device Effect
UP	Unanticipated Problem
US(A)	United States (of America)
UV	Ultraviolet

1 STUDY SUMMARY

1.1 Synopsis

Title:	Aerosol Biocontainment Device (ABCD) with Aerosol Clearance for Aerosol Generating Procedures
Short Title:	Aerosol BioContainment Device (ABCD)
Study Description:	The primary goal of this study is to assess use of a biocontainment device for planned airway procedures under general anesthesia. This will serve as a platform for using this device as a novel biocontainment and aerosol evacuation system as part of rapid sequence intubation protocols for COVID-19 patients. We hypothesize that airway procedures with the aerosol biocontainment device will be safe and effective with airway procedure times approaching times for airway procedures without the device.
Objectives:	The primary objectives of this study are: 1) Assess changes in airway procedure time with and without the biocontainment device as a function of repeated utilization and as a function of patient-associated airway factors (i.*e.* Mallampati score, hyomental distance, neck mobility, BMI) and user-associated airway factors (i.*e.* experience of user, airway device used, induction sequence) 2) Assess adverse events, adverse device events associated with biocontainment device use. Secondary objectives include: 1) Assess the subject's comfort with using the biocontainment device. 2) Assess for additional healthcare and cognitive burden imposed by the device. 3) Survey of patient's post-procedure on experience being inside the device. Exploratory objectives include gathering specific feedback regarding possible design modifications for further iterations and design improvements with the engineering team.
Primary Endpoint:	The primary endpoints of this study are: 1. Measuring the time for performing an airway procedure with the biocontainment device when accounting for patient and user-specific factors. 2. Quantifying the number of AEs or ADEs over time to assess device safety.
Secondary Endpoints:	The secondary endpoints include: 1. Median Likert ratings from device use survey questions that assess user subject device comfort. 2. Median Likert ratings from device use survey questions that assess user subject healthcare burden with the device. 3. Median Likert rating of the patient questionnaire results to assess patient experience in the device.

Study Population:	Frontline healthcare workers (anesthesiologists, CRNAs) involved in intubation (aerosol generating procedure) of COVID-19 negative patients undergoing scheduled procedures involving airway procedures under general anesthesia.
Description of Sites/Facilities	Trial sites to include HUP and PPMC locations where airway procedures under general anesthesia of COVID-19-negative patients will take place. This trial will be limited to Penn Medicine affiliated hospitals and take place solely within the United States.
Enrolling Participants:	Participants will include user subjects: anesthesiologists (attending, resident and fellow) and CRNAs performing airway procedures and patient subjects: patients undergoing scheduled airway procedures under general anesthesia.
Description of Study Intervention:	The intervention consists of an Aerosol BioContainment Device (ABCD) that will be placed around a patient prior to the airway procedure and remain in place throughout the airway procedure. The ABCD is manufactured by National Flag and consists of a re-useable frame with a disposable, plastic torso drape. This is a new device that has not been used previously in a healthcare setting.
Study Duration:	3 months
Participant Duration:	12 weeks

1.3 Schema

Week 1 through Week 4	Enrollment and Training

- Total n=5 anesthesiologists, 10 CRNAs/anesthesia residents/fellows (user subjects)
- Identify user subjects - anesthesiologists and their teams of CRNAs, anesthesia residents and fellows performing planned airway procedures under general anesthesia.
- Obtain informed consent from willing user subjects and complete intake questionnaire
- Document and record contact information for user subjects
- Review user manual and device use.

Week 1 through Week 6	Device Use and Assessment

- Protective device use and aerosol evacuation during airway procedures under general anesthesia on COVID-19-negative patients
- Patients (patient subjects) of anesthesiologists participating as user subjects in the study will be recruited on the day of procedure.
- Patient subjects will be randomized to intubation with or without the biocontainment device.
- Goal of obtaining data from 150 airway procedures under general anesthesia in the device (100 with the device and 50 without the device).
- Patient subject Data and data from record of airway procedure will be recorded after each device use
- Quality Use Survey, including documentation of any AEs will be completed by user subjects at the end of each day
- Patient experience questionnaire completed by patient subject randomized to device use within 1 week after procedure

• AE event summary reconciliation and review performed weekly • Feedback on quality use data use and user suggestions given to engineering team every two weeks • Interval assessment by the medical director of intubation data from medical record, quality use survey data, including summary of AEs, and preliminary analysis of post-training questionnaire/intake data every two weeks	
Week 4 through Week 12	Device Use and Assessment, Final Data Analysis
• Continued use and assessment of biocontainment device if needed to meet enrollment numbers • Final Feedback on device use and user suggestions given to engineering team • Final assessment of survey data and device utilization	

2 INTRODUCTION AND RATIONALE

2.1 Study Rationale

As part of addressing the COVID-19 pandemic, there is an immediate and long-term need to better protect our frontal line healthcare workers involved in intubation and care of our critically ill COVID-19 patients. Aerosol generating procedures, such as intubation or extubation, put the immediate health care workers involved in the procedure at risk of contracting COVID-19 and potentially any other patient or staff who would walk into that room for 30 minutes and upwards of several hours, depending on the room air exchange rate and concentration and rate of virus expelled by an infected patient. There are a limited number of negative pressure rooms where contaminated air can be contained or cycled out, and *this is not an option in many emergency rooms or ICUs and will not be an option if we are in tents or buildings converted to a hospital treating COVID-19 patients*. Furthermore, with disruptions in supply chains, it has been necessary in many locations to ration and re-use N95 masks and other high-level respirators required for these aerosol generating procedures. This has the potential to place our healthcare workforce at increased risk for contracting COVID-19. The purpose of this trial is to evaluate the safety and feasibility of performing airway procedures using a biocontainment and aerosol protection device. *The ultimate goal is to utilize this device an additional layer of biocontainment and aerosol protection for frontline healthcare workers during aerosol-generating procedures with patients with highly contagious infectious diseases including COVID-19.*

2.2 Background

Clinical Significance

SARS CoV2 is a novel coronavirus that is a global health threat that has killed more than a million people and threatens the lives of thousands more in the coming days, weeks, and months. This global health threat is currently a pandemic that has already fundamentally altered our lives here in America and throughout the world. There is no established or definitively proven treatment at this time for SARS CoV2, while vaccine development is months to a year away from large scale deployment.

Viral transmission occurs through three routes, contact (touching infected surface and inoculating nose with virus), droplet (spray of droplets from an infected person onto another person – usually gets into upper airway but not deeper into the lungs), and aerosol (uptake of particles 10-100 microns into the upper airways (nose, sinuses), and direct uptake into the lungs of particles under 5-10 microns in size)[1]. The titer of SARS-CoV2 and duration of exposure necessary to infect a person by either droplet, contact, or aerosol exposure is currently unknown. Viral

loads in sputum from infected patients may be elevated compared to nasopharynx samples[2] suggesting that aerosol generated from the lower respiratory tract could contain higher viral loads. There is also evidence that aerosol can lead to gross contamination of surfaces with the virus, which can also increase the risk of disease spread[3]. There is evidence from the prior SARS and MERS outbreaks of aerosol transmission of disease as well as evidence of transmission during aerosol generating procedures[4,5]. There is evidence from SARS and MERS outbreaks as well as emerging evidence from the current COVID-19 pandemic that physicians who perform aerosol generating procedures and those present at the time of the procedure are at high risk for contracting the disease[4-7]. Aerosol generated from SARS-CoV2 (the virus causing COVID-19) remains viable in the air for at least three hours and based on the half-life of virus in aerosol (one hour), there is likely viability for at least six hours in a static environment[8]. Aerosol clearance from a room is highly dependent on the number of air changes per hour (ACH), which varies from location to location within and across hospitals. There are minimum standards for air changes per hour, with operating rooms tending to have the highest number of ACH (10-15). The location of the air exchange vents and air handlers relative to the patient position as well as the size of the room, patient respiratory rate and tidal volumes and temperature differential between the room and the patient also play a role in the rate of aerosol clearance.

Aerosol generating procedures include: intubation, extubation, non-invasive positive pressure support (CPAP, BiPAP), open suctioning of any patient with a breathing tube (either endotracheal tube or tracheostomy – done multiple times a day per patient), delivering nebulizer treatments to patients, head and neck procedures involving the nose, mouth or throat, bronchoscopy, and any delivery of oxygen over 6 liters per minute. Work with tuberculosis has been the basis for much of the guidance with infectious aerosol spread[9]. However, there is sparse data on the risk of infectious aerosol spread both during and after an aerosol generating procedure with viral diseases. From the SARS outbreak in the 2000s, there is some limited retrospective data that intubation is the highest risk procedure for infection from an aerosol generating procedure. Non-invasive ventilation may also have an increased risk of contracting an airborne infection, whereas tracheostomy, sputum collection, nasal cannula delivery of oxygen and tracheostomy suctioning had equivocal data on risks of contracting an infection[10]. It is unknown if this is due to breakdown in proper PPE use and hand hygiene protocols or specifically related to an increased risk of infection from airborne virus. Within the hospital are a large cohort of healthcare providers and staff involved in aerosol generating procedures. These include anesthesiologists, nurse anesthetists, otorhinolaryngologists, critical care physicians, interventional pulmonologists, trauma surgeons and emergency room physicians, operating room nurses and scrub technicians, nurses, advanced practitioners, and respiratory therapists. Current protocols for care of patients are significantly affected by COVID-19 due to risks of exposing health care workers during aerosol generating procedures. Furthermore, there is significant anxiety within the healthcare workforce at large in this country about the limited appropriate PPE and risks of contracting this disease for both healthcare workers and their families.

There are currently no FDA cleared, readily available systems for isolation and containment of aerosols during aerosol generating procedures. Hospitals have a limited number of negative pressure rooms or rooms with high air exchange rates that can minimize aerosol spread. The best available PPE at this time would be a PAPR or N95 with face shield for all involved staff, and these would not keep the room itself free of contamination. Since the onset of the COVID-19 pandemic, a simple plexiglass box with two open hand ports has been developed by multiple groups internationally and in the USA to contain the spread of droplets during aerosol generating procedures[11]. This box does limit mobility of the user during intubation and requires training and also does not protect fully against aerosol[11].

We have designed and built a biocontainment device (**Figure 1**) that will isolate the patients head and up to the level of the shoulders (**Figure 2**) and contain droplets and aerosol while also allowing healthcare workers to safely

perform aerosol generating procedures (i.e. intubate, extubate, deliver a nebulizer treatment or suction a patient). The device has additional hand ports on both sides for an assistant to safely help the primary proceduralist. There are also dedicated ports for lines or wires associated with equipment needed for aerosol generating procedures and the hand and instrument ports self-seal after removal of arms or instrument, respectively. The device will have the ability to clear suction which is currently undergoing additional rigorous testing in a laboratory setting. The goal is to have the capability in place to use hospital wall suction to safely clear the aerosol from the chamber to further minimize healthcare worker exposure and broader contamination of the room or hospital area.

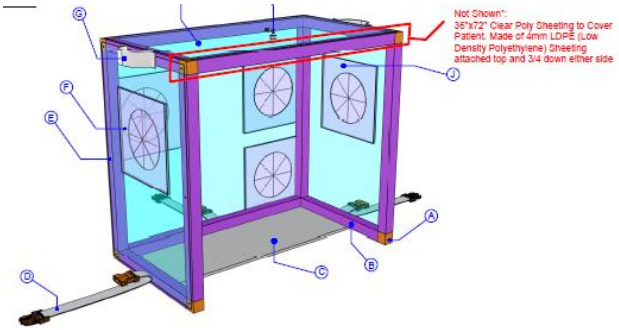

Figure 1: BioBox Device Schematic.

Figure 2: BioBox in simulated patient scenario.

Bench Data of Aerosol Evacuation and Suctioning Requirements

Particles under 100 microns are considered in the size range for infectious aerosol, however, particles in the single micron range will stay suspended for several minutes whereas particles in the 100s of nanometer and smaller range are considered small enough to "ride" the airflow and have a residence time well above tens of minutes. Coronavirus is on the order of 100 nm in diameter and exhalation of air from an infected patient could carry coronavirus on the water vapor exhaled with each breath. This condition of water vapor movement was used as an estimate for coronavirus flow in the air in a computational fluid dynamic model of virus flow from a patient's mouth assuming a baseline condition of quiet breathing (approximate airflow rate of 10 L/min). Airflow and concentration of the flow of water vapor (virus) were measured from a "patient" in an operating room setting assuming 10 air changes per hour and a room size of 6 m x 6 m x 3.5 m (**Figure 3A**). As seen in this figure, with 10 air changes per hour, the majority of the room remains safe, however, there is a danger space of approximately 1meter (~3 feet) around the patient's head where a healthcare worker would be exposed to high levels of aerosol (**Figure 3A**). Placement of the biocontainment device around the patient's head will help to contain these airborne particles within the device (**Figure 3B**), and enabling suction from the top of the unit approximately over the patients mouth at an airflow rate of 100 L/min (airflow rate from HUP wall suction), will create a streamlined movement of aerosol from the patient's mouth out of the device (**Figure 3C**), effectively containing and evacuating contaminated aerosol. Utilizing the suction continuously during the procedure will provide this streamlined movement of air and will help pull aerosol away from the healthcare provider during the procedure. There is an added benefit that this will also reduce the risk of device fogging during the procedure.

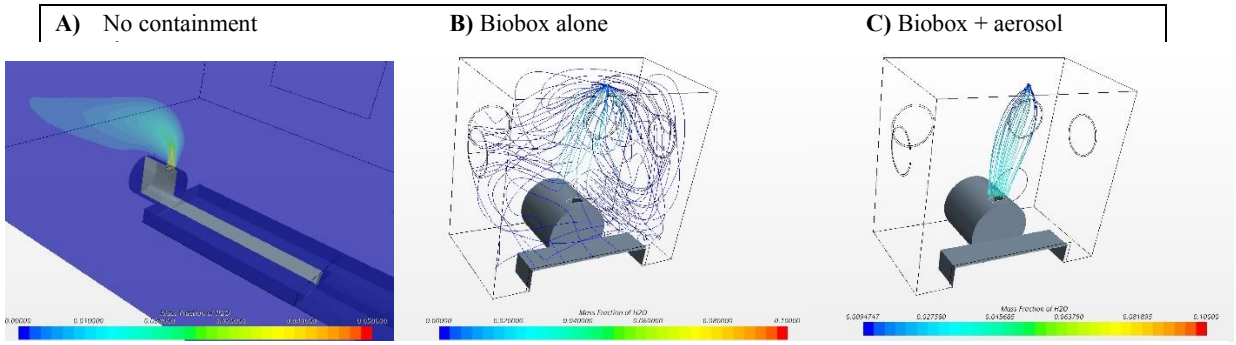

Figure 3: Computational Fluid dynamics modelling of mass fraction of water vapor exhaled by a "patient" at baseline (flow rate 10 L/minute). Flow of water vapor (virus) from the mouth in a simulated operating room (6m x 6m x 3.5m with 10 air changes /hour with (**A**) no containment, (**B**) biocontainment device alone and (**C**) biocontainment device with suction on at 100 L/min. Note the direction of airflow in sub-panel A will vary depending on the location of the air exchange vents and air handlers in the room as well as the room size. The "danger" zone for higher levels of water vapor (virus) exposure in the air is within 1 meter (~3 feet) of the patient's mouth.

Following completion of an aerosol generating procedure, the amount of time required to evacuate aerosol was calculated based on the volume of the biocontainment tent (~105 Liters), assuming minimal further aerosol generation and that there is a well-mixed environment in the device. **Figure 4** demonstrates the relationship between exhaust (suction) flow rate and amount of time required to remove 95% or 99% of aerosol. As seen in **Table 1**, wall suction rates between 50-100 L/min will be able to remove 99% of aerosol between 4.8 and 9.7 minutes post-procedure. Reducing the volume of the biocontainment device is an important factor that allows for more efficient clearance of aerosol and minimization of the amount of time the device needs to stay on a patient.

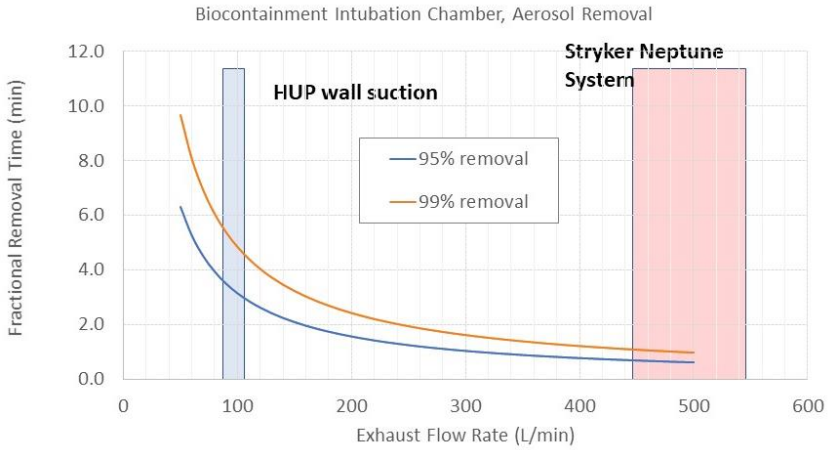

Figure 4: Time to evacuate aerosol post-procedure as a function of exhaust flow rate. Blue line depicts curve for removal of 95% of aerosol and orange curve represents curve for removal of 99% of aerosol. HUP wall suction is depicted by the blue shading and the Stryker Neptune System is depicted by the red shading.

Suction System	95% removal of aerosol	99% removal of aerosol
HUP wall suction (100L/min)	3.1 minutes	4.8 minutes
Wall suction (low) (50L/min)	6.3 minutes	9.7 minutes

Table 1: Time post-procedure for aerosol removal

We assessed droplet containment by spraying a fluorescein solution inside the device onto the inner aspects of the device frame, torso drapes and hand/instrument ports. The device appeared to contain all obvious gross droplet contamination (**Figure 5**).

Preclinical Feasibility for Use During Intubation

Figure 5: Fluorescent droplet containment in biobox as detected by UV light.

The device was tested for pre-clinical feasibility for performing intubation by an expert group of airway surgeons at HUP. The device weighs 9 lbs and could be easily lifted up by one person and placed over a patient. Assembly of the device took about 1 minute for 2 people to perform with the patient supine or upright. Assembly of the device could be performed by one person in less than 2 minutes with the patient completely supine. The device can be secured safely to an operating room table, stretcher, or hospital/ICU bed. With the safety straps in place, the device remains secure with the head elevated up to 70-degrees. Based on the current device design, there were no perceived limitations to access the arms, legs, or torso of a patient. *With the device secured, CPR could be performed in a simulated situation on a mannequin*. The device can accommodate patients of varying body habitus due to the rigid frame ending at about shoulder height and the utilization of a flexible torso drape to mold over the torso. Placement of required instruments was not impeded by the device. The largest device, an ambu bag, could easily be passed under the torso drape.

The device was designed to optimize angles of approach and mobility to perform an intubation. As a basis of comparison, the publicly described intubation box has arm ports about 10 inches apart. This is likely based on placing the hands on either side of an average sized head. Arm positioning during intubation is more easily performed when considering the forearms and hands as two limbs of a triangle converging on the airway. Based on the average length of a person's arm from fingertip to elbow (~18 inches), and ergonomic positioning to achieve right angles of the forearm at the elbows, the distance between arm ports should be farther apart than 10 inches. To accommodate wider positioning without over-extending the overall width of the device (currently 23 inches), the arm ports were positioned 15 inches apart from the midpoint of each port and the port sizes were expanded to 5 inches in diameter allowing for additional lateral and some vertical mobility of the arms in the ports. This allows for better triangulation of the hands onto the airways for a more natural approach to the airway. The novel self-sealing hand port septums allow for maintenance of chamber integrity with the larger diameter hand ports. There were no changes required in technique to safely perform intubation in a standard fashion with a mac blade in a simulated environment.

The team was subjectively comfortable with protection provided by the device. It was advised that the ventilation tubing be passed under the torso drape to limit the number of disconnects of the patient from the ventilator that would need to occur following intubation and device removal. There were no reflection or glare issues when using light sources inside the device. There was excellent visibility and optical clarity through the sides and top of the device and there are no anticipated issues with use of a videolaryngoscope or laryngoscope with adjacent video tower. Cleaning of the device with a bleach wipe did not affect optical clarity or leave streaks.

Potential Clinical Impact of Study

This trial will allow us to assess the safety and feasibility of intubation using a biocontainment and aerosol evacuation device in the controlled environment of the operating room. Briefly, the study is designed as a two-site, unblinded, randomized observational study to assess safety and feasibility of performing planned airway procedures by a small cohort of anesthesiologists with the biocontainment device in place around a patient. The goal of the study is to refine device protocols and labelling to provide frontline healthcare workers added protection with an effective biocontainment and aerosol evacuation device.

This project has the potential to have a profound positive impact on our care for COVID-19 patients. It will serve as a launching point to provide enhanced protection for our healthcare workers performing common aerosol-generating procedures for patients with COVID-19. This device may also allow for improved and easier transport of COVID-19-positive patients in the hospital for tests such as CT scans or transport between units. This additional level of protection will also provide a measure of safety and comfort to the front-line healthcare workers caring for patients with COVID-19. This trial may also serve as a basis to develop further aerosol protection systems for aerosol generating procedures in the clinic or aerosol generating surgeries in the operating room.

2.2.1 Assessment for Potential Study Products Drug-Drug, Drug-Device, Device-Device Interactions

This device does not interact with any drugs delivered to a patient. This device does not affect airflow to a patient while inside the device. This device does not contain a power source/electricity. This device has dedicated ports and flaps to accommodate instruments, cords or tubing required to perform the aerosol generating procedure. The device has the ability to connect to a suction system to evacuate aerosol contained within the device. This portion is still undergoing additional lab-based testing and suction set-up will be for simulation purposes only for this trial.

2.2.2 Clinical Adverse Event Profile

Anticipated adverse events (AEs) or adverse device effects (ADEs) associated with use of this device include, 1) injury to the patient subject (patient in ABCD) or user subject (healthcare provider), 2) patient subject claustrophobia. 3) patient subject anxiety, 4) difficulty performing intubation with or without requiring removal of the device. Serious adverse events (SAEs) or serious adverse device effects (SADEs) would include 1) major injury to the patient or provider. Unanticipated adverse device events (UADEs) would include device breakdown. Based on the pre-clinical simulations (intubation and CPR), there is a low risk of increased technical difficulty during intubation and the device remains firmly in place during chest compressions for CPR. There is minimal anticipated risk, as noted above, to the user subject or patient subject. The device will remain on a patient for the duration of an aerosol generating procedure and then for a defined period post-procedure to simulate aerosol evacuation.

2.3 Risk/Benefit Assessment

2.3.1 Known Potential Risks

Immediate Risks: There is still a risk of droplet or aerosol exposure to infectious agents, such as SARS-CoV2 (the virus causing COVID-19) with this device. This device does not eliminate that risk and does not replace current CDC guidelines for PPE during an aerosol generating procedure, proper donning, and doffing of PPE and hand hygiene. This device is intended for use *in addition to* recommended PPE during an aerosol generating procedure. Additional bench testing is ongoing to assess the efficacy of the device in containing aerosol and limiting aerosol escape.

There is a risk of device failure due to improper set-up or use of the device. There may be an increase in cognitive burden as a result of introduction of a new form of PPE which has been suggested previously as a source of risk in aerosol generating procedures[12]. The weight of the device is **9 lbs** and there is minimal risk of

injury to the user or the patient during setup and use with the device. All training material (written and audiovisual) must be reviewed and the initial survey completed prior to initiating use of the device.

There may be some variability in user comfort performing an intubation with this device. Based on our simulations and completion of the necessary training, there is likely to be minimal risk of a qualified user having device-related issues with intubation. In the event that the user feels the device is impairing their ability to safely intubate the patient, the device can be quickly removed by releasing the safety strap connectors and taking the device off the bed and proceeding to intubate without the barrier in place.

There is a risk of contamination from the device during removal of the device from the patient. PPE should be worn during removal and cleaning/disposal of the device.

There is a small risk of claustrophobia or anxiety for those patients in the device. This is a likely to be a minimal risk and this will be assessed as part of this study. All patients will be monitored while in the device and if they request to be taken out of the device or display signs of increasing anxiety/claustrophobia, the device will be removed.

Long-range Risks: There is a risk of device failure over time. Specifically, failure at seams, hand port septums, or straps. The integrity of the device should be assessed after each use and any obvious defects should be documented and the device removed from use. The free plastic sheeting over the torso will be disposable to reduce risks of cleaning a large plastic sheet and risks of the sheet developing tears or becoming dislodged from the device with repeated use. The device should be inspected after use for any physical tears or breaks in the frame or in the canopy and stored such that physical damage is limited. Parallel testing will also be ongoing in the lab setting with the engineering team as an added layer of assessing device durability, biocontainment and aerosol evacuation to get a complete picture from both a clinical use and engineering perspective on the number of times the device can be used reliably for biocontainment and aerosol evacuation.

2.3.2 Known Potential Benefits

Immediate Potential Benefits: This device offers an immediate benefit of providing an additional physical barrier for added protection of healthcare workers during aerosol generating procedures. The self-sealing hand and instrument ports offer a modular approach for enhanced safety of a patient during an aerosol generating procedure by allowing for additional assistance, if needed, during an aerosol generating procedure. Having a physical barrier in addition to standard PPE for aerosol generating procedures may also provide healthcare workers with an added layer of comfort and protection that they are better protected against contracting COVID-19 or other infectious diseases transmitted through droplet or airborne particles. This may decrease anxiety with regard to performance of aerosol generating procedures and this could improve the overall quality of the procedure.

The option for continuous suction provides a benefit of continuous evacuation of aerosol from the device during a procedure. This also offers the ability to clear contaminated air from the chamber after completion of an aerosol generating procedure to reduce the potential risk of spread of aerosol throughout the room and additional contamination of individuals and surfaces in the room.

Long-range Potential Benefits: The multiple hand and instrument ports also allows this device to be utilized for additional aerosol-generating procedures beyond intubation such as extubation, delivery of a nebulizer treatment, and open suctioning of a tracheostomy for a COVID19-treated patient. It may be feasible to use this

device for an extended period of time with positive pressure non-invasive devices such as a CPAP, BiPAP, or hiflow nasal cannula. The device in current form or with modifications outside the scope of this trial may also be useable for bronchoscopy. Use of these devices may allow for further adjustments to patient interaction protocols and allow for improved patient-care provider contacts which can enhance the quality of care and perceived level of care received by patients. There may be a long-term benefit of reduced healthcare worker risk of contracting COVID-19 or other droplet or airborne infectious diseases, which will allow for a long-term reduction in strain on the healthcare workforce by enhancing safety and wellbeing of frontline healthcare workers.

2.3.3 Assessment of Potential Risks and Benefits

The study subjects for this trial of a biocontainment device for aerosol generating procedures are frontline healthcare workers. The device is placed on top of a patient. The closest equivalent to this device is a face shield worn by a healthcare worker, which would provide no added significant risk to a patient for any procedure. This secondary "face shield" is placed over the patient as an added layer of protection during high risk procedures for generation of aerosols. Based on the results in Section 2 above, the preclinical risks of the device interfering with intubation, the most high-risk aerosol-generating procedure under investigation in this study, are small, but potentially could be serious if they occurred. **The primary goal of this study is to assess use of the device for planned airway procedures involving general anesthesia to better assess the feasibility for using this device as part of aerosol-generating procedure protocols for patients with highly transmissible (airborne or droplet) infectious diseases (i.e. COVID-19)**. The benefits of this device are adding an additional layer of PPE protection for high risk aerosol generating procedures that has the potential to reduce risk of contracting COVID-19. There is also a potential benefit of containment of infectious aerosols to reduce contamination of surfaces and equipment in rooms where aerosol generating procedures are performed which may help streamline patient care, workflow and sanitation procedures long-term.

Risk of injury to a study subject or patient from this device is minimal. The device is lightweight, sturdy with good optical clarity for performing aerosol generating procedures. Below is a breakdown of major risk/failure points and steps taken to mitigate and assess risk by topic.

Environment:

1. *Site or sub-site location for device use*. There is a future risk of non-uniform device use due to cultural and environmental differences among units and hospitals where the device will be used. The initial study will involve two sites that are in close physical proximity, work closely together and are part of the same health system (HUP and PPMC) which will help inform appropriate changes to the label/user manual for device use.

2. *Situation Urgency/Emergency*: Extubation and delivery of a nebulizer treatment or suctioning are all accomplished in an orderly and timely fashion. Intubation, depending on the urgency requires a highly coordinated and efficient response and a new device may create another layer of risk by introducing another step in the intubation process. The process for device utilization will require a work flow where the provider performing/assessing the need for intubation can understand the potential risks/benefits of proceeding with intubation. <u>The primary goal of this study is to assess use of the device for planned airway procedures under general anesthesia to better assess the feasibility for using this device as part of aerosol generating procedures for COVID-19 patients</u>.

People:

1. *Human Error*: Human error is the largest risk factor for proper use of the device. Error in understanding device function, device setup, or aerosol evacuation could lead to a false sense of security in use of the device. Improper device utilization also has a risk to cause harm to the study subject. For this reason, there is a robust audiovisual and written/pictorial training program for device use with a plan for assessment of device training. An additional goal of this study will be to assess number of device uses needed to obtain proficiency.

2. *Clinical Training and Experience*: Study subjects will have a wide range of experience and training. The goal of this study is to involve stakeholders with multiple years/levels of experience in intubation procedures. We intend to track outcomes based on these variables to assess for further needs for enhanced training, healthcare burden, and overall device utilization.

3. *Patient Risk:* There is a small risk of mild patient injury with the device as well as a mild risk of claustrophobia or anxiety to the patient in the device. Patient injury from the device, small risk of abrasion or contusion if the patient sits up inside the device is unlikely to occur, and would be an adverse event if it were to occur. The preclinical feasibility indicates that the most technically challenging procedure of intubation can be performed safely with this device. All patients will be monitored while in the device and if they request to be taken out of the device or display signs of increasing anxiety/claustrophobia, the device will be removed.

Materials:

1. *Supply Chain***:** Failure to secure a reliable supply chain for disposable elements of the device could result in inability to use device to fullest capacity and reduce effectiveness of protection against droplet and aerosol. Goal is to ensure reliable inventory of disposable components by keeping accurate logs of device use and remaining supplies, have an accurate estimate of need and burn rate for supplies and give manufacturing partner(s) adequate lead time for all components to be produced, shipped, and deployed in a timely fashion.

Methods:

1. *Device availability:* Each site/sub-site that is part of the study will have a designated storage location for units and associated disposable equipment. Given the restrictions on non-clinical staff in the hospital at this time, research coordinators/team members will not be onsite to bring equipment from storage to the room. The study PIs or subIs or study users will bring the device and associated components to the room for the procedure.

2. *Inability to perform intubation*: There is a small risk of inability to perform intubation with this device. The device has been designed to optimize hand positioning and mobility to triangulate the hands toward the patient's airway. The device safety straps have a quickly release function to rapidly remove the device and proceed with intubation if needed in the event the user has difficulty performing an intubation with the device in place.

Equipment:

1. *Device Failure*: Failure of the device is another potential source of risk. Device failure comes in multiple forms including structural failure due to repetitive use, damage during transport, damage during storage, manufacturing defects, damage during shipping. The design of the device has been simplified extensively to reduce the number of potential moving parts and structural failure points. The frame of the device also should not be susceptible to failure from repetitive cleaning over the course of the study period. To track any issues with a device, each device will have a unique identifier number that will be recorded on the Quality Use Survey with each device use. Devices will be inspected after being cleaned prior to storage for any signs of failure. The hand and instrument ports as well as the torso drape are additional point of device failure from repetitive use. The torso drape is a single use item that can be easily disposed of in a biohazard waste bin. The hand ports, frame and siding will be monitored and if signs of device failure/breakdown, the device will be logged as broken and taken out of circulation.

3 STUDY OBJECTIVES AND ENDPOINTS

The objectives of this study are to evaluate efficacy of training and use by frontline healthcare workers of a biocontainment system that provides additional protection during aerosol-generating procedures with COVID-19 patients. The primary objectives of this study are: 1) Assess changes in airway procedure times with and without the biocontainment device as a function of repeated utilization and as a function of patient-associated airway factors (Mallampati score, hyomental distance, neck mobility, BMI) and user-associated airway factors (experience of user, airway device used, induction sequence) and 2) Assess adverse events, adverse device events associated with biocontainment device use. Secondary objectives include: 1) Assess the subject's comfort with using the biocontainment device, 2) Assess for additional healthcare and cognitive burden imposed by the device. 3) Survey of patient's post-procedure on experience being inside the device. Exploratory objective includes gathering specific feedback regarding possible design modifications for further iterations and design improvements with the engineering team.

OBJECTIVES	**ENDPOINTS**	**JUSTIFICATION FOR ENDPOINTS**
Primary		
1. Assess changes in airway procedure times with and without the biocontainment device as a function of repeated utilization and as a function of patient-associated airway factors (Mallampati score, hyomental distance, neck mobility, BMI) and user-associated airway factors (experience of user, airway device used, induction sequence). 2. Assess adverse events, adverse device events associated with using the biocontainment device.	1. Measuring the time for performing an airway procedure with the biocontainment device when accounting for patient and user-specific factors. Sub-analysis, based on user experience level. 2. Quantifying the number of AEs or ADEs over time to assess device safety. Breakdown of AEs/ADEs as a function of time and by user subject.	These endpoints were chosen to assess the safety and efficacy of biocontainment device use over time. This will help assess the viability of the device as an additional layer of protection for aerosol-generating procedures.
Secondary		
1. Assess the user subject's comfort with using the biocontainment device. 2. Assess for additional healthcare and cognitive burden imposed by the device.	1. Median Likert ratings from device use survey questions that assess user subject device comfort.	These endpoints will provide additional information on the perceived quality of the device relative to

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Survey of patient's post-procedure on experience being inside the device	2. Median Likert ratings from device use survey questions that assess user subject healthcare burden with the device. Sub-analysis based on user experience level 3. Median Likert rating of the patient questionnaire results to assess patient experience in the device.	increased healthcare burden for frontline healthcare workers as well as any perceived patient discomfort.
Exploratory		
1.Assess feedback on device for iterative engineering and design improvements	Obtain broad feedback from end users on device use, function and design. Take information back to the engineering team for further design iterations or offshoots for other aerosol generating procedure applications.	To provide feedback for further device improvement and future projects.

4 STUDY PLAN

4.1 Study Design

This is a multi-site (HUP, PPMC), unblinded, randomized, observational study performed in a controlled environment in the operating room. The hypothesis is that rapid sequence intubation or other urgent airway procedures performed with the biocontainment device will be safe and can be performed in an equivalent manner to urgent airway procedures without the biocontainment device. Methods to minimize bias include randomizing patients to intubation with or without the biocontainment device. Stratification of results will be performed as described in Section 9.4.7 below.

4.2 Scientific Rationale for Study Design

Briefly, the protocol is designed as a safety and feasibility study of airway procedures under general anesthesia using a biocontainment and aerosol evacuation device. The goal of the study is to refine device protocols and labelling with the goal of providing frontline healthcare workers additional protection.

4.3 End of Study Definition

A participant is considered to have completed the study if he or she has completed all phases of the study including the last user questionnaire after final use of the device as shown in the Schedule of Activities (SoA), Appendix Section 12.1.

5 STUDY POPULATION

5.1 Inclusion Criteria

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

A) User Subjects (healthcare workers):

1. Anesthesiologist, anesthesia resident, anesthesia fellow, or CRNA at the Hospital of the University of

Pennsylvania or PPMC who has signed and dated informed consent.

B) Patient Subjects:
1. Provision of signed and dated informed consent form
2. Stated willingness to comply with all study procedures and availability for the duration of the study
3. ASA I, II, III
4. Undergoing planned procedure involving an airway procedure under general anesthesia
5. Age 18 years or older

5.2 Exclusion Criteria

An individual who meets any of the following criteria will be excluded from participation in this study.

A) User Subjects (healthcare workers):
1. Pregnancy (due to potential risks from lifting the device)

B) Patient Subjects:
1. Known history of difficult airway
2. Anticipated difficult airway management for any reason
3. COVID-19 positive status
4. Planned prolonged intubation post-surgery or anticipated inability to answer patient questionnaire within 1 week of intubation.

5.3 Lifestyle Considerations

There are no associated lifestyle considerations required for patients participating in this study as their direct device involvement is limited to the single time in the device. No limitations on interactions outside of the hospital will be required by the device users or patients.

5.4 Screen Failures

Screen failures are defined as participants who consent to participate in the clinical trial but are not subsequently randomly assigned to the study intervention or entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

5.5 Strategies for Recruitment and Retention

User Subject Recruitment and Retention

User-subjects will be recruited from within the department of anesthesia at HUP or PPMC. They will be approached in person or via email asking for participants in a trial of a biocontainment device for planned airway procedures under general anesthesia. Information provided will include length of time for study participation, participation in device training session, participant eligibility including willingness to use the device during procedures and lift up to 10 lbs, and participant requirements in the study (completion of surveys post-utilization and training). Healthcare workers (user subjects) will be recruited based solely on these criteria

and will include attending physicians, residents, fellows, and CRNA. No specific gender, age, race or ethnicity criteria will be used in the recruitment of subjects. Fifteen (15) to twenty (20) user subjects will be recruited at the study sites over the first month of the study. We anticipate full recruitment during this time. If targets are not met during the first month, recruitment will be ongoing during the second month of the study. Healthcare workers will be recruited solely on a voluntary basis with the option to withdraw at any time from the study without any form of penalty. The consent process will explicitly state that volunteering to participate in the study, declining to participate in the study, or withdrawal from the study will not affect employment status or access to appropriate PPE as determined by hospital protocols. This study is voluntary and no compensation or additional incentives will be provided.

Patient Subject Recruitment and Retention

Patient-subjects will be recruited from among the patients assigned to a recruited anesthesiologist's case-load. Given the constraints and timing of these assignments, the patient-subjects will need to be recruited on the day of the procedure. Patients will be approached by a study investigator or designee and asked about willingness to participate in study testing a new droplet and aerosol containment device for the anesthesia airway portion of the procedure. They will be informed that use of the device will not affect or influence their medical care. No specific gender, age, race, or ethnicity criteria will be used in the recruitment of subjects. The goal is to recruit 150 patients over weeks 1-6 of the study. We anticipate full recruitment during this time. Patient participation after completion of the study intervention in the operating room will be in the form of a survey with the goal for survey completion within 1-week of the intervention. Patients will be recruited solely on a voluntary basis with the option to withdraw at any time from the study without any form of penalty. This study is voluntary and no compensation or additional incentives will be provided.

6 STUDY INTERVENTION

6.1 Study Intervention(s) Administration

6.1.1 Study Intervention Description

The intervention consists of a biocontainment and aerosol clearance device that will be tested in the controlled setting to assess feasibility to perform airway procedures under general anesthesia with the device. There is no specific control device for this product. The control condition for this intervention will consist of airway procedures per routine clinical protocols without the biocontainment device. This study will be performed initially in locations where a patient would undergo a scheduled airway procedure under general anesthesia on non-COVID-19 patients. All participants in this study as well as non-participants who are present in the room during the airway procedure (aerosol-generating procedure) will continue to use appropriate level of PPE per hospital protocols and policies. This device does not replace standard aerosol-protecting PPE. The device likely falls into a class II device classification with the closest FDA-approved device consisting of a face shield. This device will be used as part of an abbreviated IDE as there is minimal risk to the subject as well as minimal risk to a patient during use of the device by a study subject (see **risk/benefit assessment** **Section 2.3** above). The device is not commercially available and is being used as part of this study.

The dimensions of the device are 23 inches (Width) x 20.5 inches (Height) x 13.5 inches (Depth). The frame is composed of aluminum with clear polycarbonate sides and top. The front of the box has two hand ports and one instrument port. The sides of the box have one hand port each. The top has a single suction port for aerosol evacuation. Hand and instrument port covers are multilayered vinyl and self-sealing. Suction tubing for

simulation of aerosol evacuation consists of standard suction tubing (Conmed tubing ¼ inch inner diameter) and the sheeting to cover the upper torso/close off the distal end of the device consists of a disposable, clear plastic sheet. This is a new device without a specific model number. Validation studies for this device are described in Section 2.2 above.

6.1.2 Dosing and Administration

The biocontainment device is designed to fit over the head and neck of a person and should accommodate shoulder width up to 23 inches (average biacromial distance in the United States is 14.1 inches for women and 16.1 inches for men). The portion of the device over the torso has a drop-down sheet that will fit over all patients regardless of body habitus and will function to contain droplet and aerosol. The biocontainment device has functionality to remove aerosol during and after a procedure. The device is designed to utilize the wall suction system, assuming wall suction at 70 L/min (rate at HUP – 100 L/min). The device is currently undergoing additional laboratory testing to assess aerosol containment and evacuation. The device will be connected to wall suction during this trial. Standard ¼ inch inner diameter suction tubing currently utilized in the hospital is attached to the suction port on the top of the device by an assistant or primary proceduralist. The suction tubing is connected to the wall suction. For the purposes of this trial on COVID-19 negative patients, this will represent an active suction process with aerosol evacuation which, in theory, would remain on for the duration of the procedure and the device and suction remain in place for 11 minutes post-procedure to ensure evacuation of 99.9% of aerosols (See **Figure 2 in Section 2 above**).

6.2 Preparation/Handling/Storage/Accountability

6.2.1 Acquisition and accountability

The biocontainment devices will be manufactured and shipped to the study sponsor. Devices will be distributed to designated storage areas in participating study site as designated by the site PIs/subIs. All devices will have a unique identification number for tracking of device location and use. Cleaning and storage of devices will be performed as described in the protocol (**See Section 6.2.4 below**). At the completion of the study, all devices will be cleaned as per the study protocol, placed in plastic/storage bags and stored by the sponsor in a designated locked, clean room prior to handling by other team members. Following evaluation of the devices by the PIs or their designees as well as the engineering team, the devices will be stored for an additional 3 months in a locked, clean room. When the entire study is deemed complete, the devices will be disposed of as biohazardous waste.

6.2.2 Formulation, Appearance, Packaging, and Labeling

The device will be manufactured by **National Flag/SBI.** The device will come as a re-useable frame with disposable plastic torso drape. The frame and hand and instrument ports can be cleaned with an antiviral wipe. Hospital grade suction tubing and a disposable torso drape will be provided with each device. Device labeling will include a unique identifier number on each device, clear indicators for orienting the device appropriately around the patient's head and clear markers for placement of suction tubing and the drape for sealing the distal portion of the containment device over the patient's torso. The device will come with a laminated quick-guide card with pictorial and written instructions for use as a quick reference. There will also be a laminated quick reference card for proper removal and cleaning of the device with an antiviral wipe, proper disposal of suction tubing and disposal of the torso drape.

6.2.3 Product Storage and Stability

The frame of the device will be stored in the designated storage area of the study site when not in use. Unused disposable suction tubing and torso draping will be stored along with the device in the designated units. The products are inert without moving parts or electronic components and will be stable for the duration of the study.

6.2.4 Device Preparation, Use, Removal and Cleaning

Device Assembly: The biocontainment device should be brought into the room prior to the procedure. Additional materials needed include the torso drape and the suction tubing (one or two tubing packets will be required depending on distance form device to wall suction).

The patient should be in position and secured properly per site protocol (i.e. with a safety strap with arms and legs appropriately positioned per protocol for procedures on an operating room table). Once this has occurred, the patient should be fully supine with the bed fully level at 0-degrees. The patient's head and the foam headrest should be gently lifted and the biocontainment device base slid under the foam headrest such that the base is centered on the operating room table and squarely on the "head" portion of the operating room table. The primary operator holds the device in place, and secures the front (head side) safety strap to the head of the bed. The left and right straps should then be secured on each side of the bed. Once the biocontainment device is secured, the torso drape should be applied and secured around the patient's torso, leaving small air holes around the patient's arms and the side of the device. To simulate use of the suction, the suction tubing should be secured to the suction port on top of the device on one end and the wall suction nozzle on the other end and the wall suction should be turned on.

Device Use: The anesthesia team should then ensure they have all equipment needed for the airway procedure readily available. The user team should then proceed with airway management technique deemed medically appropriate by the attending anesthesiologist. Note, the ventilator tubing should come out the open torso side under the torso drape. Ensure that air vents around the arms remain open during this time to pull clean air into the biocontainment device. All airway procedure related equipment can be removed during this time.

Device Removal: Following completion of procedure, the suction tubing should be disconnected from the wall and then from the device and disposed of in biohazard waste. The torso drape should be removed carefully and disposed of in biohazard waste. With two people and the patient flat at 0-degrees, the first user should hold the biocontainment device in place while the second person removes the safety strap from around the operating room table. A second member of the procedure team should gently hold the patient's head and the foam headrest, as per standard protocol for adjusting a sedated patient's head, and the first person should gently slide the device out from underneath the patient's head. The device should be placed gently out of the way for cleaning and storage.

Device Cleaning: Wearing gloves, the outside of the biocontainment device should be wiped clean with an antiviral cleaning wipe (bleach or peroxide based). The nylon strap should also be fully wiped down, rolled up and secured in a loop. Attention should be given to carefully wiping down the external layers of the hand and instrument ports. Following cleaning of the outside of the box, an antiviral wipe should then be used to carefully clean the inside of the box paying special attention to clean both layers of the inner aspect of the hand and instrument septums. The device should be allowed to air dry prior to storage and re-use.

Device Storage: See Section 6.2.3 "Product Storage and Stability" above.

6.3 Measures to Minimize Bias: Randomization and Blinding

Randomization will be done to assign patients to intubation with or without the biocontainment device in a 2:1 fashion. This will allow for analysis of patient-related intubation factors as well as user-related intubation factors as part of the feasibility analysis. Blinding is not possible with this study as all users and patients will be aware of the presence of the device intervention. To help minimize bias in the data analysis, results of all data analysis will be assessed by a neutral, third-party with expertise in statistical analysis.

6.4 Study Intervention Compliance

Use of the device will be assessed based on review of videos of the procedures, completion of quality use surveys by user subjects, and completion of the surveys by patient subjects. Each device will have a unique identifier and will be assigned to a specific attending anesthesiologist. The unique device identifier and corresponding attending anesthesiologist for each device will be recorded electronically with each quality use survey. A device use log will be established electronically from this data. If a device needs to be replaced, this will be noted in the electronic log and the new device unique ID number will be added to the electronic device record. Due to constraints entering the hospital at this time by research personnel, completeness of the electronic device logs will be assessed every other week for the duration of the study.

6.5 Concomitant Therapy

User subjects will continue to utilize standard PPE for intubation in the operating room as per hospital policy.

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1 Discontinuation of Study Intervention

Discontinuation from active participation using the study device does not mean discontinuation from the study, and remaining study questionnaires not yet completed at the time of discontinuation should be completed as indicated by the study protocol. Discontinuation of device use would occur if the subject user is unable to perform the airway procedure with the device in place. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE) or ADE.

The data to be collected at the time of study intervention discontinuation will include the following:

- Completion of remaining study questionnaires, collection of patient clinical data and data regarding the intubation procedure from the medical record.

7.2 Participant Discontinuation/Withdrawal from the Study

Participants are free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a user subject from the study for the following reasons:

- Significant biocontainment device use non-compliance
- If any clinical adverse event (AE) or ADE, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation
- Participant unable to participate with device use for > 2 weeks.

An investigator may discontinue or withdraw a patient subject from the study for the following reasons:

- If any clinical adverse event (AE) or ADE, or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant
- If the participant meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation

The reason for participant discontinuation or withdrawal from the study will be recorded on the Study Withdrawal Case Report Form (CRF). Patient subjects who sign the informed consent form and are randomized to use the biocontainment device but do not utilize the biocontainment device may be replaced. Patient subjects who sign the informed consent form and are randomized and use the biocontainment device, and subsequently withdraw, or are withdrawn or discontinued from the study, will be replaced.

7.3 Lost to Follow-Up

A participant will be considered lost to follow-up if he or she fails to complete study questionnaires and is unable to be contacted by the study site staff.

The following actions must be taken if a participant fails to comply with completing the study questionnaires:

- The PI will attempt to contact the participant and assist with completion of the questionnaires and counsel the participant on the importance of completing the surveys and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant. These contact attempts should be documented in the participant's study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENT AND PROCEDURES

8.1 Efficacy Assessments

User Subject Enrollment: Anesthesiologists (attendings, fellows, residents) and CRNAs who perform airway procedures under general anesthesia will be screened and recruited to the study as described in **Section 5** above. The anesthesia attendings work in teams with the residents and CRNAs and therefore, each anesthesia attending user subject will be assigned a unique identifier number and a unique biocontainment device that also has a unique ID number. This information will be collected as part of the device use forms to track the use of each device during the trial. User data to be collected includes first and last name, contact phone number and email address, age, gender, years of experience, healthcare degree, and training level.

User Subject Device Training: User subjects will undergo training on use of the biocontainment device as described in the Device preparation, use cleaning and storage **Section 6.2.4**. This will include in person or video demonstration of device use, review of a written user guide and an opportunity to setup and use a demo unit. Training will also include reviewing reporting any AEs, SAEs, ADEs or UADEs to the PI or qualified designee.

Patient Subject Recruitment: Patients who are undergoing airway procedures under general anesthesia who are assigned to the user subject's usual case-load will be recruited on the day of the procedure for the study. Inclusion and exclusion criteria will be as described above in Section 5. Recruitment will take place on the day of the procedure as cases and assigned providers can shift at the last minute and this will help ensure enrollment efficiency for patient subjects in the study. The on-site participation of the patient in the trial is limited to the actual scheduled procedure that includes an airway procedure under general anesthesia.

Airway procedure and patient data collection: Patient data and data from the anesthesia data record will be collected by PIs or their qualified designee post-airway procedure. As a result of social distancing and minimizing personnel due to COVID-19, it may not be possible to have a member of the research team present to observe and record data from each procedure. The airway procedures will be recorded using a GoPro camera placed in a fixed position. Data from the memory card will be transferred to an institutionally secured and managed network drive. Device use data will be collected from the videos by the PI or qualified designee. This data will include length of time to setup the device, length of time to perform the airway procedure, length of time to remove the device, number of times hand ports were used per procedure, and positioning of the torso drape. Patient data collected from the medical record will include patient demographics, contact information (phone and email), age, gender, race, co-morbid conditions (i.e. cardiac disease, lung disease, diabetes, BMI), smoking status. Airway procedure-related data that will also be collected will include BMI, hyomental distance, Mallampati score, type of airway procedure performed, number of attempts to perform the airway procedure, devices used for airway procedure, use of mask ventilation, anesthesia sequence used, and experience level of person performing the airway procedure.

Quality Use Survey and Safety Data Collection: As part of the study, user subjects will complete a Quality Use Survey after each day using the device. The results of the survey will be transferred from hard copies or REDCap to electronic format in CTMS for storage. This survey will collect user information on device functionality, perceived benefit of device use, healthcare burden associated with the device and safety data associated with device use. Safety data collected will include: 1) injury to the patient subject (patient in ABCD) or user subject (healthcare provider), 2) healthcare provider perceived patient subject anxiety or claustrophobia, 3) difficulty performing intubation with or without requiring removal of the device, 4) observed device defects or failures (i.e. broken strap, crack in plexiglass, break in hand ports).

Patient Subject Experience Survey: The patient subject's randomized to device use will be asked in the recovery room post-procedure or receive a phone call or email with REDCap survey link from a qualified study coordinator to answer a short patient experience survey where the data will be collected in REDCap and subsequently transcribed into CTMS. Data collected will include: 1) overall comfort in the device, 2) sensation of increased anxiety, 3) sensation of claustrophobia, 4) perceived safety in the device, 5) any difficulties seeing or hearing while in the device, 6) any additional comments or suggestions regarding the experience in the device. All data will be collected on a Likert scale and stored in CTMS.

Patient subjects' medical records medical will be accessed as part of the study. Personal and medical data collected as part of the study will be stored in a de-identified fashion on an institutionally secured and managed network drive and/or computer.

As part of this study, user subjects' medical records will NOT be accessed. Personal data including age, and gender, will be collected as part of the initial data collection instrument and stored in de-identified fashion on an institutionally secured and managed network drive and/or computer.

8.2 Safety and Other Assessments

Unanticipated problems posing risks to subjects will be reported to the Penn IRB using the form: "Unanticipated Problems Posing Risks to Subjects or Others Including Reportable Adverse Events" or as a written report of the event (including a description of the event with information regarding its fulfillment of the above criteria, follow-up/resolution and need for revision to consent form and/or other study documentation).

Copies of each report and documentation of IRB notification and receipt will be kept in the Clinical Investigator's study file.

The following events are reportable to the Penn IRB:

- Breach of confidentiality
- Change to the protocol taken without prior IRB review to eliminate apparent immediate hazard to a research participant.
- Protocol violation (meaning an accidental or unintentional deviation from the IRB approved protocol) that in the opinion of the investigator placed one or more participants at increased risk or affects the rights or welfare of subjects.

This study will be unblinded. The Sponsor monitors the safety and clinical efficacy of the protective device and analyze outcome measures to determine whether or not the trial should proceed or be aborted. Study questionnaires will be completed after training and questionnaires on device utilization will be completed after each device use and transferred into electronic format. Dedicated research personnel will be present for each device. Data collection and monitoring will occur remotely. The trial will continue if and only if no clinically significant adverse events or unanticipated device failures are observed. The interval assessment of design changes based on subject feedback will not be incorporated into the current design used for this study. Subjects would be informed of device modifications and updated user instructions and training would be provided.

It is the responsibility of the Sponsor to oversee the safety of the study at their site. This safety monitoring will include careful assessment and appropriate reporting of adverse events as noted above, as well as the construction and implementation of a site data and safety-monitoring plan. Medical monitoring will include a regular assessment of the number and type of adverse or serious adverse events.

Electronic data will be stored on an institutionally secured and managed drive and/or in the Velos/PennCTMS system. Only authorized study personnel will have access.

8.3 Adverse Events and Serious Adverse Events

8.3.1 Definitions

8.3.1.1 Adverse Event/Adverse Device Effect

An ***adverse event*** (AE) or adverse device effect (ADE) is any untoward medical occurrence (sign, symptom, or experience) that develops or worsens in severity associated with the use of the biocontainment device, whether or not considered intervention related. Intercurrent illnesses or injuries should be regarded as adverse events. A pre-existing condition should be recorded as an adverse event if the frequency, intensity or the character of the condition changes. Abnormal results of the intervention are considered to be adverse events if the abnormality:

- results in study withdrawal
- is associated with a serious adverse event
- is associated with clinical signs or symptoms
- leads to additional treatment or to further resource utilization (diagnostic tests/procedures)
- is considered by the investigator to be of clinical significance

8.3.1.2 Serious Adverse Events (SAE)

Adverse events are classified as serious or non-serious.
A ***serious adverse event*** is any AE that is:

- fatal
- life-threatening
- requires or prolongs hospital stay
- results in persistent or significant disability or incapacity
- a congenital anomaly or birth defect
- an important medical event
- required intervention to prevent permanent impairment or damage to participant or subject

Important medical events are those that may not be immediately life threatening, but are clearly of major clinical significance. They may jeopardize the subject, and may require intervention to prevent one of the other serious outcomes noted above. For example, drug overdose or abuse, a seizure that did not result in inpatient hospitalization, or intensive treatment of bronchospasm in an emergency department would typically be considered serious.

All adverse events that do not meet any of the criteria for serious should be regarded as **non-serious adverse events.**

8.3.1.3 Unanticipated Adverse Device Effect (UADE)

An unanticipated adverse device effect (UADE) is any serious adverse effect on health or safety, or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

8.3.2 Classification of an Adverse Event

8.3.2.1 Severity of Event

Adverse events will be classified based on the defined grading system:

- Mild: events require minimal or no treatment and do not interfere with the participant's daily activities
- Moderate: events result in low level of inconvenience or cause some inference with functioning
- Severe: events interrupt a participant's usual daily activity. Severe events are usually potentially life-threatening or incapacitating. Please note, the term "severe" does not necessarily equate to "serious".

8.3.2.2 Relationship to Study Intervention

All adverse events (AEs) and ADEs must have their relationship to the study device assessed by the PI who examines and evaluates the participant based on temporal relationship and his/her clinical judgment. The degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be considered.

- Definitely Related – The AE/ADE is known to occur with the device.
- Probably Related – There is a reasonable possibility that the device caused the AE, or there is a temporal relationship between the device use and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the device and the AE/ADE.
- Possibly Related - There is a possibility that the device caused the AE, or there is a temporal relationship between the device use and event. There is no evidence to suggest a causal relationship between the device and the AE/ADE but an alternate etiology has not yet been established.
- Unrelated – There is not a reasonable possibility that the use of the device caused the event, there is no temporal relationship between the use of the device and event onset, or an alternate etiology has been established.

8.3.2.3 Expectedness

Expected adverse events associated with this study that will be tracked and reported include:

1. Minor injury to the patient subject or provider
2. Patient claustrophobia
3. Patient anxiety
4. Difficulty performing intubation with the device in place
5. Need to remove the biocontainment device to safely perform intubation

Potential SAEs associated with this study would include:
1. Major physical injury to patient or provider due to device failure.

A UADE for this device would be breakdown or malfunction of the device during use.

The Sponsor medical director is responsible for determining whether an adverse event (AE) or ADE is expected or unexpected. An AE or ADE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the risk information listed in the Investigational Plan.

8.3.3 Time Period and Frequency for Event Assessment and Follow-Up

Safety will be assessed by monitoring and recording potential adverse effects using the quality use survey and the patient survey questionnaire as defined in Section 1.3. Participants will be monitored by these questionnaires. Any adverse events/ADEs are captured and shared with study PIs and the Sponsor. AEs and SAEs will be assessed for daily and completeness of surveys (data integrity) will be assessed weekly.

The investigator will seek information on adverse events by non-directive questioning. Adverse events may also be detected when they are volunteered by the clinician utilizing the device. Information on all adverse events will be recorded in the source documentation. To the extent possible, adverse events will be recorded as a diagnosis and symptoms used to make the diagnosis recorded within the diagnosis event.

As much as possible, each adverse event or follow-up information will be evaluated to determine:

1. Severity grade (as described in Section 8.3.2.1 above)
2. Duration (start and end dates)
3. Relationship to the study treatment or process – (As described in Section 8.3.2.2 above)
4. Expectedness to study treatment or process – [Unexpected – if the event severity and/or frequency is not described in the investigator brochure (if applicable) or protocol].
5. Action taken with respect to investigational device or process (none, permanently discontinued, unknown, not applicable)
6. Whether the event is serious

Once an adverse event is detected, it should be followed until its resolution or until it is judged to be permanent, and assessment should be made weekly (or more frequently, if necessary) of any changes in severity, the suspected relationship to the study treatment, the interventions required to treat it, and the outcome.

8.3.4 Adverse Event Reporting

Reporting Period

Adverse events will be reported from the time of informed consent until study completion.

Investigator Reporting: Notifying the Study Sponsor and via the Medical Director.

Every SAE/UADE, regardless of suspected causality (e.g., relationship to study product(s)) must be reported to the medical director and sponsor within 24 hours of learning of its occurrence.
Recurrent episodes, complications, or progression of the initial SAE must be reported to the Sponsor as a follow-up to the original episode within 24 hours of the investigator receiving the follow-up information. A SAE/UADE considered completely unrelated to a previously reported one should be reported separately as a new event.

Send the SAE report to the Medical Director.

New information regarding the SAE or UADE will be reported as it becomes available and in the same manner that the initial SAE (i.e., MedWatch form). The investigator must follow the event to resolution or until the event is deemed and documented irreversible, whichever is longer.

Investigator Reporting: Local Reporting Requirements

The investigator will report AEs/ADEs and SAEs/UADES to the IRB/EC of record and other local regulatory groups per the local requirements. Additional reporting/requirements include: failure to obtain ICF, device recall/repair/disposal, change in risk determination, or FDA or IRB withdrawal of the study.

8.3.5 Serious Adverse Event Reporting

The study PI will immediately report to the sponsor any serious adverse event or UADE, whether or not considered biocontainment device related, including those listed in the protocol and must include an assessment of whether there is a reasonable possibility that the biocontainment device caused the event.

New information regarding the SAE or UADE will be reported as it becomes available and in the same manner that the initial SAE/UADE (i.e. SAE form). All serious adverse events (SAEs) and UADEs will be followed until satisfactory resolution or until the site investigator deems the event to be chronic or the participant is stable. Other supporting documentation of the event may be requested by the study sponsor and should be provided as soon as possible.

The SAE and UADE reports along with the PI's assessment are to be sent to the Sponsor medical director within 24 hours. AEs and ADEs are to be entered into CTMS weekly, no later than 7 calendar days after each event. The sponsor and medical director will review these events no less than weekly.

The study investigator shall complete an Unanticipated Adverse Device Effect Form and submit to the study sponsor and medical director and to the reviewing Institutional Review Board (IRB) per IRB policy. The study sponsor is responsible for conducting an evaluation of an SAE/UADE and shall report the results of such evaluation to all reviewing IRBs and FDA as applicable.

8.3.6 Reporting Events to Participants

SAEs and UADEs will be reported to study user subjects within 24-hours of assessment completion by the Study sponsor and medical director.

8.3.7 Events of Special Interest

Not Applicable.

8.3.8 Reporting of Pregnancy

Potential User-Subjects who are pregnant are excluded from this trial due to any potential risks associated with lifting the device. If a study participant becomes pregnant, they should inform the PI team. They do not need to disclose pregnancy status as the reason for study withdrawal.

9 STATISTICAL CONSIDERATIONS

9.1 Statistical Hypotheses

We hypothesize that the biocontainment device will be a safe and effective option for performing airway procedures in patients while also providing additional protection during an aerosol generating procedure.

Primary Efficacy Endpoints:

1. We hypothesize that the time to perform an airway procedure with the biocontainment device will be equivalent to time for airway procedure without the biocontainment device. Alternatively, there will be prolonged airway procedures times with the device. This endpoint will be analyzed every two weeks.

2. We anticipate that the number of AEs or ADEs will be low and will also decrease over time. This endpoint will be analyzed on a weekly basis.

Secondary Efficacy Endpoints:

1. We hypothesize that the median Likert ratings for User subject device comfort will be weighted toward "strongly agree". Alternatively, we will see ratings favoring "neutral" or "disagree" for user subject device comfort.
2. We hypothesize that the median Likert ratings for User subject additional healthcare burden comfort will be weighted toward "strongly disagree". Alternatively, we will see ratings favoring "neutral" or "agree" on increased healthcare burden.
3. The median Likert ratings for the Patient Experience survey will be weighted toward minimal patient discomfort or anxiety. Alternatively, we will see ratings favoring increased patient discomfort or anxiety inside the device.
3. We anticipate that the median Likert ratings of the patient experience post-survey will indicate overall good user comfort and low levels of anxiety or claustrophobia in the device.

9.2 Sample Size Determination

Statistical calculations:
Sample size (for unknown population size) was determined based upon a 95% confidence level (Z-score 1.96), standard deviation of 0.5, and a margin of error (confidence interval) of 10%. [qualtrics.com/experience-management/research/determine-sample-size]

- Necessary Sample Size = $((\text{Z-score})^2 * \text{StdDev}*(1-\text{StdDev}))/(\text{margin of error})^2$
  - $((1.96)^2 * 0.5*(1-0.5))/(0.1)^2 =$
  - $(3.8416 * 0.25)/(0.01)=$
  - 96.04
  - **At least 97 performed airway procedures are needed to have adequate power to test our hypotheses for this study**

We will screen at least 175 patients, and assuming a 10-15% drop-out/screen failure rate, plan to enroll at least 150 patient subjects on a rolling basis during weeks 2 - 6 of the trial to evaluate the use of a novel biocontainment and aerosol evacuation system. The study should be adequately powered to assess secondary endpoints. Some of the sub-analyses may be underpowered depending on the characteristics of the recruited patients.

At defined intervals (see Section 1.3 Schema), we will perform interim analysis to determine changes to sample size based on subject drop out/withdrawal.

9.3 Populations for Analyses

For this study, a per-protocol analysis dataset will be obtained. Participants (user and patient subjects) who complied with the protocol will be used to create a dataset. This population for analyses will in effect allow us to analyze outcomes related to the advantages and disadvantages of the protective device of interest. For example, the number of proceduralists who utilized the protective device, overall device utilization and perceived comfort level, added healthcare burden and training level with the device.

9.4 Statistical Analyses

9.4.1 General Approach

Descriptive statistics:

- The number of subjects who utilized the protective device will be included; the level of experience and training of user subjects will be included.
- Patient subject baseline demographics, co-morbidities, smoking status, and intubation-related factors will be included.
- Objective data regarding total time for the airway procedure, number of intubation/LMA/extubation attempts, airway device used (i.e. intubation blade used and size of ETT) will be included.
- The user subjects comfort level for device use will be graded on a continuous scale, and the mean comfort level calculated as well as the range.
- The patient subjects comfort level and experience in the device will be graded on a continuous scale, and the mean comfort/experience level calculated as well as the range.
- Categories for various healthcare burdens will be provided as options for participants; the mean for most common burden will be identified; the percentage for each burden subtype will also be identified.

Inferential Tests

- A p-value of 0.05 and 95% confidence interval will be utilized when determining if the protective device results in an improvement in outcomes measures, i.e. a decrease in the number of COVID-19 cases by participants.
- Chi-square testing or ANOVA will be used.

Covariates will be collected on participants, including but not limited to subspecialty training, years of experience as a resident, fellow, or attending, as well as gender.

Assumption of normality of data points will be determined using Q-Q plots. If there are limitations to performing assumptions of normality, then appropriate non-parametric corrections would be performed.

9.4.2 Analysis of the Primary Efficacy Endpoint(s)

Primary Endpoints:

1. Assessment of time to complete an airway procedure with or without the biocontainment device. The time is measured as a single quantitative measure at the end of the procedure. The initial starting time (T0) is defined as “time the mask is removed from the patient just prior to initiation of the airway procedure”. End time (T1) is defined as the time that the airway procedure is completed with a secure airway defined as the

time the airway device is secured to the airway circuit. Data will be presented as median amount of time for a given procedure with or without the biocontainment device and statistical significance will be determined by analysis of variance (ANOVA). Additionally, a multiple regression model will be created using covariates of subject user experience, number of prior uses with the device, and patient specific factors (co-morbid conditions, BMI, Mallampati score). This will help determine the critical factors associated with time to use the device.

2. The total number of AEs and ADEs will be presented. This will be broken down by specific AE or ADE. Logistic regression will be used to assess possible contributing factors to AEs or ADEs including subject user experience, airway procedure performed, patient-specific factors (BMI, co-morbid conditions, Mallampati score). We anticipate a low number of AEs/ADEs and as such, statistically rigorous regression analyses may be limited by a low overall number of events.

Statistical analyses will be performed on all data points, however, a sub-analysis will be performed on participants without any missing data points.

9.4.3 Analysis of the Secondary Endpoint(s)

The secondary endpoints are not dependent on the primary endpoints.

1. Device Use Survey questions that are specific to the functioning of the device are collected as ordinal data on a Likert scale. Data will be presented as the median value with standard deviation for individual question results. Aggregate (summed) results for all questions will be also be assessed using the same methodology. Statistical significance will be determined using Chi-square test. Sub-analysis will be performed based on user subject experience level.

2. Device Use Survey questions that are specific to the healthcare burden associated with the device are collected as ordinal data on a Likert scale. Data will be presented as the median value with standard deviation for individual question results. Aggregate (summed) results for all questions will be also be assessed using the same methodology. Statistical significance will be determined using Chi-square test. Sub-analysis will be performed based on user subject experience level.

3. Patient experience survey results are collected as ordinal data on a Likert scale. Data will be presented as the median value with standard deviation for individual question results. Aggregate (summed) results for all questions will be also be assessed using the same methodology. Statistical significance will be determined using Chi-square test. Sub-analysis will be performed based on patient age, gender, co-morbid conditions, type of airway procedure performed.

Statistical analyses will be performed on all data points, however, a sub-analysis will be performed on participants without any missing data points.

9.4.4 Safety Analyses

Safety analyses is one of the primary endpoints and will be assessed as described in Section 9.4.2. Reporting of AEs, SAE, ADEs, UADEs is as described in Section 8.2.

9.4.5 Planned Interim Analyses

An interim analysis will be performed after 50% enrollment (approximately 4 weeks) on primary and secondary outcomes. If the total number of AEs or ADEs is trending upward over time, the study would be paused until further assessment of AE/ADEs by the study Sponsor or their qualified designee would be performed as described in Section 8.

9.4.6 Sub-Group Analyses

Primary and secondary endpoints will be analyzed in the context of gender (males versus females) age, and co-morbid conditions for patient subjects, and years of experience of the user subject.

9.4.7 Tabulation of Individual Participant Data

Individual participant data will be listed by measure and by time point.

9.4.8 Exploratory Analyses

Exploratory analyses will be performed throughout the study, namely assessing broad feedback on the device from end users for iterative engineering and design improvement. Modifications to the device are not planned during the trial period, and device changes will be judged based upon continual assessment via user feedback as described in the protocol above.

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 Regulatory, Ethical, and Study Oversight Considerations

10.1.1 Informed Consent Process

10.1.1.1 Consent and Other Informational Documents Provided to Participants

Consent forms describing in detail the rationale for the biocontainment device, use of the device, and risks are given to the participant. Additionally, written documentation of informed consent is required prior to participating in the study. No prescreening consent process is required. The following consent materials are submitted with this protocol: 1) User Subject Informed Consent, 2) Patient Subject Informed Consent. At this time, the primary subject of the intervention is the healthcare provider (user subject). Patient subject specific-data is collected and data from a patient survey will also be collected. Therefore, a separate consent will also be obtained from the patient.

10.1.1.2 Consent Procedures and Documentation

Informed consent 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. Consent forms will be Institutional Review Board (IRB)-approved and the participant will be asked to read and review the document. The investigator will explain the research study to the participant and answer any questions that may arise. A verbal 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. Participants will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants should have the opportunity to

discuss the study with their family or surrogates or think about it prior to agreeing to participate. The participant will sign the informed consent document prior to any procedures being done specifically for the study. Participants must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document will be given to the participants for their records. The informed consent process will be conducted and documented in the source document (including the date), and the form signed, before the participant undergoes any study-specific procedures. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

10.1.2 Study Discontinuation and Closure

This study may be temporarily suspended or prematurely terminated by the Sponsor or the PI at any site if there is sufficient reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the suspending or terminating party to the study participants, investigator, the Investigational New Drug (IND) or Investigational Device Exemption (IDE) sponsor and regulatory authorities, if applicable. If the study is prematurely terminated or suspended, the Principal Investigator (PI) will promptly inform study participants, the Institutional Review Board (IRB), and sponsor and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants
- Demonstration of efficacy that would warrant stopping
- Insufficient compliance to protocol requirements
- Data that are not sufficiently complete and/or evaluable
- Determination that the primary endpoint has been met
- Determination of futility
- Determination of SAE associated with device functionality as described in Section 7
- PI Contractual or GCP Breach

Study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB and/or Food and Drug Administration (FDA).]

In terminating the study, the Sponsor and the Principal Investigator will assure that adequate consideration is given to the protection of the subjects' interests.

10.1.3 Confidentiality and Privacy

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor(s) and their interventions. This confidentiality is extended to cover the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, the study records of the participants in this study. Access to personal medical records is not necessary for this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements. No documents are to be destroyed without Sponsor written consent.

Information about study subjects will be kept confidential and managed according to the requirements of the Health Insurance Portability and Accountability Act of 1996 (HIPAA). Those regulations require a signed subject authorization informing the subject of the following:

- What protected health information (PHI) will be collected from subjects in this study
- Who will have access to that information and why
- Who will use or disclose that information
- The rights of a research subject to revoke their authorization for use of their PHI.

In the event that a subject revokes authorization to collect or use PHI, the investigator, by regulation, retains the ability to use all information collected prior to the revocation of subject authorization. For subjects who have revoked authorization to collect or use PHI, attempts should be made to obtain permission to collect at least vital status (i.e. that the subject is alive) at the end of their scheduled study period.

Study participant research data, which is for purposes of statistical analysis and scientific reporting, will be transmitted to and stored securely in a Velos/Penn CTMS database. Video data will be secured on HIPAA-compliant Penn servers. This will not include the participant's contact or identifying information. Rather, individual participants and their research data will be identified by a unique study identification number. Each user subject and patient subject will have a unique identifier number.

Patient IDs

The study data entry and study management systems used by clinical sites and by Otorhinolaryngology research staff will be secured and password protected. At the end of the study, all study databases will be de-identified and archived at the Department of Otorhinolaryngology.

10.1.4 Future Use of Stored Data

De-identified Data collected for this study will be analyzed and then stored in a University HIPAA compliant, Velos/Penn CTMS database accessible only to authorized study personnel. No video data will be stored for longer than 14 days. After the study is completed, the de-identified, archived data will be available for use other researchers including those outside of the study upon written request. Permission to transmit and use the de-identified data will be included in the informed consent.

10.1.5 Safety Oversight

Safety oversight will be under the direction of the Sponsor and medical director.

10.1.6 Clinical Sponsor Monitoring

Sponsor monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), with International Conference on Harmonisation Good Clinical Practice (ICH GCP), and with applicable regulatory requirement(s).

10.1.7 Quality Assurance and Quality Control

All monitoring and audits are to be performed according to ICH GCP E6(R2).

Each clinical site will perform internal quality management of study conduct, data collection, documentation and completion. An individualized quality management plan will be developed to describe a site's quality management.

Quality control (QC) procedures will be implemented beginning with the data entry system and data QC checks that will be run on the database will be generated. Any missing data or data anomalies will be communicated to the site(s) for clarification/resolution. This will be accomplished by the database research coordinator.

Following written Standard Operating Procedures (SOPs), the monitors will verify that the clinical trial is conducted and data are generated, and specimens are collected, documented (recorded), and reported in compliance with the protocol, International Conference on Harmonisation Good Clinical Practice (ICH GCP), and applicable regulatory requirements.

The investigational site will provide direct access to all trial related sites, source data/documents, and reports for the purpose of monitoring and auditing by the sponsor, and inspection by local and regulatory authorities.

10.1.8 Data Handling and Record Keeping

10.1.8.1 Data Collection and Management Responsibilities

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported.

Hardcopies of the study questionnaires will be provided at each site for use as source document for data recording, for each participant enrolled in the study. Data recorded in the electronic case report form (eCRF) derived from source documents should be consistent with the data recorded on the source documents. All paper data/survey collection forms will be stored in a locked cabinet in a locked room with access only be qualified study personnel.

Clinical and survey data will be entered into a 21 CFR Part 11-compliant electronic data capture system (EDC) that includes individual user account level password protection. This EDC (Velos version 9) supports programmable data entry validation rules and edit checks to identify data entry errors.

All video recordings will be captured using a GoPro camera. Data will be transferred from the flash storage card to a HIPAA-compliant server behind the Penn Medicine firewall. Videos will be labelled with the de-identified unique patient ID number. Original videos will be deleted from the flash storage device upon upload

to the server. Videos will be analyzed with data points recorded in CTMS. All videos will be deleted within 14 days of download to the server.

10.1.8.2 Study Records Retention

Study documents should be retained for a minimum of 2 years after the last approval of a marketing application in an International Conference on Harmonization (ICH) region and until there are no pending or contemplated marketing applications in an ICH region or until at least 2 years have elapsed since the formal discontinuation of clinical development of the biocontainment device for aerosol generating procedures. These documents should be retained for a longer period, however, if required by local regulations. No records will be destroyed without the written consent of the sponsor, if applicable. It is the responsibility of the sponsor to inform the investigator when these documents no longer need to be retained.

10.1.9 Protocol Deviations

The PI and the study team should document all scenarios where the protocol is not followed and provide, in particular:

- Who deviated from the protocol
- What was the deviation
- When did the deviation occur
- How did the deviation happen
- What is the impact of the deviation
- A root cause analysis of why the deviation occurred

If the assessment is determined to be of limited impact (minor deviation), the documentation for this assessment and the outcome should be reported to the Sponsor at the time of annual report. Reporting to the IRB should follow specific local requirements.

If the assessment results in a determination that any of the following are potentially affected, the deviation would be considered of significant impact:

- having the potential to adversely affect subject safety; OR
- increases risks to participants; OR
- adversely affects the integrity of the data; OR
- violates the rights and welfare of participants, OR
- affects the subject's willingness to participate in research.
- there is a potential for an overall impact on the research that should be shared with the IRB for consideration and development of next best steps to address it

10.1.10 Publication and Data Sharing Policy

The Sponsor must approve all sharing of information/data prior to its occurrence.

10.1.11 Conflict of Interest Policy

The independence of this study from any actual or perceived influence, such as by the pharmaceutical or manufacturing industries, is critical. Therefore, any actual conflict of interest of persons who have a role in the design, conduct, analysis, publication, or any aspect of this trial will be disclosed to the Sponsor and managed.

Furthermore, persons who have a perceived conflict of interest will be required to have such conflicts managed in a way that is appropriate to their participation in the design and conduct of this trial.

10.2 Protocol Amendment History

Protocol modifications, except those intended to reduce immediate risk to study subjects, may be made only by the Sponsor team, with final approval from Michael Kohanski, MD, or the Medical Director. A protocol change intended to eliminate an apparent immediate hazard to subjects may be implemented immediately, provided the Sponsor and IRB/IEC is notified within 5 days.

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12 APPENDIX

12.1 Schedule of Activities (SoA)

Procedures	Screening/Enrollment User Subjects Week -1 to -4	Screening/Enrollment Patient Subjects Week1-12	Airway Procedure performed week 1-12
Informed consent	X	X	
Intake Questionnaire	X		
Device training	X		
Baseline Patient Data Collection		X	
Randomization			X
Administer study intervention			X
Collect airway procedure data from video and anesthesia records			X
Device Use Survey (user subjects)			X
Patient experience survey			X
AE, ADE review and evaluation			X

END OF DOCUMENT