Harvard University

# **Detailed Guidance for Human Subject Research: Respirometry and Spirometry**

This is specific guidance for preparing, operating, and cleaning respirometry and spirometry devices. In addition to the device specific procedures illustrated below, general human subject research guidance and research lab specific guidance will be followed during all research activities.

**Pre-Visit Screening Procedures**

* Call the participant and complete the Coronavirus Pre-Visit Screening Form using the participant script prior to visit.
* All study team members complete Coronavirus Screening Form.

**General Procedures**

* All study team members and the participant wash their hands upon arrival and after any physical contacts with other people.
* All study team members and the participant wear university-supplied surgical-grade facemasks at all times. Anyone who wants to take off the mask (for taking breaks or drinking water) does so at least 6 ft away from others and in advance notifies all the others present in the testing location to ensure adequate distancing during the break.
	1. Additional PPE such as face shields, goggles, sterile gloves, and gowns may be used for the participant and/or the study team members in any part of the study visit.
	2. After every use of reusable PPE (e.g. face shields), they are cleaned and sanitized using Lysol Disinfecting Wipes/Spray or equivalent.
		1. Note: See [EPA (US Environmental Protection Agency) website](https://www.epa.gov/pesticide-registration/list-n-disinfectants-use-against-sars-cov-2) for the full list of disinfectants for use against SARS-CoV-2.
	3. One exception to wearing surgical-grade facemask is when the participant wears a respirometry/spirometry mask. The respirometry/spirometry masks will be equipped with antibacterial/antiviral filters and cleaned/sanitized after every use. See below for details.
* During the study visit, up to two study team members can be present at the testing location, but no close contact occurs between them (i.e. the two persons cannot work on the same task together) and they should maintain a 6 ft distance at all times.
* During the study visit, only one designated study team member can make close contact (less than 6 ft apart) with the participant for all procedures that require close contact. Close contact should be minimized, and only occurs as outlined in **red** below and when otherwise required to ensure the participant’s safety.
	1. During close contact, the designated study team member wears a face shield, and if possible, the designated study team member and the participant face opposite directions.
	2. When additional PPE (e.g. face shields) are used during close contact, the designated study team member (i) first puts on his/her own PPE while maintaining 6 ft distancing, (ii) approaches to the participant and dons PPE for the participant, (iii) carries out the close contact tasks, (iv) doffs the PPE from the participant, and (v) takes 6 ft distancing from the participant and then takes off his/her own PPE.
* The participant’s personal belongings are placed in a designated storage space, and the study team members should not touch them.
	1. The participant may be asked to bring their own bottle of water. It will be placed near the testing site where the participant can access during breaks, and same with the other belongings, the study team members should not touch the water bottle.
* All materials are handled on a clean/sanitized surface, e.g. desks or benches. Anything below the waist level is considered as unclean surfaces.
* After every study visit, all non-disposable items used in the testing should be cleaned/sanitized and stored in sealable containers. Each container will have a label and a log to track when and who cleaned the contents, and the containers shouldn’t be re-open until the next use; otherwise, the contents should be cleaned/sanitized again.

**Procedures for Sable Respirometry Systems**

* Preparation
	1. One person calibrates the Sable Systems devices prior to the experiment. In particular the flow generator will be turned on to generate negative pressure (i.e. a vacuum) prior to interaction with the participant. Thus, once the mask is placed on the participant, he/she will only be inhaling filtered air (see below). Additionally, once the mask is placed over the nose and mouth, all exhaled air will be isolated from the researchers and expelled from the laboratory (see below).
	2. The Sable Systems Respirometry devices will be set up following order:
		1. We will use only masks without inspiratory valves to allow for air filtration prior to inhalation/exhalation by the participant. Specifically, inspired air that enters the mask will come through a 6 ft tube with a disposable antibacterial/antiviral filter placed between the initial 6 ft tube and the participant mask (with a rubber connector) to isolate the atmosphere from the inhaled/exhaled gas by the participant. This tube will be sterilized between experiments in bleach solution as described below.
		2. Exhaled air from the participant mask attaches to a 6 ft tube connecting to the flow generator (Flowkit);
			1. The exhaust air from the Flowkit is vented from the Flowkit out of the laboratory window via additional tubing and an additional pump;
		3. Subsampled air from the Flowkit enters the subsampler;
		4. Air from the subsampler is filtered through CO2 and H2O scrubs before entering an O2-analyzer and CO2-analyzer.
* Operation
	1. Before the data collection,
		1. The designated study team member (wearing full PPE) makes close contact with the participant for up to 2 minutes to fit the respirometry mask safely on the participant. To limit exposure, the mask will be handed to the participant who will fit it over his/her mouth and nose, isolating exhaled air from the researchers.
		2. The participant takes the surgical-grade facemask off and without breathing immediately dons the respirometry mask by themselves to minimize close contact. While masks are switched, the study team members will remain at least 6 ft away from the participant.
		3. Once the mask is over the participant’s nose and mouth, the researcher may need to help adjust the mask for a secure and safe fit, attaching the straps that secure the mask to the participant’s face. During this procedure, the participant holds the mask firmly against his/her face to maintain a tight seal. Doing so isolates the exhaled air from the researchers and makes sure the participant inhales purified air.
		4. O2/CO2 delay calibration process is done remotely to eliminate close contact.
	2. During the data collection,
		1. A study team member remotely monitors flow rate, energy expenditure and VO2 values using LabChart software.
	3. After data collection,
		1. The participant removes the respirometry mask and dons the surgical-grade facemask by themselves to minimize close contact. While switching between the two masks, the participant tries not to breathe in or out, and the study team members stay at least 6 ft from the participant.
		2. If needed, the designated study team member may make close contact with the participant for up to 2 minutes to help loosen/detach the straps holding the mask in place. Again, during this procedure, the participant holds the mask firmly against his/her face to maintain a tight seal. Doing so isolates any exhaled air from the researchers and makes sure the participant inhales purified air.
* Cleaning
	1. When cleaning, study team members wear disposable gowns and sterile gloves per CDC recommendation.
	2. One person cleans and sanitizes all hard components (device, cables, etc.) using Lysol Disinfecting Wipes/Spray or equivalent.
	3. One person cleans and sanitizes the respirometry mask, the mask straps, both 6 ft tubes attached to the mask, and the rubber connector for the antibacterial/antiviral filter, using Enzol detergent and CIDEX OPA. All equipment must be fully submerged in the disinfectant solution for a minimum of 10 minutes to ensure decontamination.
		1. Note: Enzol detergent and CIDEX OPA are not listed in EPA website as disinfectants for use against SARS-CoV-2. However, there are supporting data that suggest CIDEX OPA effectively kills lipid-type coronavirus such as SARS-CoV-2, and this is the recommended method of cleaning COSMED components by the supplier.
	4. Once the components are removed from the disinfectant, they air dry for 48 hours. They are then stored in a sealable container and with the date and time noted
	5. All dates of cleaning will be added to the cleaning log.

**Procedures for COSMED Respirometry Systems**

* Preparation
	1. One person prepares and calibrates the COSMED device.
		1. An antibacterial/antiviral filter is placed between the COSMED mask and the rest of the components (sampling line, turbine, inlet/outlet, etc.) to filter the inhaled/exhaled gas, using a 3D-printed connector provided by COSMED.
		2. Only the COSMED masks without inspiratory valves can be used to isolate the atmosphere from the inhaled/exhaled gas by the participant.
* Operation
	1. Before the data collection,
		1. The designated study team member makes close contact with the participant for up to 5 minutes to don the COSMED portable unit and hand over the COSMED mask to the participant.
		2. The participant takes the surgical-grade facemask off and dons the COSMED mask by themselves to minimize close contact. While switching between the two masks, the study team members keep at least 6 ft away from the participant.
		3. O2/CO2 delay calibration process is done remotely by COSMED OMNIA software to minimize close contact.
	2. During the data collection,
		1. A study team member remotely monitors VE value using COSMED OMNIA software and checks if it is lower than 100 L/min at all times.
			1. If not, stop the condition immediately and take a break.
		2. The designated study team member may make additional close contact with the participant for up to 3 minutes to replace the battery for the COSMED portable unit.
		3. The participant may be asked to change the disposable antibacterial/antiviral filter in between test conditions. A clean, unused, and packaged filter will be provided to the participant at necessary intervals. While the filter is being replaced, study team members will keep at least 6 ft away from the participant. A waste receptacle will be made available for the participant to dispose of the used filter.
	3. After the data collection,
		1. The participant takes the COSMED mask off and dons the surgical-grade facemask back by themselves to minimize close contact. While switching between the two masks, the study team members keep at least 6 ft away from the participant.
		2. The designated study team member makes close contact with the participant for up to 5 minutes to doff the COSMED portable unit.
* Cleaning
	1. When cleaning, study team members wear disposable gowns and sterile gloves per CDC recommendation.
	2. All used antibacterial/antiviral filters will be disposed of immediately after use.
	3. One person cleans and sanitizes the rest of the hard/non-porous components (device, cables, etc.) and textile components (harness, straps, etc.) using Lysol Disinfecting Wipes/Spray or equivalent. The COSMED sampling lines will be cleaned using Lysol Disinfecting Wipes/Spray or equivalent and will be stored in a sealed container for 72 hours before reuse, to mitigate any risk of contamination.
	4. One person cleans and sanitizes the COSMED mask, the COSMED mask straps, turbine, turbine cap, and the connector for the antibacterial/antiviral filter, using Enzol detergent and CIDEX OPA. They are soaked in Enzol detergent for more than 5 minutes and then soaked in CIDEX OPA for more than 10 minutes.
		1. Note: Enzol detergent and CIDEX OPA are not listed in EPA website as disinfectants for use against SARS-CoV-2. However, there are supporting data that suggest CIDEX OPA effectively kills lipid-type coronavirus such as SARS-CoV-2, and this is the recommended method of cleaning COSMED components by the supplier.
		2. COSMED mask straps are cleaned only by Enzol detergent, following the supplier’s recommendation.
	5. After drying them all, store the COSMED components in a sealable container and add time and date to the cleaning log.

**Procedures for Spirometry**

* Preparation
	1. One person calibrates the spirometry device prior to the participant’s arrival.
	2. The spirometry device will be set up following order:
		1. A participant mask with a one-way valve attaches to a 6-foot tube. The one-way valve set-up will have all expired air directed into the spirometer, thereby isolating expired air from the researchers;
		2. The 6 ft tube attaches to the spirometer.
	3. A disposable antibacterial/antiviral filter is placed over the intake valve on the participant mask (with a rubber connector) to isolate the atmosphere from the inhaled/exhaled gas by the participant.
	4. An additional disposable antibacterial/antiviral filter is placed between the release valve and the 6-foot tube to purify the exhaled air.
* Operation
	1. Before the data collection,
		1. The designated study team member makes close contact with the participant for up to 2 minutes to fit the mask safely on the participant. To limit exposure, the mask will be handed to the participant who will fit it over his/her mouth and nose, isolating exhaled air from the researchers via attached filters.
		2. The participant takes the surgical-grade facemask off and dons the mask by themselves to minimize close contact. While switching between the two masks, the participant tries not to breathe in or out as much as they can, and the study team members keep safe distance to the participant.
		3. Once the mask is over the participant’s nose and mouth, the researcher will help adjust the mask for a secure and safe fit, attacking the straps that secure the mask to the participant’s face.
			1. Note: During this procedure, the participant holds the mask firmly against his/her face to maintain a tight seal. Doing so isolates the exhaled air from the researchers and makes sure the participant inhales purified air.
	2. During the data collection,
		1. A study team member remotely monitors flow rate and tidal volume using LabChart software.
	3. After the data collection,
		1. The participant removes the mask and dons the surgical-grade facemask by themselves to minimize close contact. While switching between the two masks, the participant tries not to breathe in or out as much as they can, and the study team members keep safe distance from the participant.
		2. The designated study team member makes close contact with the participant for up to 2 minutes to help loosen/detach the straps holding the mask in place.
			1. Note: During this procedure, the participant holds the mask firmly against his/her face to maintain a tight seal. Doing so isolates any exhaled air from the researchers and makes sure the participant inhales purified air.
* Cleaning
	1. When cleaning, study team members wear disposable gowns and sterile gloves per CDC recommendation.
	2. One person cleans and sanitizes the hard components (device, cables, etc.) using Lysol Disinfecting Wipes/Spray or equivalent.
	3. One person cleans and sanitizes the mask, the mask straps, both 6-foot tubes attached to the mask, and the rubber connector for the antibacterial/antiviral filter, using Enzol detergent and CIDEX OPA. All equipment must be fully submerged in the disinfectant solution and remain so for a minimum of 10 minutes to ensure decontamination.
		1. Note: Enzol detergent and CIDEX OPA are not listed in EPA website as disinfectants for use against SARS-CoV-2. However, there are supporting data that suggest CIDEX OPA effectively kills lipid-type coronavirus such as SARS-CoV-2, and this is the recommended method of cleaning COSMED components by the supplier.
	4. Once the components are removed from the disinfectant, they air dry for 48-hours. They are then stored in in a sealable container and add time
	5. All dates of cleaning will be added to the cleaning log.

**Additional considerations depending on the type of experiments**

* Indoor treadmill testing
	+ Treadmills that can be remotely controlled by study team members should be used.
	+ The lab space will be divided into the participant's space (including the treadmill) and the study team members’ space, with any necessary close contact only occurring at the boundary. At least 6 ft must separate the treadmill and the study team members’ space, and these spaces will be marked on the floor. In case that 6 ft distance is not achievable, a plexiglass shield should be installed between the participant and study team members to achieve adequate isolation. During the data collection, no study team member enters the participant’s space unless otherwise required to ensure the participant’s safety.
	+ For Bertec instrumented treadmills, the designated study team member may enter the 6-ft boundary for up to 3 minutes to lock/unlock the treadmill before/after adjusting the slope of the treadmill.
	+ In case of using a safety harness, the designated study team member may make additional close contact with the participant for up to 5 minutes to don and doff the harness and connect it to the overhead hanger.
	+ In case of using a heart rate monitor, the designated study team member may make additional close contact with the participant for up to 5 minutes to don and doff the heart rate monitor.
* Indoor overground testing
	+ The lab space should be divided into the participant's space (e.g. the overground walking path) and the study team members’ space, with any necessary close contact only occurring at the boundary. At least 6 ft must separate the participant and the study team members’ space, and these spaces will be marked on the floor. In case that 6 ft distance is not achievable, a plexiglass shield should be installed between the spaces to achieve adequate isolation. During the data collection, no study team member enters the participant’s space unless otherwise required to ensure the participant’s safety.
		- In case of changing settings inside of the participant’s space during the study visit, the study team asks the participant to move away from the testing space so that the designated study team may enter the participant’s space while still maintaining 6 ft distancing.
	+ In case of using a safety harness, the designated study team member may make additional close contact with the participant for up to 5 minutes to don and doff the harness and connect it to the overhead hanger.
	+ In case of using a heart rate monitor, the designated study team member may make additional close contact with the participant for up to 5 minutes to don and doff the heart rate monitor.
* Outdoor overground testing
	+ The study team should check their own IRB-approved protocol for safety procedures for outdoor testings, e.g. the minimum number of study team members present, presence of CPR-trained members, etc.
	+ The study team selects relatively less crowded IRB-approved testing sites/routes, such as Middlesex Fells Reservation (4 Woodland Rd, Stoneham, MA 02180) or Mount Auburn Cemetery (580 Mt Auburn St, Cambridge, MA 02138), and testing should be scheduled avoiding the location’s popular times.
	+ Sealable containers should be used for transporting materials and devices. After testing, uncleaned materials are packed in sealed containers and brought back to a designated space for handling and cleaning these materials, e.g. motion capture lab. When cleaning, the containers used for transporting uncleaned materials should also be cleaned and sanitized using Lysol Disinfecting Wipes/Spray or equivalent.
	+ Except for the close contact instances outlined above, all study team members and the participant should keep 6 ft distance throughout the testing. Whenever possible, keep adequate distance from other pedestrians as well, e.g. to stop and wait until other pedestrian(s) to pass by.