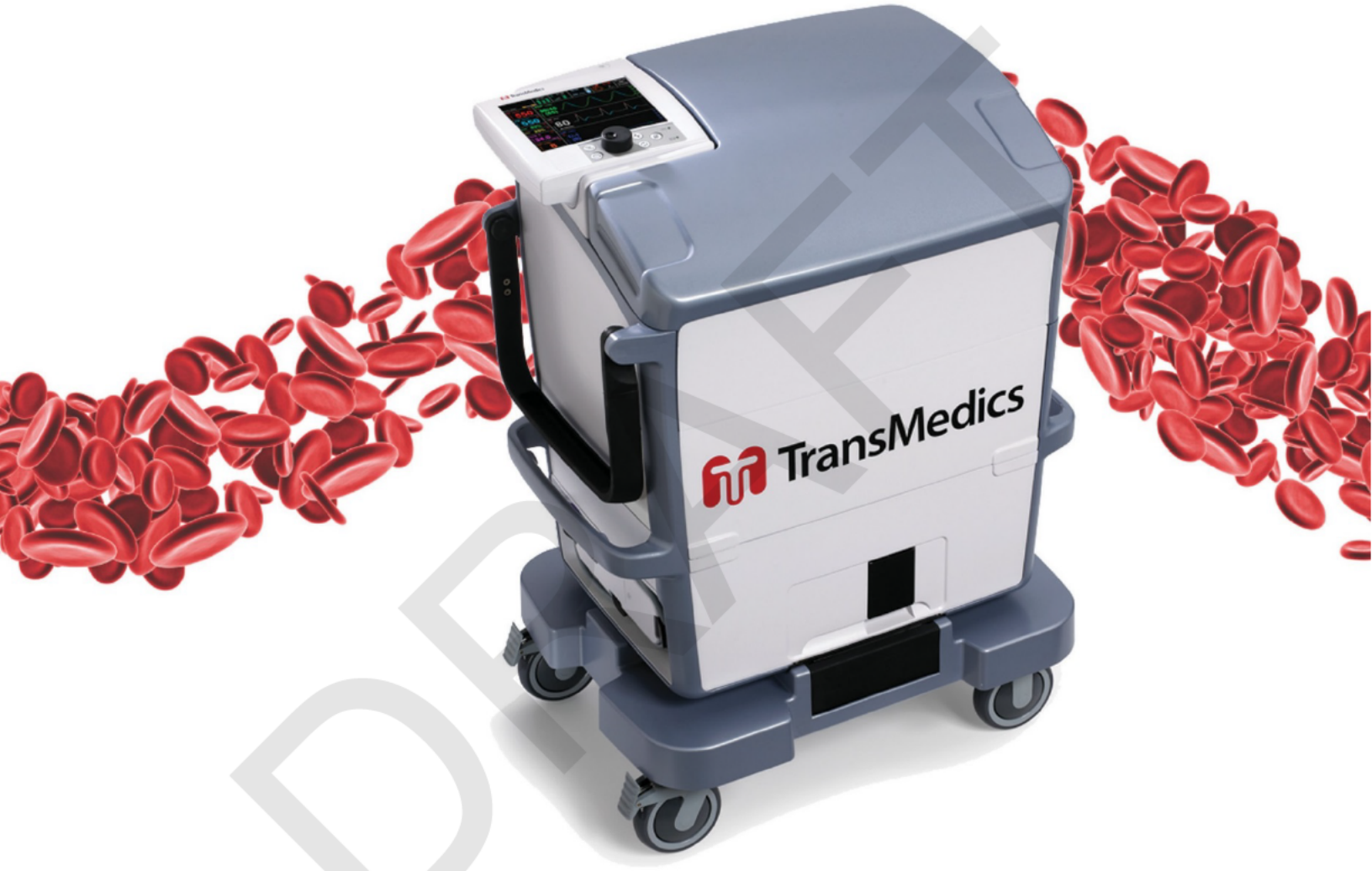
TransMedics® Organ Care System™

Clinical User Guide: OCS™ Lung System

Software Version 3.1.1
PN 100004071 Rev 2
REF 2102



CE (b) (4)

TransMedics

Manufacturer's Address:

TransMedics, Inc.
200 Minuteman Rd., Suite 302, Andover, MA 01810, USA
(b) (4)
Web: www.transmedics.com

This device complies with the Medical Device Directive 93/42 EEC.

(b) (4)
EC REP
(b) (4)

Patents:

U.S. Patents 6,046,046, 6,100,082; International Patents EU, UK, FR, ES, IT, BE, DK, FI, IE, LU, MC, NL, PT, CH, SE 1017274, DE 69819759.3-08, AU728233, ATE253819; Additional Patents Pending.

Manual PN & Rev
PN 100004070 REV 2

CAUTION: United States federal law restricts this device to sale by or on the order of a physician.

TABLE OF CONTENTS

GLOSSARY OF TERMS 10

1. CHAPTER 1: READ THIS FIRST 13

1.1. Intended Audience 13
1.2. Indications for Use 13
1.3. Contraindication 13
1.4. Warning 13
1.5. Using This Manual 13
1.6. Related Documents 13
1.7. Conventions 13
1.8. Customer Comments 14
1.9. Supplies 14
1.10. Contacting TransMedics 15

2. CHAPTER 2: OVERVIEW OF OCS™ LUNG SYSTEM 16

2.1. Overview of OCS™ Lung System Preservation Process 16
2.2. Overview of (b) (4) and (b) (4) 16
2.3. Clinical Study of the OCS™ Lung System 17

3. CHAPTER 3: ACTIVITIES PERFORMED BEFORE DEPARTURE TO DONOR SITE 18

3.1. Procedure Overview Checklist 18
3.1.1. For Clinical Support 18
3.1.2. OCS™ Lung Console Checklist 18
3.2. OCS™ Lung Gas Cylinders 19
3.2.1. (b) (4) Gas Cylinder 19
3.2.2. (b) (4) Gas Cylinder 19
3.3. OCS™ Lung Solution & Additives Checklists 21
3.3.1. For Donor Lung Flush 21
3.3.2. OCS™ Lung Perfusate & Additives 21
3.3.3. Perfusate Corrective Medications Checklist– (As needed & after every blood sample check) 22
3.4. Leukocyte Reduced Packed Red Blood Cells (pRBCs) Checklist 22
3.5. OCS™ (b) (4) Set Checklists 22
3.6. Run Bag Checklist and Contents 23
3.7. Transport Considerations 23
3.8. Preparing the OCS™ Lung System for Travel to Donor Site 24

4. CHAPTER 4: ACTIVITIES PERFORMED AT DONOR SITE 25

4.1. Unpacking, Installation, and OCS™ Lung System Setup 25
4.1.1. Unpacking and Inspecting the (b) (4) Set (LPS) 25
4.1.2. Unpacking and Inspecting the Sterile Components 25
4.1.3. To Open the LPM Packaging 25
4.2. To Install the LPM on the OCS™ Lung System 26
4.3. Attaching the Probes 29
4.3.1. Attaching the Pump Flow Probe 29
4.3.2. Attaching the SaO_2/Hematocrit and SvO_2/Hematocrit Probes 30

4.4. Running the OCS™ Lung System Self Test 31
4.5. Assessing Lungs in the Donor Chest 32
4.6. Preparing the OCS™ Lung System for (b) (4) 33
4.6.1. Priming the OCS™ LPM 33
4.6.2. Pause Preservation Mode 33
4.6.3. Priming the (b) (4) Module 35
4.6.4. Start of Perfusate Circulation 35
4.6.5. Injecting Additives Into the Perfusate and Preparing for Use 37
4.6.6. Evaluating Hematocrit and Reservoir Volume Level 39
4.6.7. Obtaining a Priming (Pre-Instrumentation) Blood Sample 39
4.6.8. Priming Blood Sample 39
4.7. Harvesting Donor Lungs 39
4.7.1. Administering Heparin 40
4.7.2. Donor Lung Flush, Clamping Trachea, and Stopping Ventilation 40
4.7.3. Preparing the Lung for the OCS™ Lung System (Cannulation & Instrumentation) 40
4.7.4. Securing TransMedics® Cannulae to Lung 40
4.7.5. Connecting and Securing the Trachea Cannula 41
4.7.6. Pulmonary Artery (PA) Cannulation 42
4.7.7. PA Reconstruction and Cannulation 43
4.8. Draping the Work Area In Preparation for Instrumentation 43
4.9. Instrumenting Lungs on the OCS™ Lung System 44
4.9.1. Instrumentation Sequence Overview 45
4.9.2. Connecting Trachea Cannula and PA Cannula to OCS™ Lung System 46
4.9.3. Initial Stabilization Overview 46
4.9.4. Warming the Lungs 47
4.9.5. Ventilation Start on the OCS™ Lung System 47
4.9.6. Bronchoscope Monitoring Mode (Overview) 48
4.9.7. Wrapping the Lung 48
4.9.8. Steps of Lung Wrapping 48
4.9.9. Applying Banded Bags/Sterile Covers 49
4.9.10. End of the Initial Stabilization Phase 50
4.10. Initial (Baseline) Monitoring Overview 51
4.10.1. Assessing Lungs at Donor's site Prior to Transport 51
4.10.2. Continuous Monitoring Mode Timing and Settings 51
4.11. Continuous Monitoring Mode 52
4.11.1. Steps of Performing Continuous Monitoring Mode (Baseline at donor site) 52
4.12. Preservation Mode 54

5. CHAPTER 5: ACTIVITIES PERFORMED DURING TRANSPORT 56

5.1. Preparing for Transport 56
5.2. Managing the Lung and OCS™ Lung System During Transport 57
5.2.1. Throughout Transport Ensure and Monitor the Following: 58

6. CHAPTER 6: ACTIVITIES PERFORMED AT RECIPIENT SITE 59

6.1. Recipient Site Evaluation 59
6.1.1. Final Recruitment in Preservation Mode 59

6.2. Final Monitoring/Overview 60
6.2.1. 1-Continuous Monitoring Mode Timing and Settings 60
Performing Continuous Monitoring Mode (Final): 60
6.2.2. 2-Physical Bronchoscope Monitoring 61
6.2.3. 3-Physical Assessment in Organ Chamber 62
6.3. Final Implantation Decision 63
6.4 [redacted] Termination Options 63
6.4.1. 1- Double Lung Cooling Techniques 64
6.4.1.1. A- Double Lung Flush Using Cold Buffered OCS™ Lung Solution 64
6.4.1.2. B- Lung Perfusate Cooling on the OCS™ Lung System Followed by Cold Flush 68
6.4.2. 2- Cooling One Lung at a Time While Perfusing the Second Lung 69
6.5. Performing the Shut-Down Protocol 71
6.6. Preparing the OCS™ Lung System for Shutdown 71
6.7. Removing the Probes from Tubing 71
6.8. Disconnecting the Ventilator Lines 72
6.9. Turning off the [redacted] Gas 72
6.10. Removing and Disposing of the [redacted] Module 72
6.11. Preparing the OCS™ Lung System for Storage 72
6.12. Steps of Resetting the OCS™ Lung System 73

7. CHAPTER 7: CRITICAL SCENARIOS AND TROUBLESHOOTING 74

7.1. If PEEP Can Not be Maintained During Preservation 74
7.2. If Mean PAP, VR and/or PAWP is Rising at Same Ventilation and Perfusion Settings 75
7.3. To Recruit Lungs with Atelectasis 75

APPENDIX A. OCS™ LUNG SYSTEM INSPIRE STUDY 76

1. Study Objectives and Endpoints 76
2. Secondary Effectiveness Endpoints 76
3. Safety Endpoint 76
4. Study Population 77
5. Study Treatments 77
6. Analysis Populations 77
7. Demographic and Baseline Information 79
8. Donor [redacted] Characteristics & Critical Times 82
9. Primary Effectiveness Endpoint & Related Analyses 82
10. Patient Survival at Day 30 83
11. OCS Lung System Reduces the Incidence of PGD3 84
12. Safety Endpoint was Met 85
13. In-Hospital and Longer-Term Survival 86
14. Reduction in Mechanical Ventilation, ICU Stay and Hospital Stay 88
15. Freedom from BOS through 24 Months 88
16. Summary of Benefits and Risks of OCS Lung System 89
17. Summary of Adverse Events 90
18. Summary of INSPIRE Clinical Study 94

APPENDIX B. BODY WEIGHT FORMULA 96

LIST OF TABLES

Table 1: OCS™ Lung Solution Manufacturing Composition 21
Table 2: Additives 21
Table 3: Prophylactic Medications 22
Table 4: Priming Overview 34
Table 5: Additives for Perfusate Injections 37
Table 6: (b) (4) Tool Set 40
Table 7: Initial Stabilization Settings 46
Table 8: Setting Alarms 55
Table 9: Recipient Demographic and Baseline Characteristics (mITT Population) 79
Table 10: Donor Demographic and Baseline Characteristics (ITT Population, N=349, Combined Cohort) 81
Table 11: Safety Endpoint Analysis – (Average Number of LGRSAEs through the 30 days post-transplantation per patient) in Combined Cohort Safety Population 85
Table 12: Adverse Events by Type of Event; Safety Population (N=319) 90
Table 13: Adjudicated Serious Adverse Events by Preferred Term that occurred in ≥1% of Subjects; Safety Population (N=319) 91

LIST OF FIGURES

Figure 1: OCS™ Lung System Preservation Process Overview 16
Figure 2: Circulation and Ventilation Overview 17
Figure 3: (b) (4) Cylinder with Additional Differentiating Labels from (b) (4) Cylinder 20
Figure 4: Lifting the OCS™ Lung Console off the Mobile Base 24
Figure 5: OCS™ Lung System Probes Pulled to the Side of the LPM 26
Figure 6: Pump Head, Ventilator Actuator of the OCS™ Lung Console (A) and the Bellows Plate of the LPM (B) 27
Figure 7: Holding Clips Engaging with the LPM (A) and Ventilator Actuator Engaged with the Bellows Plate of the LPM (B) 27
Figure 8: Ventilator Lines Connection Port 28
Figure 9: Proper Connection vs. Wrong Correction of Ventilator Lines 28
Figure 10: Clamp onto the Oxygenator Recirculation Line 29
Figure 11: Closing the PA Flush Port 29
Figure 12: Pump Flow Position 30

Figure 13: SaO_2/HCT and SvO_2/HCT Probes 31
Figure 14: Wireless Monitor Controls 32
Figure 15: Pause Preservation Mode 33
Figure 16: (b) (4) Module Priming Inlet Port 35
Figure 17: Pulmonary Artery Stopcock in Open Position 37
Figure 18: Additive Injections 38
Figure 19: Reservoir of the (b) (4) Module 39
Figure 20: Tracheal Cannula Procedure 41
Figure 21: Cannula Alignment 42
Figure 22: Cannula-Tip Positioning 42
Figure 23: Reconstructed PA 43
Figure 24: Sterile Drape (Unfolding and Draping) 44
Figure 25: Sequence of Instrumentation 45
Figure 26: Steps of Lung Wrapping 48
Figure 27: Applying the Sterile Covers/Banded Bags 50
Figure 28: Continuous Monitoring Mode 52
Figure 29: Connecting (b) (4) Gas Cylinder to the Monitoring Port of OCS™ Lung System 52
Figure 30: Sampling From the Arterial Sampling Port between 120-180 sec in Continuous Monitoring Mode 54
Figure 31: Preservation Mode 54
Figure 32: Monitor Picture with Bottom Graphic Frame Set in Preservation Mode to display VR Trend vs. PAWP Trend 58
Figure 33: Bronchoscope Examination on the OCS™ Lung System through a Bronchoscope Port 62
Figure 34: PA Vent Line in Close Position 64
Figure 35: Connecting the Lung Flush Collection Bag to the Oxygenator Recirculation Line 64
Figure 36: De-airing the Termination Flush Port 65
Figure 37: Making a Wet-to-Wet Connection 65
Figure 38: Delivering Flush Solution 66
Figure 39: Clamping the PA Line 66
Figure 40: Monitor Screen Showing Pump is Turned off in the Pump Adjust Menu 67
Figure 41: Connecting the Recirculation line to an OR Heat Exchanger 69
Figure 42: Monitor in Situation with Un-maintained PEEP 74

Figure 43: Lung Injury with Blood Froth....75
Figure 44: INSPIRE Trial Enrollment Detailed Consort Diagram....78
Figure 45: Total Cross Clamp and Ischemic Times on Transplanted Lungs (As Treated Population)....82
Figure 46: Composite of All Cause Patient Survival at 30 days Post-Transplant and Absence of PGD grade 3 in The First 72 Hours (Primary Effectiveness Endpoint) (PP Population)....83
Figure 47: Survival at 30 Days in INSPIRE Trial (INSPIRE and Combined Cohorts, mITT and PP populations)....83
Figure 48: Incidence of PGD3 within 72 hours (INSPIRE and Combined Cohorts, PP Population)....84
Figure 49: Incidence of PGD3 within 72 hours (ITT Population, INSPIRE and Combined Cohorts)....85
Figure 50: 30-Day and In-Hospital Survival for OCS and Control Groups (INSPIRE Cohort and Combined Cohort)....86
Figure 51: Causes of Death for OCS and Control Groups (30-Day and In-hospital) – mITT Population, Combined Cohort....87
Figure 52: K-M Survival for OCS and Control groups at 24 Months (Combined Cohort PP Population)....87
Figure 53: Improvements in Ventilation Time, ICU Time and Hospitalization (PP, Combined Cohort)....88
Figure 54: BOS-Free Probability through 24 Months (PP, Combined Cohort)....88

LIST OF SYMBOLS IN THIS GUIDE

Symbol	Meaning
	Run/Standby button on Wireless Monitor
	Wireless Bluetooth link between the monitor and the OCS Lung system
	ON position for OCS™ Lung Console
	(b) (4) [redacted] icon on the Wireless Monitor screen
	(b) (4) [redacted] icon on the Wireless Monitor screen

	(b) (4) [redacted] mode icon on the Wireless Monitor screen
	(b) (4) [redacted] mode icon on the Wireless Monitor screen
	Pump Adjust button on Wireless Monitor
	Main configuration button on Wireless Monitor

GLOSSARY OF TERMS

Term	Meaning
ABG	Arterial Blood Gas
(b) (4)	(b) (4)
Bronchoscope Port	Port on the (b) (4) Module through which a Bronchoscope probe may be inserted to inspect the interior of the lung
Circuit	Refers to the perfusate loop in the (b) (4) Module
(b) (4)	(b) (4) Medical professionals may evaluate the capabilities of the lungs according to their clinical judgment by comparing the base O_2 saturation of the deoxygenated perfusate to the O_2 saturation of the perfusate exiting the lung.
(b) (4)	(b) (4) .
(b) (4)	A removable SD Data card used to store perfusion, ventilation, and monitoring parameters from the current session, which can be downloaded and analyzed on a personal computer
FiO_2	Fraction of inspired oxygen
HCT%	Hematocrit, expressed as a percentage by volume
L/min	Liters/minute
LPM	(b) (4) Module
MDI Port	Metered Dose Inhaler port on the (b) (4) Module through which MDI drugs may be injected into the lungs
mL/hr	Milliliters per hour
mL/min	Milliliters per minute
mmHg	Millimeters of mercury
Mobile Base	The removable Mobile Base has four wheels, with brakes on the front wheels. The Mobile Base can be installed as needed during system use. During transport, raise the two-position handle to push the system. With the Mobile Base removed, you can set the system flat or carry it with the lift handles.
Organ Care System	The Organ Care System (OCS™) houses the removable Wireless Monitor, circulatory pump driver, multi- mode ventilator, drive and control, batteries, data card, gas delivery subsystem, and reusable flow and pulse oximeter probes. When in active use, it houses the disposable (b) (4) Module.
PA	Pulmonary artery
PaO_2	Partial pressure of oxygen in mmHg in arterial (oxygenated) perfusate.
PAP	Pulmonary Artery Pressure. The perfusate pressure in mmHg at the Pulmonary Artery cannula as the perfusate flows into the lungs.
(b) (4)	(b) (4)
PAWP	Peak Air Way Pressure. (b) (4) PAWP

Term	Meaning
	corresponds to Peak Inspiratory Pressure on mechanical ventilators
PEEP	Positive End Expiratory Pressure. (b) (4) e
Perfusate	The fluid pumped through the lung that delivers dissolved gases and nutrients.
Power-cycle	To Power-cycle the lung system, use the On/Off switch on the side of the OCS™ Lung Console to turn the system OFF (b) (4), and then turn it ON.
(b) (4)	(b) (4)
Priming Inlet Port	Port on the (b) (4) Module through which priming solution and other large-volume perfusate components flow into the reservoir
Priming Solution	The sterile OCS™ Lung Solution added to the reservoir through the priming inlet port to preserve the lungs supplemented with other perfusate components.
(b) (4)	.
Pump Flow Probe	A probe that you attach to the (b) (4) Module. It is used to measure OCS™ Lung System Pump flow.
PvO_2	Partial pressure of oxygen gas in mmHg in venous (deoxygenated) perfusate.
RR	Respiration Rate. Number of respiration cycles per minute in units of breaths/minute
Run Mode	Power mode where the system is on, the Wireless Monitor is active, and the pump and ventilator are able to operate
SaO_2	Oxygen saturation of arterial (oxygenated) perfusate, expressed as a percentage and measured at the outflow of the lung (b) (4)
SaO_2/Hematocrit Probe	An OCS™ Lung System probe that you attach to the (b) (4) Module. It is used to measure the arterial oxygen saturation and the hematocrit of the perfusate (b) (4)
Session	A session is created in internal system memory when the system is set to Run Mode. Every time Run Mode is entered, you can choose whether to continue using the last session file or create a new one. In ordinary circumstances, data from all of the procedures associated with an organ should be documented in only one session. (b) (4)
Standby-Cycle	To Standby-cycle the system, press to switch from Run Mode to Standby Mode and then back to Run Mode. The system will automatically run the Self Test.
Standby Mode	A power mode where the system is on but the Wireless Monitor is off and no ventilation or perfusion may be performed. Standby Mode is the mode used during OCS™ Lung System storage; organs cannot be preserved in this mode. The OCS™ must be plugged in to AC power to avoid battery depletion when storing the lung system in this mode.
SvO_2	Oxygen saturation of venous (deoxygenated) perfusate, expressed as a percentage and measured (b) (4)

Term	Meaning
SvO_2/Hematocrit Probe	An OCS™ Lung System probe that you attach to the (b) (4) Module. It is used to measure the venous oxygen saturation and hematocrit of the perfusate (b) (4)
Temp	Temperature of perfusate supplied to the lung, displayed on the Wireless Monitor in degrees Celsius
TV	Tidal Volume. The volume of air breathed in and out of the lungs during a respiration cycle.
VR	Vascular Resistance. This is a measure of the resistance to flow that must be overcome to push perfusate through the vasculature of the lungs. (b) (4)
Waveform	Real-time waveforms display continuously updated data. The waveforms are drawn from left to right with the most current data. An update bar displays the oldest data first. If more than one graphic frame is configured to show real-time waveforms, the update bars are automatically synchronized. The RESP waveform is always displayed in the top-most frame on the Wireless Monitor. Use the Configuration Menu to configure which of the following waveforms are displayed in the middle and bottom frames on the Wireless Monitor.
Wireless Monitor	A small, dockable monitoring system with an LCD screen and controls for configuring system functions and screen displays, and for adjusting system settings during preservation. When removed from its docking station on the OCS™ Lung Console, the Wireless Monitor operates wirelessly, powered by its own battery.

1. CHAPTER 1: READ THIS FIRST

This chapter contains important information about the documentation for your TransMedics® Organ Care System (OCS™) and about contacting TransMedics.

1.1. Intended Audience

The OCS™ Lung System is intended for use only by qualified healthcare professionals specializing in organ transplants and trained on the use of the lung system. The system enables medical professionals to monitor key parameters that may be useful in assessing organ status and evaluating lung function according to their clinical judgment. This device can only be purchased upon order of a physician. A TransMedics representative must install and activate each newly purchased OCS™ Lung System before a qualified health care professional can use it.

Before using the system, review this *TransMedics Clinical User Guide: OCS™ Lung System* and the *TransMedics Technical User Guide: OCS™ Lung System*, noting the Warnings and Cautions throughout the guides.

1.2. Indications for Use

The TransMedics® Organ Care System (OCS™) Lung System is a portable organ perfusion, ventilation, and monitoring medical device intended to preserve donor lungs in a near physiologic, ventilated, and perfused state for transplantation.

1.3. Contraindication

Moderate to severe donor lung injury with air leak (as seen on radiological studies, bronchial examination or final visual assessment in donor's chest) to avoid:

- Perfusate leakage at injured segments into the airways and potential edema formation
- Inability to recruit donor lungs due to air leak

1.4. Warning

Only trained users are allowed to use of the OCS™ Lung System.

1.5. Using This Manual

This manual provides detailed instructions regarding Clinical use of the OCS™ Lung System.

For a system overview, understanding the Wireless Monitor controls and functions see the *TransMedics Technical User Guide: OCS™ Lung System.*

1.6. Related Documents

TransMedics Technical User Guide: OCS™ Lung System.

1.7. Conventions

The system, OCS™ Lung System, the lung system, and OCS™ are used interchangeably throughout this manual to refer to the TransMedics OCS™ Lung System.

The system uses consistent conventions throughout the interface and accompanying documentation to make it easy for you to learn and use.

WARNING—A Warning alerts you to a potential serious outcome, adverse event or safety hazard. Failure to observe a warning may result in loss of organ, death or serious injury.

CAUTION—A Caution alerts you to situations where special care is necessary for the safe and effective use of the product. Failure to observe a caution may result in minor or moderate personal injury or damage to the product or other property, and possibly a risk of more serious injury.

NOTE—A Note brings your attention to important information that will help you operate the system more effectively.

1.8. Customer Comments

If you have a question about the documentation or you discover an error in the documentation, please call:

(b) (4)

V 2

1.9. Supplies

The components, accessories, and supplies required when using the OCS™ Lung System must be used in accordance with this user manual, associated documents, and accepted medical standards.

CAUTION—Only accessories and supplies purchased from or recommended by TransMedics, Inc. are to be used with the TransMedics OCS™ Lung System. Use of accessories and supplies other than those supplied by or recommended by TransMedics may cause system malfunction and invalidate the TransMedics warranty.

For details on what is included with your OCS™ Lung System and (b) (4) Set, see the *TransMedics Technical User Guide: OCS™ Lung System*.

To order additional parts and supplies, see Appendix A of the *TransMedics Technical User Guide: OCS™ Lung System.* Other materials, not supplied by TransMedics, are required to operate the OCS™ Lung System. See Section 3.

1.10. Contacting TransMedics

1—For Customer Clinical Support:
Please contact TransMedics prior to departure to donor site on one of the following numbers:
(b)(4)Proprietary Information [redacted]

2—For Customer Service:
Please contact TransMedics at (b) (4) [redacted]
You can also contact one of the following offices for referral to a customer service representative, or visit the TransMedics Web site: www.transmedics.com.

Corporate and North American Headquarters
TransMedics, Inc.
200 Minuteman Road, Suite 302
Andover, MA 01810, USA
(b) (4) [redacted]

(b) (4) [redacted]

2. CHAPTER 2: OVERVIEW OF OCS™ LUNG SYSTEM

The TransMedics® Organ Care System (OCS™) Lung System is a portable organ perfusion, ventilation and monitoring medical device intended to preserve donor lungs in a near physiologic, ventilated and perfused state for transplantation. The system enables medical professionals to monitor key parameters that may be useful in assessing organ status and evaluating lung function according to their clinical judgment.

2.1. Overview of OCS™ Lung System Preservation Process

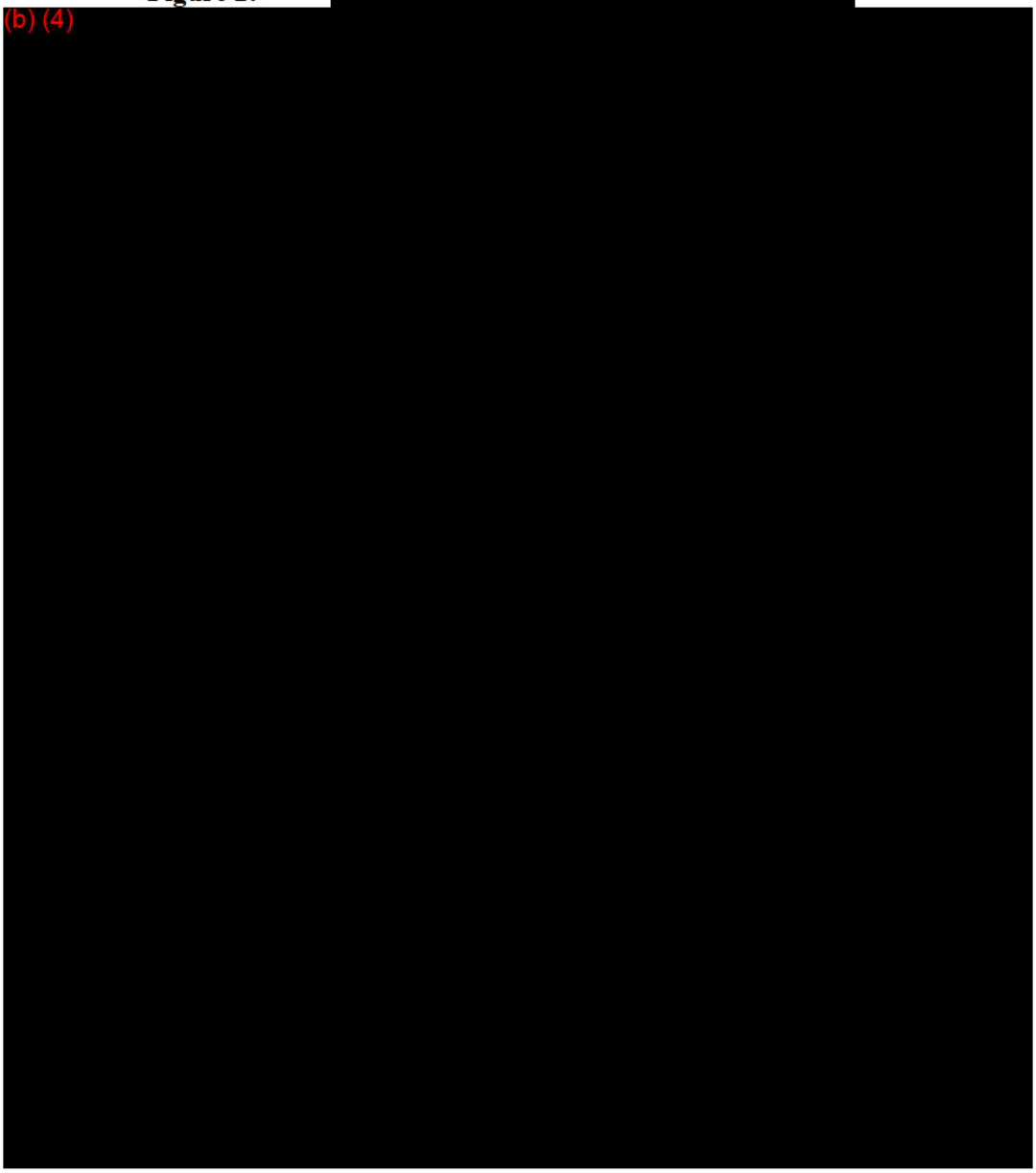
Figure 1 illustrates the various activities performed at the Donor Site, in transport and after returning to the Recipient Site.

2.2. Overview of Perfusion and Ventilation

The OCS™ Lung System preserves ventilated lungs using warm oxygenated cellular perfusate. The system supports several ventilator modes to ensure both preservation and monitoring of lung function during retrieval. Ventilator modes of the lung system include the following: (b) (4)

e. Figure 2 shows an overview of the circulation and ventilation.

Figure 2: (b) (4)



2.3. Clinical Study of the OCS™ Lung System

The safety and effectiveness of the OCS™ Lung System was studied as part of a randomized, controlled, multi-center study of 320 subjects at 21 investigational sites in the United States, Canada, Australia and the European Union.

A summary of the study and the results are provided in Appendix A of this document.

NOTE—It is essential that you carefully review the study results in Appendix A: OCS™ Lung System INSPIRE Study. If you have any questions about these results, please contact TransMedics.

3. CHAPTER 3: ACTIVITIES PERFORMED BEFORE DEPARTURE TO DONOR SITE

Adequate preparation ensures the smoothest possible organ retrieval run with the OCS™ Lung System. This chapter provides information on the checklists and tasks that are performed at the recipient site prior departure to the donor site.

3.1. Procedure Overview Checklist

3.1.1. For Clinical Support

1. Contact TransMedics prior to departure to donor site

(b) (4) [redacted]

2. Ensure you have an updated application on a fully charged OCS™ training iPad
3. OCS™ Lung Console, removable cover and 3 fully charged OCS™ Lung System batteries
4. (b) (4) [redacted] Gas cylinder (>30% full) and (b) (4) [redacted] Gas cylinder (>50% full). For less gas, replace or take a spare cylinder
5. OCS™ Lung Solution and medications
6. Leukocyte reduced packed red blood cells (pRBCs) – ABO type matched to transplant recipient
7. OCS™ (b) (4) [redacted] Module (LPM) and Accessory Sets

(b) (4) [redacted]

8. OCS™ Run Bag and contents

3.1.2. OCS™ Lung Console Checklist

1. OCS™ Lung System passes Self Test and is set to Run Mode
2. With the OCS™ Wireless Monitor correctly docked on the lung system and in Standby mode, press the  button on the Monitor to set the OCS™ Lung System to Run Mode
3. Ensure Bluetooth is enabled on the Wireless Monitor 
4. Check date, time and adjust as needed
5. Check status of three fully charged OCS™ Lung System batteries:
   a. Press the test button (located on the front of each battery) to check battery charge.
   b. Battery status will be displayed on the Wireless Monitor once the Lung System is set to Run Mode.

c. For detailed instructions on checking the battery status and charging the batteries, see the *TransMedics Technical User Guide: OCS™ Lung System*.

NOTE—Each fully charged battery provides a minimum of 80 minutes of power, totaling four hours of power with three fully charged batteries under normal operating conditions. Additional batteries can be ordered from TransMedics® as needed.

6. The OCS™ Lung System has a TransMedics approved Data Card
7. The OCS™ [redacted] Gas cylinder is installed properly inside the gas compartment. Open the cylinder to check the status of the [redacted] Gas on the Monitor.
8. After OCS™ Lung Console check, switch back to Standby Mode by pressing  on the Monitor until the [redacted] Module is installed

3.2. OCS™ Lung Gas Cylinders

3.2.1. [redacted] Gas Cylinder

The [redacted] gas is composed of 12% [redacted] The Preservation gas is used by the system during Priming to oxygenate the perfusate and throughout Transportation to ventilate lungs. The [redacted] Gas cylinder needs to be installed inside the gas compartment of the OCS™ Lung Console before using the system.

A full [redacted] Gas cylinder contains [redacted].

[redacted] Gas Cylinder checklist:

1. Ensure the [redacted] Gas cylinder is ≥ 30% full (at least 900 psi); otherwise, replace or take a spare full cylinder and store in the Run Bag.
   - Open the [redacted] Gas cylinder valve with the gas cylinder wrench, located in the front of the gas compartment, and check the level on the gas gauge. To open the valve, turn it in counter-clockwise direction.
   - Looking at the [redacted] Gas status icon on the Wireless Monitor after opening the cylinder's valve can also check the Preservation gas level.
2. Close the cylinder's valve (turn in clockwise direction) after check and until Priming at the donor's site.

NOTE—For more information, see "Estimating the Remaining Preservation Gas Supply" in the *TransMedics Technical User Guide: OCS™ Lung System*. Replace the cylinder if necessary. Close gas valve after check and after use.

3.2.2. [redacted] Gas Cylinder

The [redacted] gas is composed of [redacted] Gas is needed to assess oxygenation capacity of lungs preserved on the OCS™ Lung System: in either [redacted] Mode or [redacted] Mode. In order to be used, the

Monitoring cylinder needs to be connected to the lung system using the Monitoring Gas Regulator kit.

A full (b) (4) Gas Cylinder contains (b) (4)

(b) (4) Gas Cylinder checklist:

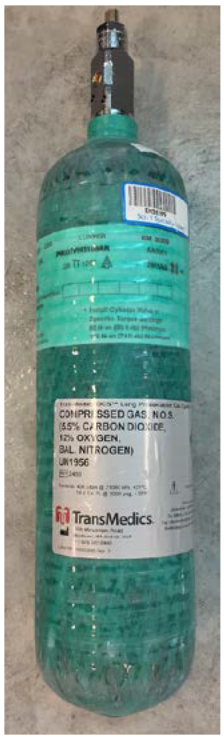
1. Ensure the (b) (4) cylinder is ≥ 50% full (At least 1500 psi) before departure to donor site. Otherwise, replace or take a spare.
2. Regulator and green line (Monitoring Regulator Kit) are attached to the cylinder before usage.
3. All components are stored in the retrieval Run Bag.

WARNING—Please note the different color of the labels on the (b) (4) and the (b) (4) gas cylinders, to ensure installing the correct cylinder inside the OCS™ Lung Console.

To avoid the inadvertent insertion of the (b) (4) gas cylinder into the OCS™ Lung Console, an additional label is placed around the (b) (4) Gas Cylinder to prevent it from fitting into the Lung Console's Preservation Gas compartment.

NO attempts should be taken to remove this additional label at any time. See Figure 3.

Figure 3: (b) (4) Cylinder with Additional Differentiating Labels from (b) (4)



(b) (4) Gas Cylinder

(b) (4) Gas Cylinder with Additional Label

3.3. OCS™ Lung Solution & Additives Checklists

3.3.1. For Donor Lung Flush

- Use (b) (4) of cold buffered* OCS™ Lung Solution for antegrade flush supplemented with 50 mg of nitroglycerin in the first flush bag.
- Use (b) (4) of cold buffered* OCS™ Lung Solution for retrograde flush.

** Use 10 mEq of $NaHCO_3$ or 1 mmol of THAM/L (tromethamine) to buffer solution immediately before usage*

3.3.2. OCS™ Lung Perfusate & Additives

- (b) (4) of Buffered* OCS™ Lung Solution

  ** Use 10 mEq of $NaHCO_3$ or 1 mmol of THAM/L to buffer solution*
- 3 units of leukocyte reduced, CMV negative, ABO typed pRBCs

Table 1: OCS™ Lung Solution Manufacturing Composition

(b) (4)

CAUTION—The OCS™ Lung Solution is ONLY intended for use with OCS™ Lung System. The OCS™ Lung Solution is NOT intended for intravenous injection.

Table 2: Additives

(b) (4)

Table 3: Prophylactic Medications

(b) (4)

[redacted]

3.3.3. Perfusate Corrective Medications Checklist– (As needed & after every blood sample check)

(b) (4)

[redacted]

3.4. Leukocyte Reduced Packed Red Blood Cells (pRBCs) Checklist

1. (b Units are required to use with the OCS™ Lung System
2. ABO compatible (to transplant recipient)
3. Tested Cytomegalo Virus (CMV) Negative
4. Leukocyte reduced
5. Stored in a cooler during transport

3.5. OCS™ (b) (4) Set Checklists

1. Check the expiration date and check for any obvious shipping damage on the (b) (4) Set (LPS).
2. If the date has expired or if any damage is found to a packaged LPS, do not use this LPS.
3. Installing the (b) (4) Module (LPM) prior departure to donor site is optional. For details of installing the LPM, refer to Section 4.
4. If the LPM is installed before departure to donor site, Accessory Sets shipped with the corresponding LPS should be stored in the OCS™ Run Bag to be used at the donor site.
5. Accessory Set packages should not be opened until just before use at the donor site.
6. Once the LPM is installed, switch the OCS™ Lung System to Run Mode and verify that the lung system passes the Self Test.
   a. If displayed errors indicate problems, refer to the Troubleshooting chapter in the *TransMedics Technical User Guide: OCS™ Lung System*.
7. If no errors display, select “New Session File” and confirm the following:
   a. Ventilator Mode is defaulted to Pause Preservation

b. [redacted]

[redacted]

8. Switch back to Standby Mode until the module is ready for Priming at the donor site.

WARNING—Without a Sterile OCS™ [redacted] Set (LPM and Accessory Sets) the OCS® Lung System cannot be used.

3.6. Run Bag Checklist and Contents

1. [redacted] of OCS™ Lung Solution with buffering agents [redacted] (For LPM Priming)
2. Medications and additives listed in Table 1
3. OCS™ [redacted] Gas cylinder (≥ 50% full) & Monitoring Gas Regulator Kit
4. Sterile syringes, needles, gloves, alcohol wipes and petroleum jelly/Vaseline®
5. OCS™ Lung Accessory Sets (if the LPM is installed before departure to donor site):

[redacted]

6. Sterile (OCS™ Lung Manual Inflation Set)/Ambu Bag
7. [redacted]
8. [redacted]

3.7. Transport Considerations

When selecting a transport vehicle, consider the following:

1. Identify a level area large enough to accommodate the OCS™ Lung Console (with its mobile base removed), approximately 29" x 19" x 29" (72 cm x 46 cm x 72 cm).
2. Position the OCS™ Lung System for access to its gas and batteries, if possible.
3. Secure the OCS™ Lung Console to the vehicle to immobilize it during transport, [redacted]
4. Install the OCS™ Lung Console cover [redacted]

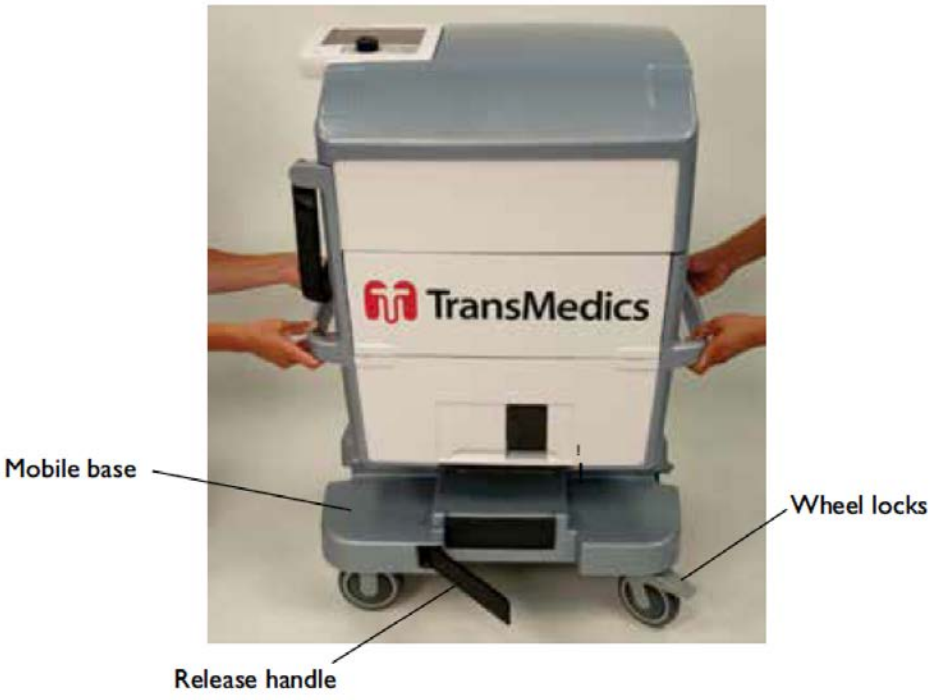
[redacted]

3.8. Preparing the OCS™ Lung System for Travel to Donor Site

1. Press the Run/Standby button on the docked Monitor to set the lung system back to Standby Mode.
2. Unplug the OCS™ Lung Console from the AC receptacle and wind the power cord around the power cord wrap.
3. With the Mobile Base installed, (b) (4), raise the handle and push the Lung Console to the loading area.
4. Lock the Mobile Base wheels (b) (4).
5. Disconnect the Mobile Base from the OCS™ Lung Console (b) (4).
6. With two people using the right and left lift handles, lift the OCS™ Lung System into the transport vehicle.
7. Position the OCS™ Lung Console level in the vehicle and secure it (b) (4).
8. Remember to take the Mobile Base with you for use at the donor site.

For additional information on safely transporting the OCS™ Lung System, including temperature and humidity limits, see the *TransMedics Technical User Guide: OCS™ Lung System.*

Figure 4: Lifting the OCS™ Lung Console off the Mobile Base



4. CHAPTER 4: ACTIVITIES PERFORMED AT DONOR SITE

This chapter provides instructions for the tasks that are performed at the donor site to retrieve, preserve, monitor and assess the lungs' function throughout transport.

NOTE— The (b) (4) Module (LPM) may be installed in the OCS™ Lung System before going to the donor site. (b) (4)

4.1. Unpacking, Installation, and OCS™ Lung System Setup

This section provides instructions for unpacking the (b) (4) Set, installing the (b) (4) Module, attaching the probes, and running the system Self Test.

4.1.1. Unpacking and Inspecting the (b) (4) Set (LPS)

Accessories packaged and shipped with the (b) (4) Set should be unpacked immediately before use.

For illustrations and descriptions of the components included in the (b) (4) Set, see the *TransMedics Technical User Guide: OCS™ Lung System*.

4.1.2. Unpacking and Inspecting the Sterile Components

1. Inspect the packaging of each sterilized component for tears or breaks in the seal that might compromise sterility. If any tears or damage are found, do not use the damaged item.

CAUTION—Check the expiration date on each package. If the date has expired, do not use the item.

2. Unpack each sterilized component immediately before use.
3. Open the (b) (4) components ONLY in a sterile field, using sterile technique.

4.1.3. To Open the LPM Packaging

1. Check the expiration date and inspect for any obvious shipping damage. If the date has expired or if any damage is found, do not use the LPM.
2. Partially lift the bagged LPM out of the box, supporting the bottom of the module on the foam insert.
3. Open the bag (b) (4)
4. Carefully remove the LPM from the bag and discard the bag.
5. Supporting the bottom of the LPM on the foam insert inside the box, grasp the corner of the foam wrapped around the (b) (4) Module and tear off the foam.

6. Remove the foam block from the rear of the LPM.
7. (b) (4)

(b) (4)

4.2. To Install the LPM on the OCS™ Lung System

For photos of the back and front of the (b) (4) Module and its location inside the OCS™ Lung System, see the *TransMedics Technical User Guide: OCS™ Lung System.*

1. Stabilize the OCS™ Lung Console by pressing the wheel brakes on the mobile base down.
2. Remove the OCS™ Lung Console cover and lower the front panel of the system.
3. Keep the system in STANDBY mode (b) (4) and thus facilitates installing and engaging the module to the OCS™ Lung Console.
4. Pull the saturation and flow probes cables to the left to avoid getting them in the user's way while engaging the module to the ventilator's arm. See Figure 5.

Figure 5: OCS™ Lung System Probes Pulled to the Side of the LPM

(b) (4)

(b) (4)

Figure 6: Pump Head, Ventilator Actuator of the OCS™ Lung Console (A) and the Bellows Plate of the LPM (B)

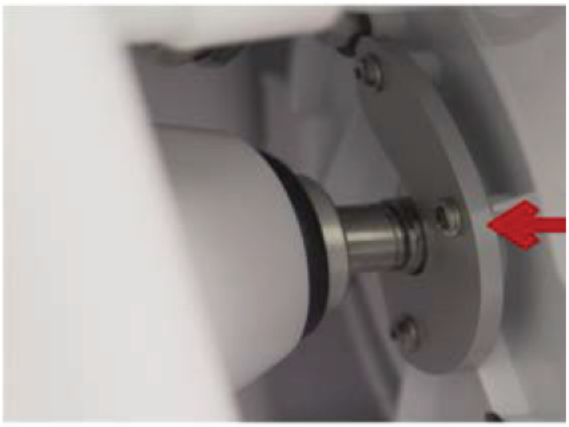
A

B

6. Push the Module backwards after ensuring proper alignment of the OCS™ Lung System holding clips with the LPM's recesses to keep it in place. See Figure 7. (b) (4)

Figure 7: Holding Clips Engaging with the LPM (A) and Ventilator Actuator Engaged with the Bellows Plate of the LPM (B)

A

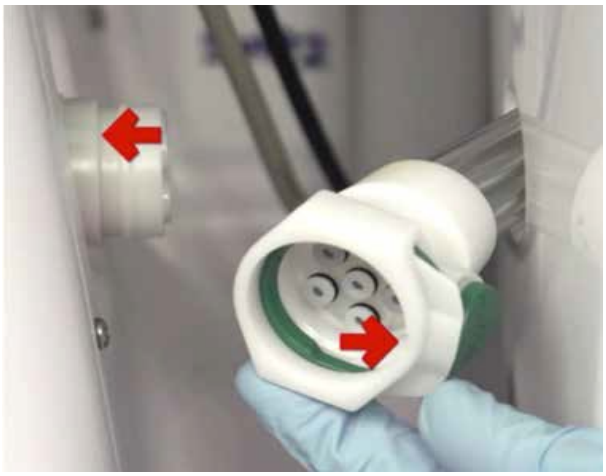


B

(b) (4)

(b) (4) See Figure 8.

Figure 8: Ventilator Lines Connection Port



(b) (4)

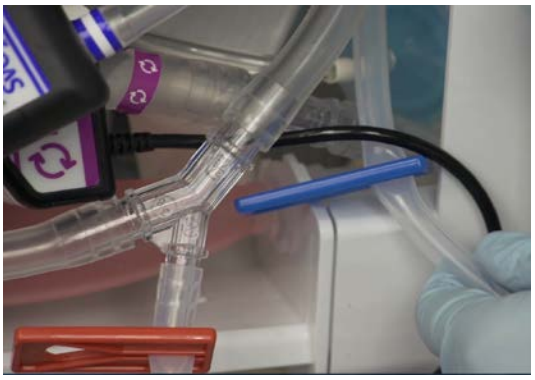
Figure 9: (b) (4)

Proper Connection
(Green release button pointing to 10 O'Clock)

Wrong Connection
(Green release button pointing upwards)

9. Expose the Oxygenator Recirculation line of the module and release its clamps to be opened. Push the blue and the red clamps all the way up on the recirculation line and store in clamped on position. See Figure 10.

Figure 10: Clamp onto the Oxygenator Recirculation Line



10. Close the pulmonary artery flush port as seen in Figure 11.

Figure 11: Closing the PA Flush Port

4.3. Attaching the Probes

This section provides detailed instructions on attaching the pump flow probe, the SaO_2/Hematocrit probe, and the SvO_2/Hematocrit sensor/probe to the tubing on the module.

4.3.1. Attaching the Pump Flow Probe

The pump flow probe is installed between the purple bands (between the perfusate warmer and the gas exchanger).

1. Apply a small amount of petroleum jelly to the inside of the probe.
2. Locate the color-coded bands on the LPM that match the color of the probe label.

> **CAUTION—** Apply ONLY petroleum jelly/Vaseline® to the inside of the flow probe. Using any other coupling gel, such as silicone grease or ultrasound gel, may damage the pump flow probe.

Align the probe between the bands so that the double lines on the probe label are next to the band with double lines on the tubing (Figure 12).

3. Insert the tubing into the sensing cavity and close the lid.

4. Make sure the lid is completely closed and the latch is secure. The fit should be tight, with the full tubing cross-section contacting all inner surfaces of the sensing window. The tubing will be slightly compressed into a rectangular shape.
5. Once fluid is flowing through the tubing during priming, check the Wireless Monitor display to make sure that the desired flow parameters are being displayed.

Figure 12: Pump Flow Position

4.3.2. Attaching the SaO_2/Hematocrit and SvO_2/Hematocrit Probes

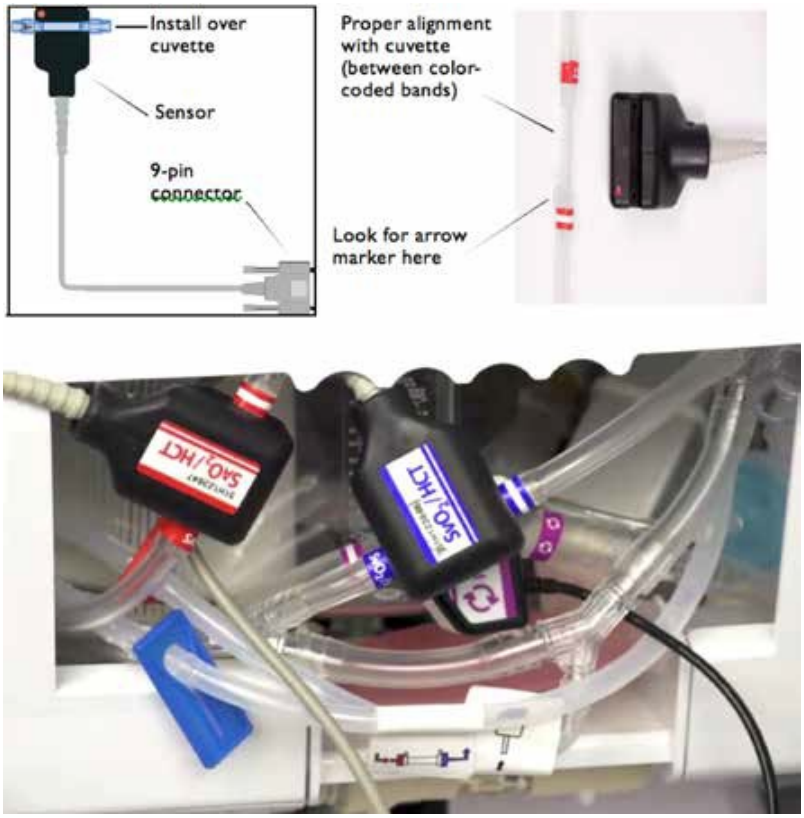
The SaO_2/Hematocrit and SvO_2/Hematocrit optical probes are designed to be clipped onto cuvettes that are incorporated into the LPM's tubing. The cuvette is marked with colored bands at each end. The color of the bands should match the color of the label on the corresponding probe. Align the probe between the bands so that the double lines on the probe label are next to the band with double lines on the tubing.

The probes are attached to the following locations:

1. Clip the SvO_2/Hematocrit probe to the cuvette between the blue bands on the line between the gas exchanger and the pulmonary artery (PA) inflow.
2. Clip the SaO_2/Hematocrit probe to the cuvette between the red bands between the left atrial (LA) drain and the reservoir.

Figure 13 shows the SvO_2/Hematocrit and SaO_2/Hematocrit probe components and the probes attached to the tubing.

Figure 13: SaO_2/HCT and SvO_2/HCT Probes



CAUTION—Ensure the saturation probes are securely connected to the cuvette.

4.4. Running the OCS™ Lung System Self Test

After the LPM is fully installed, run the system Self Test again to make sure that the system is operating properly.

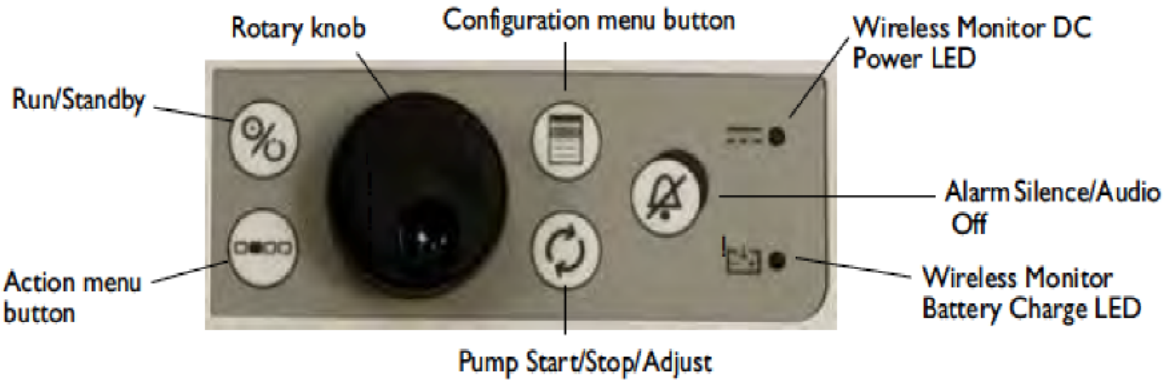
To run the system Self Test:

1. Make sure the Wireless Monitor is docked to the OCS™ Lung Console and the lung system is in Standby Mode. Figure 14 shows the controls of the Wireless Monitor.
2. Make sure the ON/OFF switch on the OCS™ Lung Console is in the 'ON'  position.
3. Press the  button on the Monitor. The system performs a Self Test and displays system transitional status messages. If errors are encountered, error messages are displayed.
4. If displayed errors indicate problems, refer to the Troubleshooting chapter in the *TransMedics Technical User Guide: OCS™ Lung System*.
5. If no errors display, select "New Session File" to proceed.
6. Start a "New Session File" and confirm the following:

- Ventilator Mode is defaulted to Pause Preservation. 
- NO (+++) OR (- - -) are displayed on the Monitor for PAP or PAWP readings

CAUTION—If the system detects an issue during the Self Test, a message is displayed with information about the issue until it is resolved. To resolve the issue, follow the steps in the troubleshooting section of the *TransMedics Technical User Guide: OCS™ Lung System*.

Figure 14: Wireless Monitor Controls



NOTE—The Run/Standby button  on the Wireless Monitor will NOT FUNCTION unless the Wireless Monitor is DOCKED on the OCS™ Lung System.

At the beginning of the session, the system may display messages and sound alarms related to sensor probes. These messages and alarms can be disregarded. For details of system initialization and messages, see the *TransMedics Technical User Guide: OCS™ Lung System*.

(b) (4)

[redacted]

4.5. Assessing Lungs in the Donor Chest

Use standard routine assessments of lung function and condition in the donor's chest to rule out contraindication for use of OCS™ the lung system before proceeding

Once moderate to severe lung injury is excluded and lungs are accepted, per standard donation criteria, an operator should begin preparing the OCS™ Lung System to receive the lung.

4.6. Preparing the OCS™ Lung System for (b) (4)

This section provides instructions for preparing the lung system for (b) (4).

4.6.1. Priming the OCS™ LPM

Priming overview settings are listed in Table 4.

After the LPM and the probes are installed and the Self Test is complete, the lung system will default to Pause Preservation Ventilation Mode, and the module is ready to be primed.

4.6.2. Pause Preservation Mode

The bellows remain stationary and the OCS™ Lung System achieves a static level of lung inflation (b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

NOTE—Use aseptic technique when performing the following procedure.

(b) (4)

[redacted]

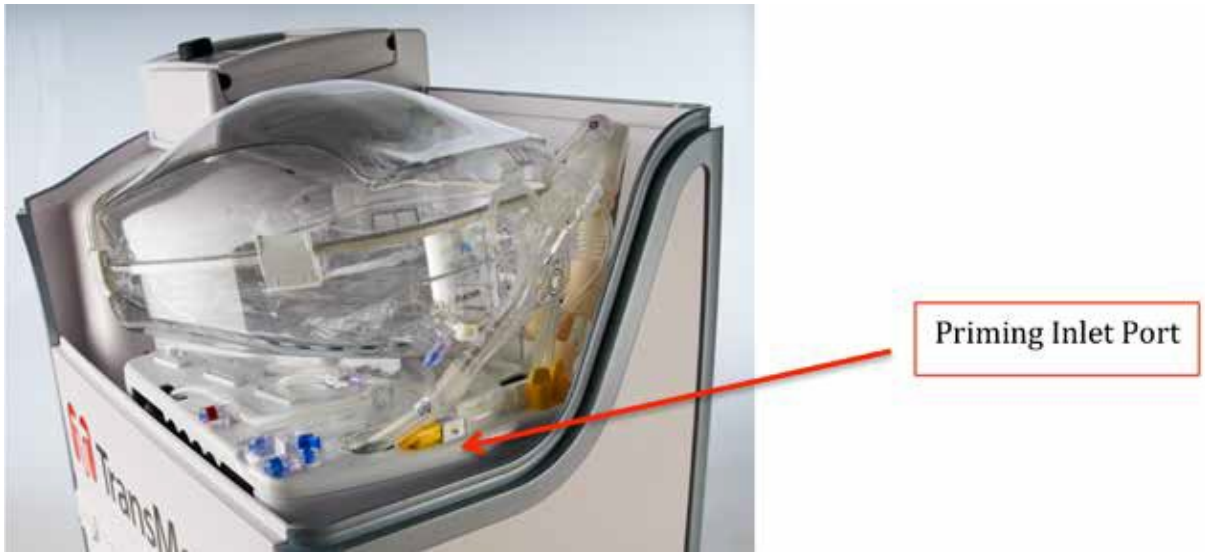
***NOTE—**For a suggested ideal body weight formula, see Appendix B: Body Weight Formula (Devine's Formula for donor's height above 150 cm (5 feet).

4.6.3. Priming the (b) (4) Module

For Priming the LPM, the (b) (4) Initiation Set needs to be used to transfer the Priming Solutions as follows:

1. Open one of the packaged Dual Vented Prime Lines in the (b) (4) Initiation Set.
2. Close the clamps on the Dual Vented Prime Line.
3. Insert the piercing spike of the Dual Vented prime line into the buffered OCS™ Lung solution bags, using a twisting motion until the set is firmly seated.
4. Remove the yellow protective cap from the (b) (4) Module's Priming Inlet Port (Figure 16).
5. Connect the outlet from the Dual Vented Prime line into the Priming Inlet port.
6. When ready to prime the LPM, open the Dual Vented Prime Line's clamp and start by adding 1.5 -2L of buffered OCS™ Lung Solution to the reservoir.
7. Add the 3 units of ABO compatible (to the recipient) leukocyte reduced pRBCs after adding the OCS™ Lung Solution using a set of the Dual Vented Prime Lines.
8. Clamp and cover the Priming Inlet Port of the LPM with one the provided spare covers on the modules. Reposition the covered Priming Inlet Port back in its recess.
9. Turn on the Pump to start circulating, mixing, and warming the perfusate.

Figure 16: (b) (4) Module Priming Inlet Port



4.6.4. Start of Perfusate Circulation

1. Make sure the gas exchanger vent on the LPM remains open.
2. Ensure that the Termination Flush Stopcock is closed.
3. Open the (b) (4) Gas cylinder by turning its valve 180 degrees in counter-clockwise direction.
4. Always keep the OCS™ Lung System connected to AC power while at the donor site and during system Priming.

CAUTION—Ensure that the Flush stopcock is closed before turning the pump on to avoid pumping the perfusate out of the module through the Termination Flush Port.

5. Start circulation with the following settings:

   a. Press Pump adjust button  on the Wireless Monitor and adjust Pump flow to 3.0 L/min for few minutes to de-air the module, mix and warm the perfusate.

   b. Press the Configuration menu button  , highlight and select the Preservation tab using the Rotary Knob. Adjust the settings as follows for the Preservation settings:

      – (b) (4) [redacted]

      – Set the ventilation setting, as listed in Table 4, using the Rotary Knob to highlight, select, and adjust all settings.

      – Ensure that you confirm your settings by highlighting and pressing "accept," displayed at the bottom of each menu, using the Rotary Knob.

   c. Press the Configuration menu button  , highlight and select the Monitoring tab using the Rotary Knob. Adjust the settings as follows for the Monitoring settings:

      i. (b) (4) [redacted]).
      ii. Set ventilation, as listed in table 4, using the Rotary Knob to highlight, select, and adjust all settings
      iii. Confirm settings by highlighting and pressing "accept," displayed at the bottom of each menu, using the Rotary Knob

   d. Confirm that the OCS™ Lung System defaults to (b) (4) [redacted] on the Monitor. 

   e. If (b) (4) [redacted] was not configured, please refer to the *TransMedics Technical User Guide: OCS™ Lung System*.

Ensure that the PA stopcock (Blue) stays open as seen in Figure 17 to de-air PA flow. If necessary, use a syringe to initiate flow through the purge line as needed.

Figure 17: Pulmonary Artery Stopcock in Open Position

4.6.5. Injecting Additives Into the Perfusate and Preparing for Use

Table 5 describes the additives to be injected into the perfusate before use. Additives, syringes and medium gauge needles must be available at the donor site.

Table 5: (b) (4) s

(b) (4)

To inject additives into the perfusate:

1. Inject the additives listed in Table 5 through the reservoir injection port (Figure 18) using aseptic technique.

Figure 18: Additive Injections

2. Let the fluids circulate for few minutes at a flow rate of (b) (4).
3. During Priming:
   - Check for air bubbles in the perfusate. If present, tap the lines as vigorously as necessary to dislodge the trapped air for removal by the system de-foamer.
   - Once de-airing is completed, lower Pump flow to (b) (4) until preset temperature is reached (b) (4)

(b) (4)

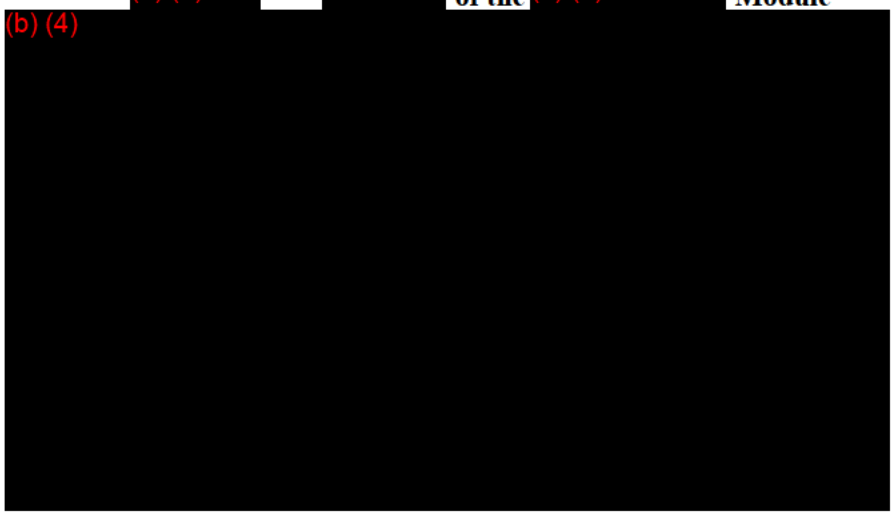
   - Make sure there are no leaks in the LPM's tubing or connections.
   - Check the Wireless Monitor to make sure it is displaying all system parameters.
   - Verify that the perfusate temperature begins to increase toward the Temp Set Point.
4. At this point, if the hematocrit (HCT) of the perfusate is above (b) (4) look for SvO_2 and SaO_2 readings that are rising to stabilize between (b) (4)
5. Obtain a priming blood sample from the arterial sample port once preset temperature (b) (4) is reached and lower Pump flow rate to around (b) (4) until lungs are instrumented.

4.6.6. Evaluating Hematocrit and Reservoir Volume Level

After components of the perfusate have been added to the reservoir and have been circulating for approximately 2-3 minutes during priming, evaluate the HCT. TransMedics recommends perfusate's HCT between (b) (4) for optimal lung evaluation.

WARNING—Maintain a volume of at least (b) (4) (Figure 19) in the reservoir at all times. Lower volumes may result in air being pumped into the organ.

(b) (4) of the (b) (4) Module



4.6.7. Obtaining a Priming (Pre-Instrumentation) Blood Sample

Using aseptic technique, take a perfusate sample from the arterial sample port (wipe port with alcohol before perfusate withdrawal). Enter the results into the OCS™ Lung Session File as needed after each sample using the Record Blood Sample function on the Action menu. For details, see *TransMedics Technical User Guide: OCS™ Lung System.*

4.6.8. Priming Blood Sample

Timing:

- After system priming and before lungs are on OCS™
- At Temp: (b) (4)

Purpose:

- Correct HCO_3 (b) (4) s
- Correct glucose (b) (4)

4.7. Harvesting Donor Lungs

This section provides detailed instructions on harvesting, cannulating, and connecting the lungs to the OCS™ Lung System.

NOTE—Use standard procedures to prepare the donor for organ explantation.

4.7.1. Administering Heparin

Per standard retrieval procedure, donor receives heparin (b) (4)) and adequate time for heparinization is allowed before explanting the lung

4.7.2. Donor Lung Flush, Clamping Trachea, and Stopping Ventilation

1. Donor Lung Flush
   - Use at least (b) (4) of cold buffered* OCS™ Lung Solution + (b) (4) for anti-grade flush.
   - Use (b) (4) of cold buffered* OCS™ Lung Solution for retrograde flush.

     (b) (4) .
2. Clamp the trachea while pulling the endotracheal tube out to stop ventilation. Explant the lung according to standard protocol.
3. Once lungs are removed, they must be prepared for instrumentation on the lung system.

4.7.3. Preparing the Lung for the OCS™ Lung System (Cannulation & Instrumentation)

A sterile operator performs back-table lung preparation while a non-sterile operator is priming and preparing the lung system for instrumenting the lungs.

4.7.4. Securing TransMedics® Cannulae to Lung

These procedures require supplies from the (b) (4) Tool Set.

You will need to supply and use the following:

- Silk tie
- Surgical clamp

Table 6 lists and describes the components in the (b) (4) Tool Set.

Table 6: (b) (4) Tool Set

Item	Description and Size
(b) (4)	
Tube Cutter	For sizing selected PA cannula
Tubing Clamps (2)	For clamping the cannula
Trachea Cannulae	(b) (4)
PA Cannula	For PA cannulation when connecting the lung to the LPM
(b) (4)	

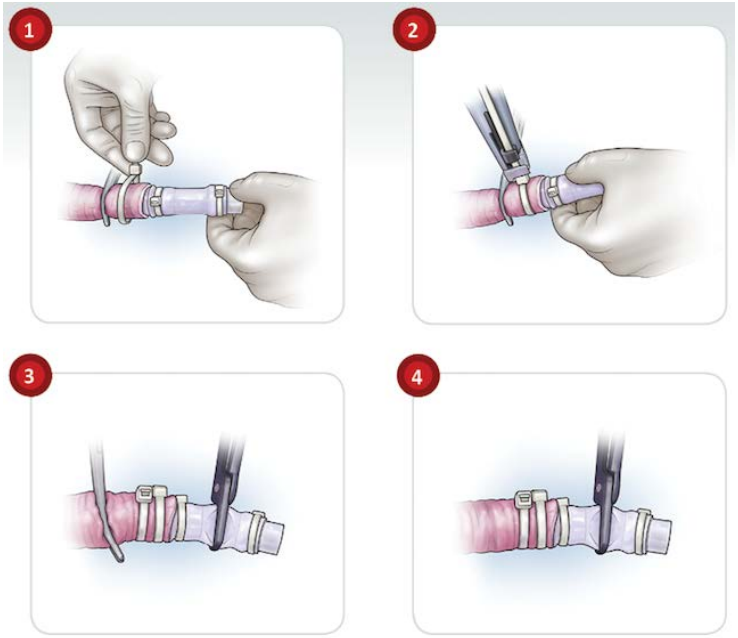
(b) (4)

4.7.5. Connecting and Securing the Trachea Cannula

To connect and secure the trachea cannula:

1. Apply second surgical clamp (b) (4) distal to the first surgical clamp (that is applied to the endotracheal tube during organ removal) and then remove first clamp.
2. Trim the trachea at the level of the lung apex, (b) (4)
3. Select the appropriate size trachea cannula, insert the largest cannula that fits into the trachea, and connect it by using the TransMedics cable tie (1 or 2) and cable tie tool (Figure 20).
4. Clamp the flexible portion of the trachea cannula with the TransMedics tubing clamp.
5. Remove the surgical clamp from the trachea.

Figure 20: Tracheal Cannula Procedure

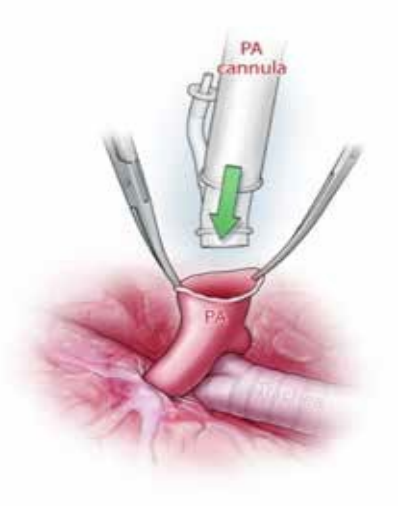


4.7.6. Pulmonary Artery (PA) Cannulation

This section provides instructions for cannulating the PA with a single cannula:

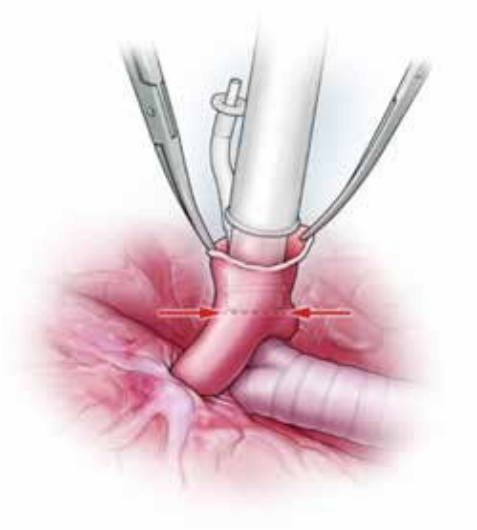
- A main pulmonary artery stump (b) (4) is needed to cannulate the PA.
- Align PA cannula in the midline with the pressure line pointing up (Figure 21).

Figure 21: Cannula Alignment



1. Position cannula tip in the main PA to ensure equal and homogeneous perfusion to both lungs (Figure 22).

Figure 22: Cannula-Tip Positioning

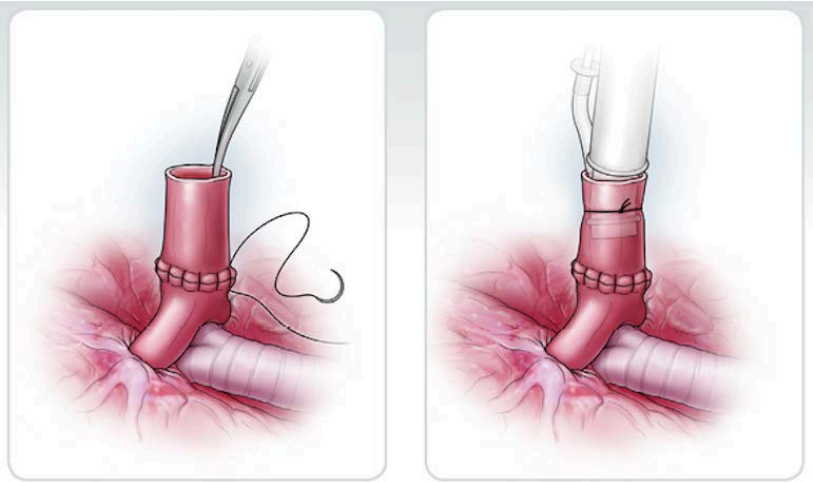


2. Secure the cannula using a silk tie or using purse string suture and a silk tie above the ridge at the tip of the PA cannula.
3. (b) (4)

4.7.7. PA Reconstruction and Cannulation

1. If the lung has a short PA, use a piece of descending aorta to reconstruct the main PA (Figure 23).
2. Secure the PA cannula into the reconstructed PA conduit as previously described.

Figure 23: Reconstructed PA



4.8. Draping the Work Area In Preparation for Instrumentation

As the PA and Trachea are being cannulated and after taking the priming blood sample from the perfusate, drape the lung system in preparation for instrumenting the lungs by a sterile surgeon.

Steps:

1. A non-sterile operator may remove the Wireless Monitor from its docking cradle.
2. Remove the strap on the sterile drape attached to the organ chamber of the LPM (Figure 24).
3. Grasp the drape at the arrow marking on the top of the drape and pull it backward away from the chamber.
4. Continue unfolding following the arrow markings printed on the drape in order and until the whole drape is extended.

Figure 24: Sterile Drape (Unfolding and Draping)

If the Wireless Monitor is to be left in its docking cradle during [redacted]:

- Assure that the clear film covers the Wireless Monitor so that the controls and screen can be easily seen and accessed in a sterile way during instrumentation.
- Use the rest of the drape to cover the system and other system surfaces outside the organ chamber.

4.9. Instrumenting Lungs on the OCS™ Lung System

1. Inspect Trachea Cannula distal to the applied tubing clamp to ensure there is no solution from the bowl trapped in this part. If seen, dry this part of the cannula before connecting the lungs to the lung system (Figure 25).

2. Confirm that the Ventilator Mode is set to [redacted] If not, press the main configuration button on the Wireless Monitor and set the Ventilator Mode [redacted]

CAUTION—DO NOT set VENTILATOR MODE to OFF at any time during the retrieval

1. Press the Pump adjust button and decrease the flow to (b) (4) if not done earlier. This will ensure gradual warming of the cold lungs once connected to the lung system.

2. Open the organ chamber and fully unfold the enclosed folds of the lung Wrap.

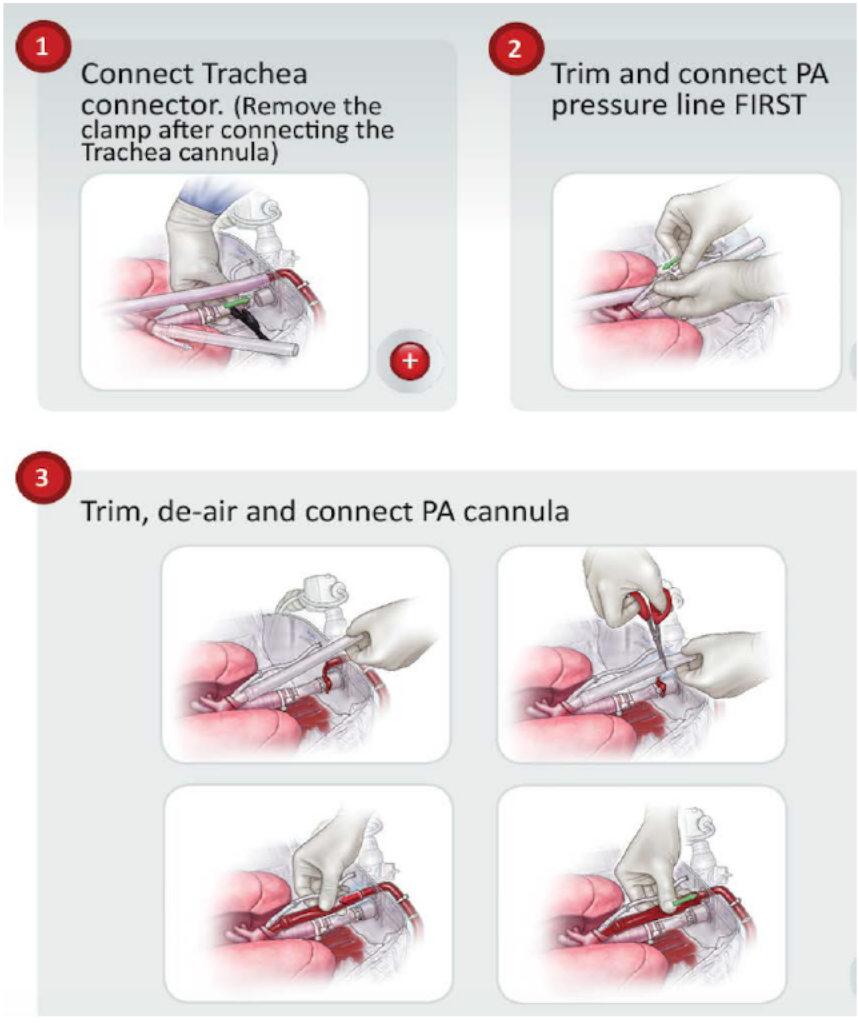
3. Keep the Prime tube connected to the PA Connector until the trachea connection is secured.

4. Place the lungs in the organ chamber with the cannulae directed toward the connection ports inside the organ chamber. (b) (4)

4.9.1. Instrumentation Sequence Overview

Figure 25 illustrates the sequence of instrumentation.

Figure 25: Sequence of Instrumentation



4.9.2. Connecting Trachea Cannula and PA Cannula to OCS™ Lung System

1. Connect the trachea cannula to the organ chamber's Trachea Connector.
2. Unclamp the trachea-tubing clamp.
3. Trim the PA pressure line to fit the lung. Connect the line between the PA pressure port on the cannula to the PA pressure port inside the Lung Organ Chamber
4. Remove the Priming tube in preparation to connect the PA cannula.
5. Trim the PA cannula (see diagram Connecting Trachea Cannula and PA Cannula to OCS™ Lung System).
6. (b) (4) [redacted]

4.9.3. Initial Stabilization Overview

Table 7 provides recommended settings for initial stabilization

(b) (4) [redacted]

4.9.4. Warming the Lungs

The lung must be warmed and fully perfused before transport (b) (4)

Refrain from ventilation until a brief equilibrium period had been (b) (4)

1. After instrumenting the lungs on the OCS™ Lung System, press the main configuration button  on the Monitor and set the perfusate Temp to (b) (4) under the Preservation menu. Confirm the new setting by acknowledging the "accept" command using the Rotary Knob.

2. Gradually increase the Pump flow rate using the Rotary Knob and after pressing the Pump adjust button  on the Monitor.
3. Target flow rate of (b) (4)

s

4. While gradually warming the lungs, press the main Configuration menu button  and set the ventilation settings to match settings in Table 7 under both Preservation and Monitoring Menu tabs (if not performed during priming).

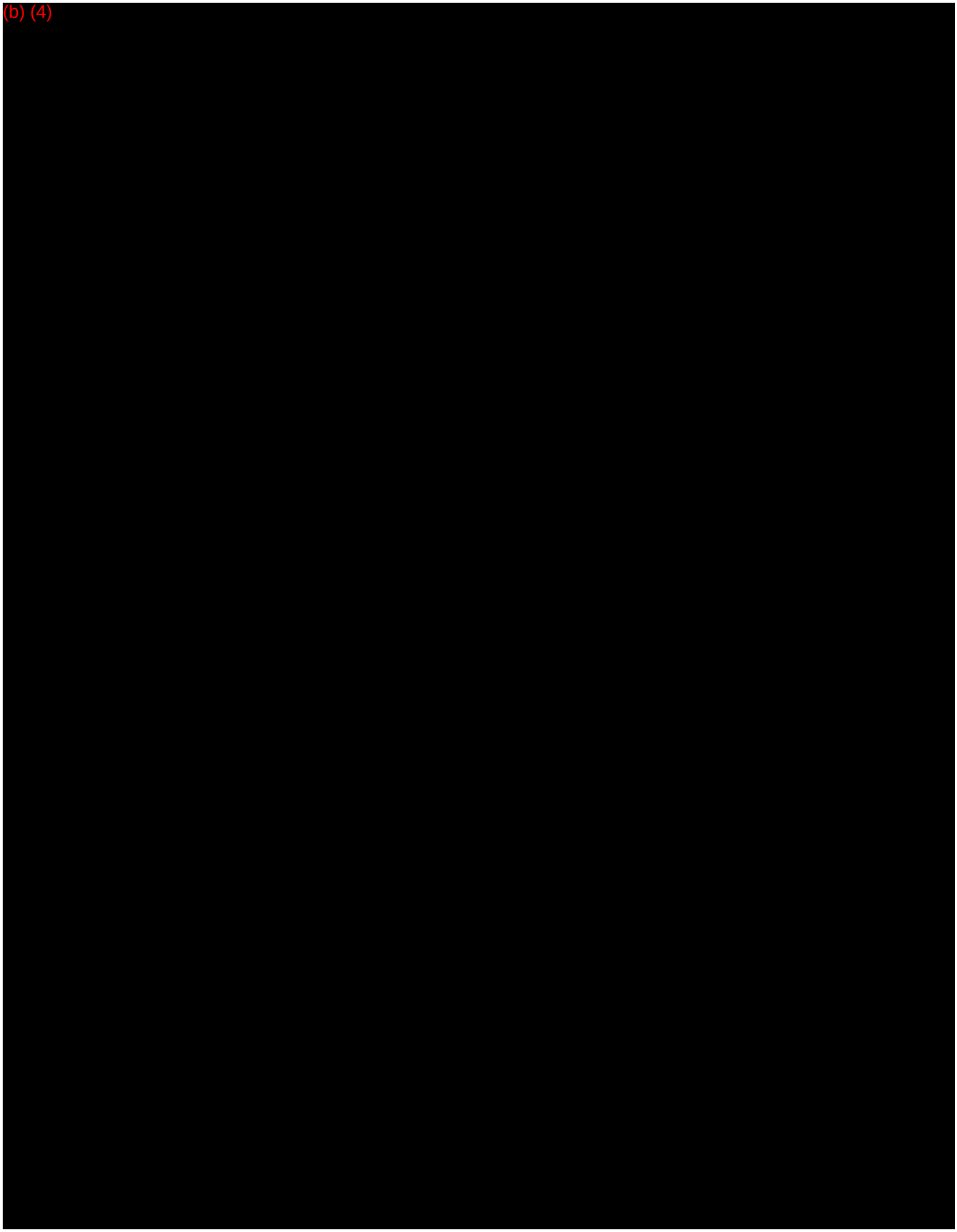
4.9.5. Ventilation Start on the OCS™ Lung System

Start of ventilation takes place after the perfusate temperature reaches (b) and the Pump flow rate reaches at leas (b) (4) . It is recommended to start ventilation in (b) (4) for the first (b minutes and while continuing to achieve a target flow rate of (b) (4)

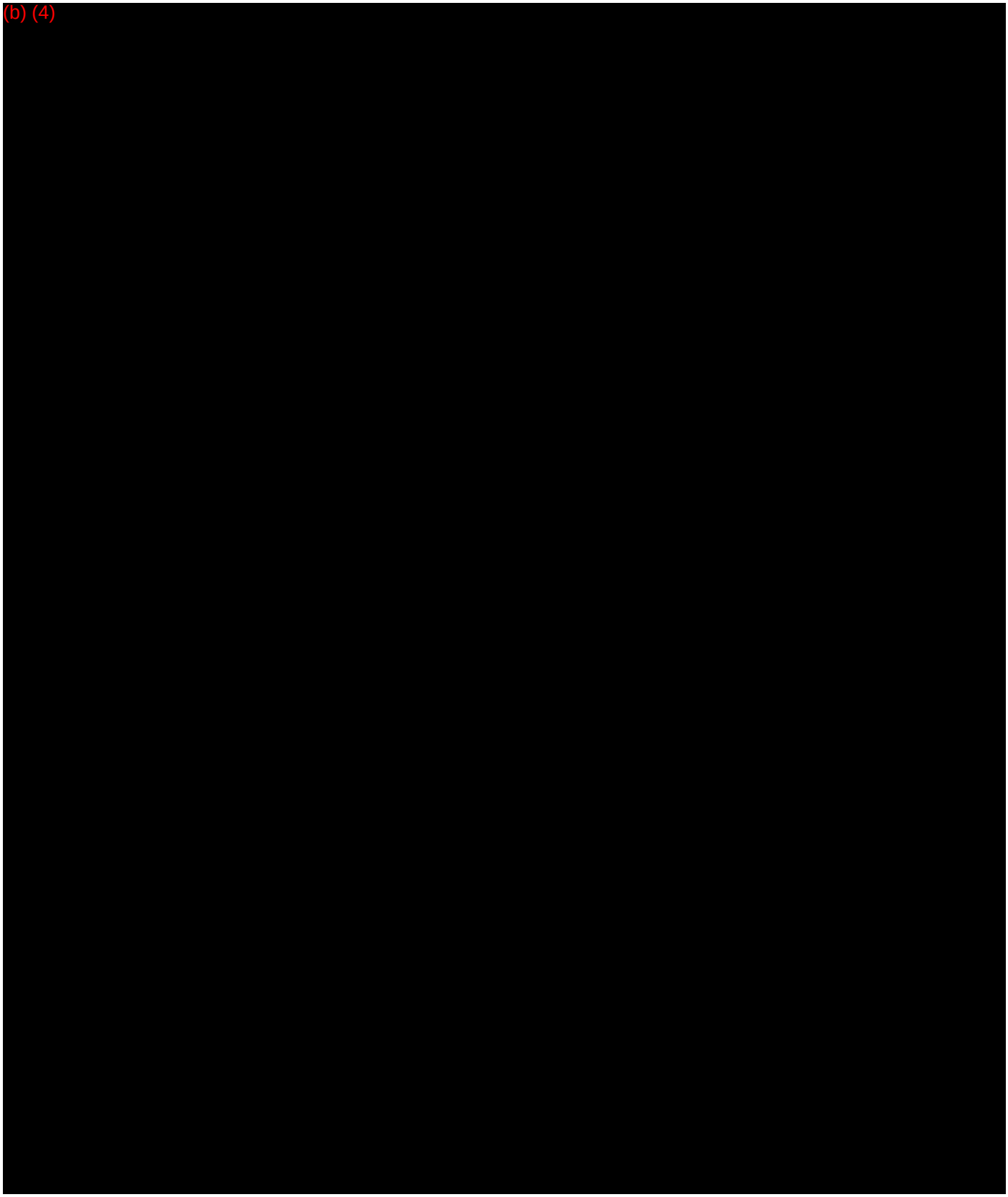
Steps:

1. Once perfusate temp reaches (b) (4) Pump flow rate reaches at least (b) (4) , press the Configuration menu button 
2. Highlight the Ventilator Mode tab using the Rotary knob.
3. Switch to (b) (4) Mode to initiate Ventilation (b) (4) .

(b) (4)



(b) (4)



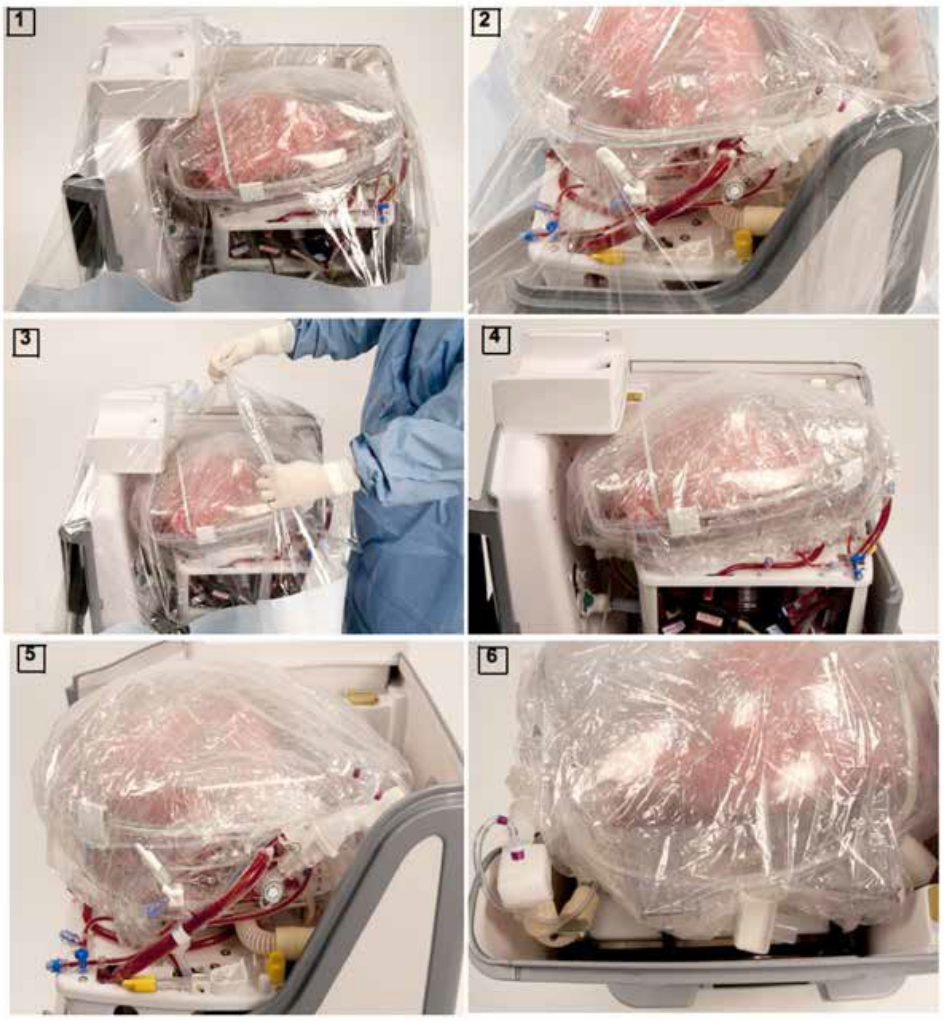
4.9.10. End of the Initial Stabilization Phase

Initial stabilization phase is considered complete after perfusate's temperature reaches (b) (4) lung ventilation started and all target ventilation and perfusion parameters are fully met.

Before proceeding to the initial /baseline monitoring of the lungs, confirm the following are shown on the Wireless Monitor:

(b) (4)

Figure 27: Applying the Sterile Covers/Banded Bags



CAUTION—Do not disconnect the OCS™ Lung System from AC power until ready to leave the donor's site

4.10. Initial (Baseline) Monitoring Overview

4.10.1. Assessing Lungs at Donor's site Prior to Transport

1. Perform an initial assessment of lung oxygenation capacity using (b) (4)

3. Bronchoscope examination can be performed if clinically needed (even at donor site) in which a bronchoscope can be introduced through a designated bronchoscope port on the LPM (b) (4) For detailed steps of performing physical bronchoscope examination, refer to Section 6.2.2.

(b) (4)

4.10.2. Continuous Monitoring Mode Timing and Settings

Timing:

- Occurs in the donor operating room (OR)
- Once the perfusate temp reaches (b) (4) and perfusion and ventilation parameters have been stabilized

PA (Pump) Flow:

- (b) (4)

(b) (4)

Ventilators' Settings:

(b) (4)

***NOTE**—For a suggested ideal body weight formula, see Appendix B: Body Weight Formula (Devine's Formula for donor's height above 150 cm (5 feet)).

4.11. (b) (4) Mode

The OCS™ Lung System continuously deoxygenates the perfusate by supplying (b) (4)

(b) (4)

4.11.1. (b) (4)

(b) (4)

(b) (4) [redacted]

(b) (4) [redacted]

(b) (4)

(b) (4)

It is recommended to always display PAWP trend versus VR trend on the bottom graphic display of the Monitor's screen during Preservation mode. Real time display of these parameters will help the OCS™ Lung System users to manage the lungs as needed during transport. For instructions on how to set or change the lower graphic display on the Monitor's screen, please refer to the *TransMedics Technical User Guide: OCS™ Lung System.*

NOTE: Vascular Resistance (VR). This is a measure of the resistance to flow that must be overcome to push perfusate through the vasculature of the lungs. (b) (4)

5. CHAPTER 5: ACTIVITIES PERFORMED DURING TRANSPORT

The OCS™ Lung System enables medical professionals to perfuse and ventilate the lungs and monitor key parameters during transport between the Donor site and the Recipient site. The instructions for transporting and caring for the lung found in the following two sections are designed to optimize the condition of the organ in preparation for transplant.

5.1. Preparing for Transport

CAUTION—Avoid leaving the OCS™ Lung System in an uncontrolled temperature environment for longer than a few minutes. During such periods, monitor the perfusate temperature and take remedial action if the temperature registers more than one or two degrees over or under the desired setting.

If the Wireless Monitor is taken out of its range (b) (4) verify upon return to range that all parameters are as expected (to detect the rare instance in which a system event occurred while out of range).

1. Close the front panel and reinstall the cover of the OCS™ Lung Console.
2. Unplug the system from AC power, and wind the power cord around the power cord wrap.
3. Have all supplies needed for transport to the recipient site (e.g.: (b) (4)).
4. Press the release buttons on the push handle, lock in the upright position and push the system to the vehicle loading area.
5. At the vehicle, set the wheel locks, (b) (4) lift the system off the base using the lift handles.

NOTE—Always use two people to lift and carry the system. Do not lift the system when it is mounted on to the Mobile Base.

(b) (4)

6. Position the OCS™ Lung Console in the vehicle (b) (4) Remember to bring the Mobile Base for use at the recipient site.
7. For remote monitoring, remove the Wireless Monitor from its docking station.

NOTE—The Wireless Monitor must be kept within (b) (4) the OCS™ Lung Console.

5.2. Managing the Lung and OCS™ Lung System During Transport

During transport, periodically check the following lung parameters on the Wireless Monitor:

- PEEP
- Mean PAP
- PAWP
- TV
- SVO_2
- SaO_2
- VR

During transport, periodically check the following lung system parameters on the Wireless Monitor:

- Pump flow
- (b) (4) gas levels
- OCS™ and Wireless Monitor battery charge status

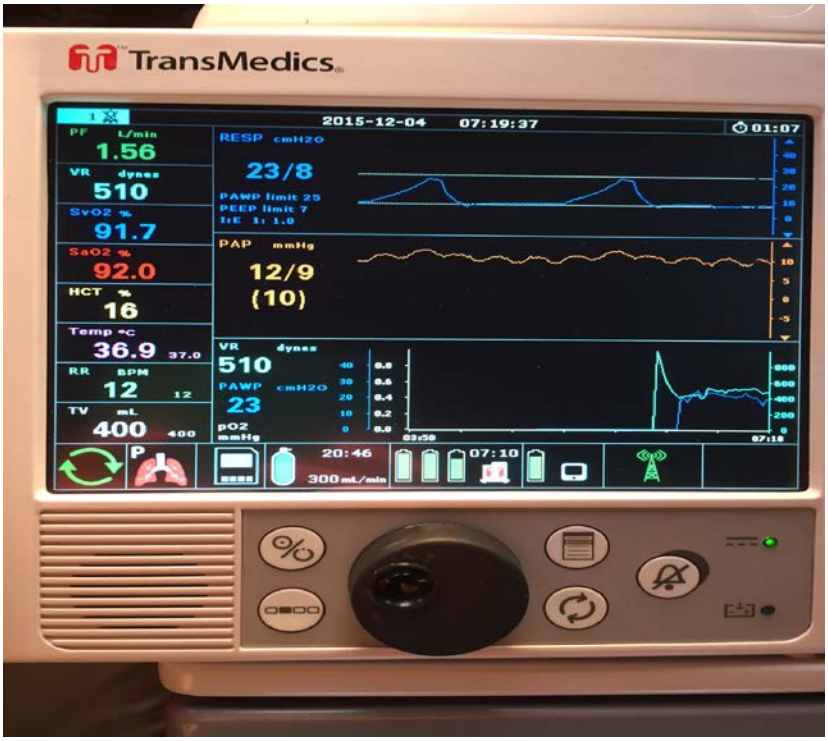
(b) (4)

5.2.1. (b) (4)

(b) (4)

It is recommended to always display PAWP trend versus VR trend on the bottom graphic display of the Monitor's screen during Preservation mode. Real time display of these parameters will help OCS™ Lung System users to manage the lungs as needed during transport (See detailed settings in Figure 32). For more information, please refer to the *TransMedics Technical User Guide: OCS™ Lung System.*

Figure 32: Monitor Picture with Bottom Graphic Frame Set in Preservation Mode to display VR Trend vs. PAWP Trend



6. CHAPTER 6: ACTIVITIES PERFORMED AT RECIPIENT SITE

The OCS™ Lung System enables medical professionals to observe whether key parameters have changed upon arrival at the recipient site or whether they have remained stable throughout transport. In the case of a double-lung, the device may be configured [redacted] to continue perfusing and ventilating the second lung while the first lung is being implanted into the recipient.

Ultimately, with the organ removed from the chamber, proper shutdown and storage ensures the lung system will be ready at short notice for the next run. This chapter provides instructions for the tasks that are performed upon returning to the recipient site.

6.1. Recipient Site Evaluation

[redacted]

Once arrived at the recipient site:

1. Plug the OCS™ Lung System into an active wall AC outlet.
2. Take a final recruitment ABG to:
   - [redacted]

6.2. (b) (4)

[redacted]

(b) (4)

[redacted]

(b) (4)

[redacted]

(b) (4)

[redacted]

(b) (4)

[redacted]

6.2.2. 2-Physical Bronchoscope Monitoring

The OCS™ Lung System has the capability of performing bronchoscope examination while the lungs are inflated on the device.

To prepare for and perform Bronchoscope examination:

1. Keep the Pump flow at (b) (4) [redacted]
2. Ensure that the OCS™ Lung System is stationary.
3. Remove the OCS™ Lung Console top cover.
4. Lower the front panel.

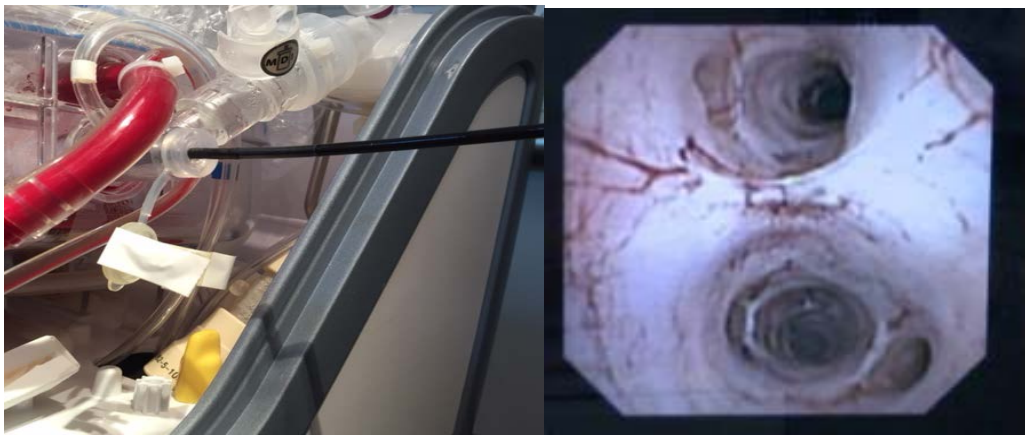
(b) (4)

[redacted]

(b) (4)

6. Insert the fiber-optic bronchoscope via the Bronchoscope port to perform bronchoscope examination as seen in Figure 33.

Figure 33: Bronchoscope Examination on the OCS™ Lung System through a Bronchoscope Port



7. After bronchoscope examination is completed, tightly secure the cap to the Bronchoscope port.
8. Switch back to Preservation Mode following the steps below:
   a. Press  to display the Configuration Menu and select the Ventilator Mode tab.

(b) (4)

6.2.3. 3-Physical Assessment in Organ Chamber

It is recommended to do visual and physical assessment at the recipient's OR prior preservation termination for final clinical implantation decision

Steps of Performing Physical Assessment and Palpation of the lungs:

(b) (4)

6. Keep the organ chamber cover closed until the lungs are ready to be disconnected from the lung system.
7. (b) (4) [redacted]

6.3. Final Implantation Decision

Implantation decision will be taken in the recipient operating room by the transplantation team after considering and reviewing **ALL** of the following methods of observations and monitoring provided by the OCS™ Lung System:

1. (b) (4) [redacted].
2. PO_2/FiO_2 ratio ≥ 300 at time of final Continuous Monitoring on the OCS™ Lung System.
3. Clinically acceptable lungs based on visual, physical and bronchoscope examination.

Once the clinical decision is made to implant the lungs, terminate the preservation session by following either one of two options:

1. **Cooling and preserving both lungs** (b) (4) [redacted]

   Cooling could be done by one of two techniques:

   - (b) (4) [redacted]

2. **Separating and cooling one lung while continuing perfusing and ventilating the second lung until the first lung is implanted.**

6.4. (b) (4) [redacted] Termination Options

General Considerations:

When disconnecting the lung from the OCS™ Lung System a sterile operator(s) performs all actions that involve the inside of the organ chamber. Non-sterile (NS) operator(s) may perform other actions.

(b) (4) [redacted]

When the surgical team is ready to accept and receive the lung for transplant, perform either one of following options in Section 6.4.1 or Section 6.4.2.

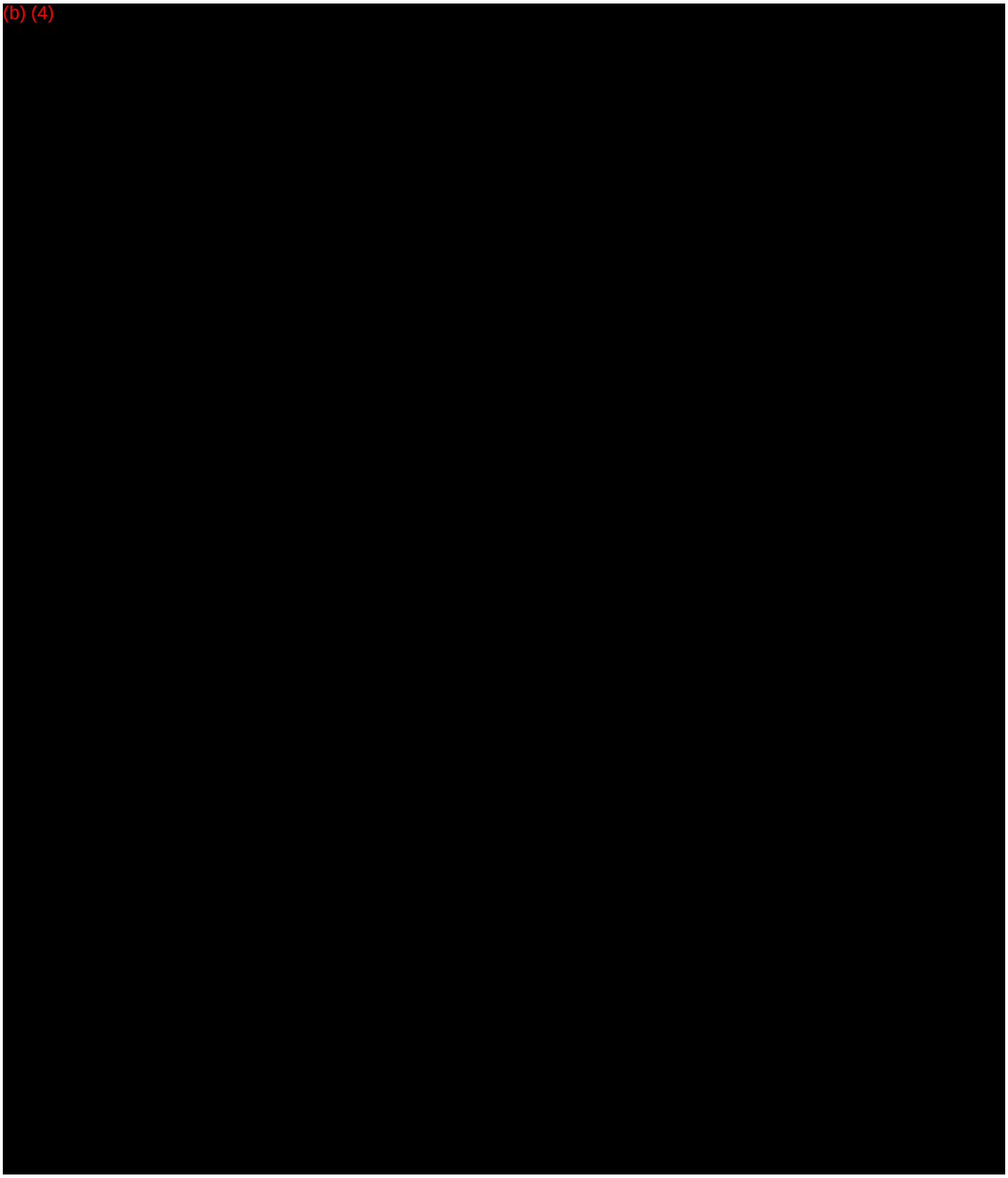
6.4.1. (b) (4)

[redacted]

(b) (4)

[redacted]

(b) (4)



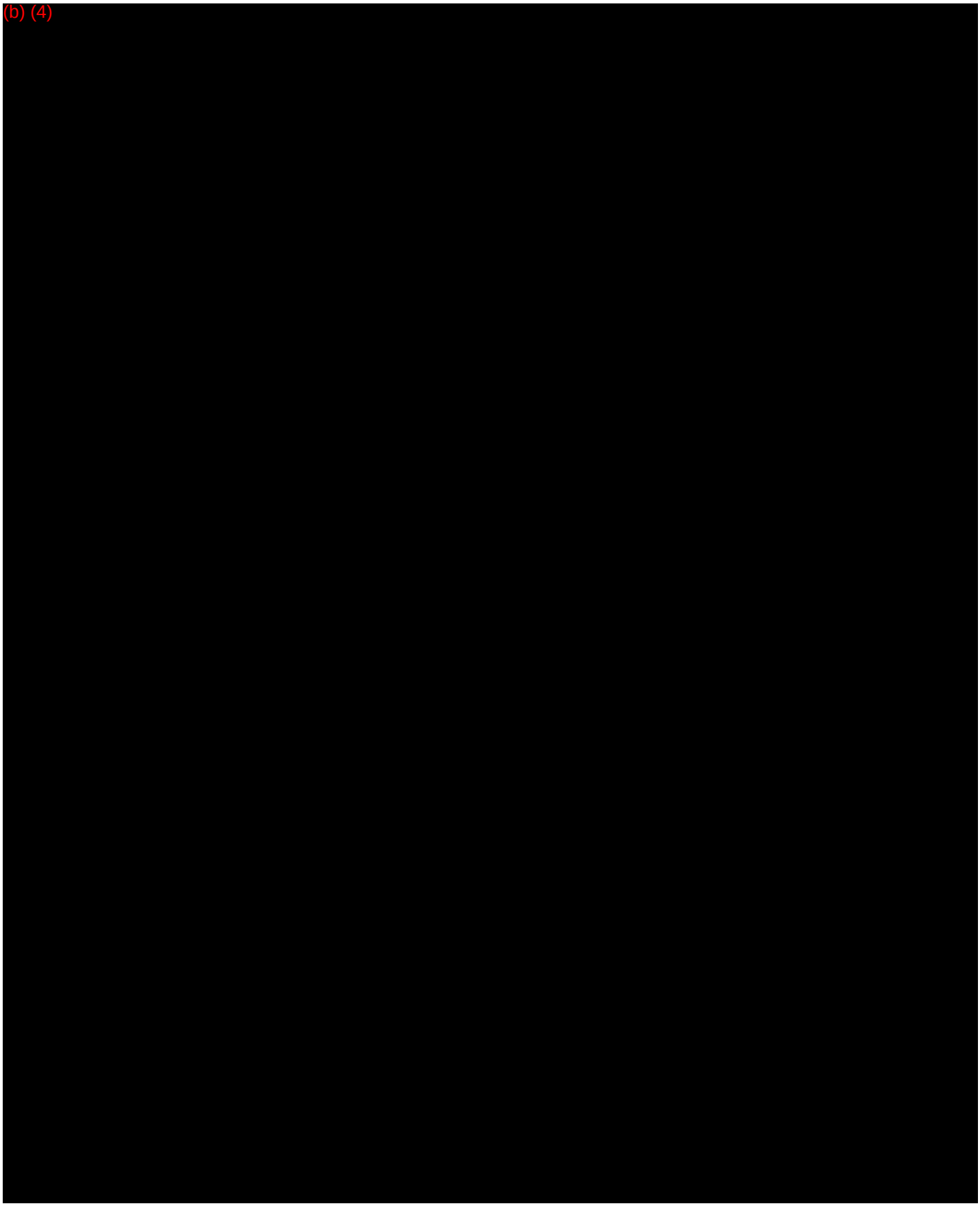
9. (b) (4) [redacted]

(b) (4) [redacted]

(b) (4)

[redacted]

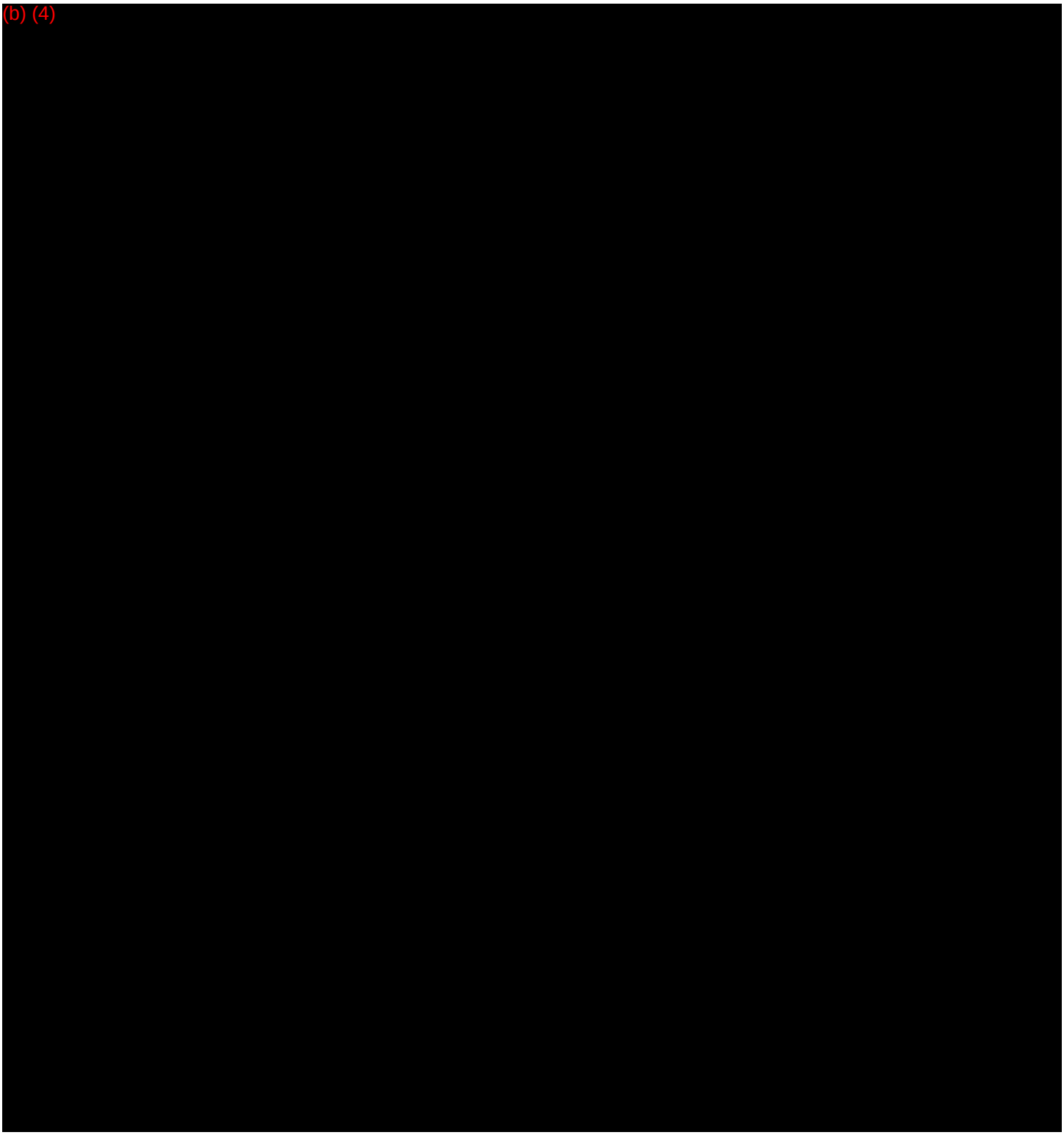
(b) (4)



(b) (4)

[redacted]

(b) (4)



6.5. Performing the Shut-Down Protocol

This section provides instructions for terminating the preservation session and shutting down the OCS™ Lung System.

Perform the following steps after the organ has been disconnected from the system:

1. Remove the sterile drape.
2. Clamp the red side of the Oxygenator Recirculation loop and disconnect the Lung Flush Collection Bag.
3. Dispose of materials according to the standard site procedure for disposal of blood contaminated materials.

6.6. Preparing the OCS™ Lung System for Shutdown

1. Once the organ has been removed press the  button while the Monitor is docked to the OCS™ Lung Console.
2. Set the lung system to Standby Mode.
3. If no data card is present, the software will provide on-screen instructions.
   a. Follow the on-screen directions to ensure that all data is downloaded to the data card.
   b. Remove the data card from the slot to the right of the Wireless Monitor-docking cradle.

6.7. Removing the Probes from Tubing

The probes are reusable and do not require sterilization since they do not directly contact perfusate. After the lung has been removed, detach the Flow, SaO_2/Hematocrit, and SvO_2/Hematocrit probes from the tubing, clean the probes as described in ***Chapter 8*** of the *TransMedics Technical User Guide: OCS™ Lung System*, and store them inside the Lung System.

To remove the Flow probe from the tubing:

1. Press the latch on the side of the probe until the probe lid opens.
2. Carefully remove the flow probe from the tubing on the (b) (4) Module, but leave it connected to the OCS™ Lung Console.

To remove the SvO_2/Hematocrit and SaO_2/Hematocrit probes from the tubing:

1. Firmly grasp the probe with one hand.
2. Use the other hand to gently remove the cuvette from the probe.
3. Carefully remove the SaO_2/Hematocrit probe and the SvO_2/Hematocrit probe from the tubing on the (b) (4) Module, but leave them connected to the OCS™ Lung Console.

6.8. Disconnecting the Ventilator Lines

NOTE—Before disconnecting the Ventilator lines, make sure the Ventilator Mode is set to OFF Mode or the OCS™ Lung System is in Standby Mode.

1. To turn the Ventilator to OFF Mode, press the  button to set the system to Standby Mode, or configure the Ventilator Mode to OFF.
2. To disconnect the Ventilator lines, press the green button and firmly pull back on the connector to release it.

6.9. Turning off the (b) (4) Gas

CAUTION—Do not over-tighten the gas valve with the cylinder wrench. Excessive tightening may damage the valve.

Always ensure that the gas cylinders are OFF after the preservation session is complete.

1. Use the cylinder wrench to shut off the (b) (4) Gas by slowly turning the shut-off valve clock- wise.
2. If the (b) (4) Gas cylinder is connected to the OCS™ Lung Console, close its valve and disconnect it from the Lung Console.

6.10. Removing and Disposing of the (b) (4) Module

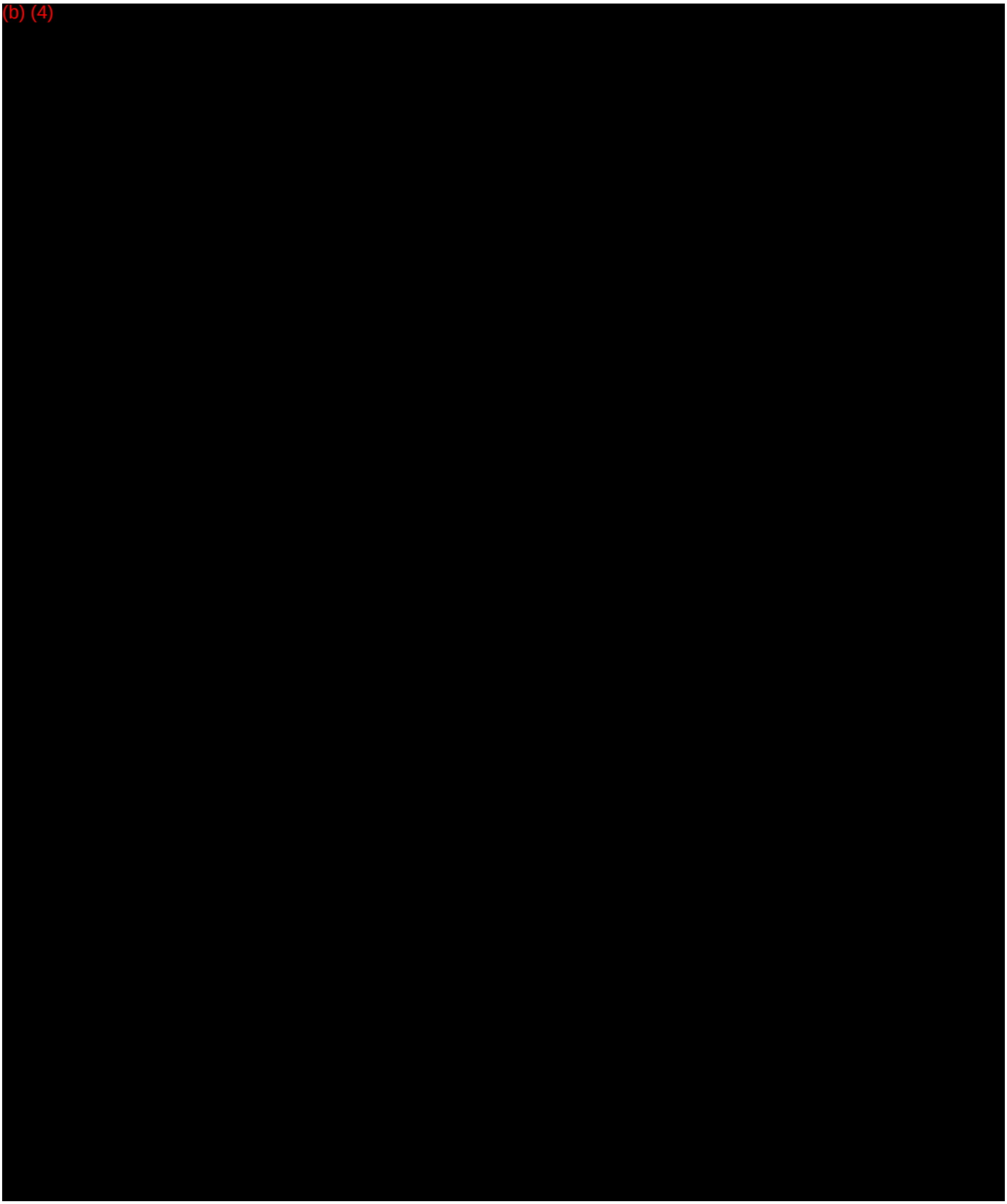
1. Facing the Lung system so that Wireless Monitor is on your left, perform the following:
   a. Press the (b) (4) Module release lever to disengage the clips that hold it in place.
   b. Hold the (b) (4) Module with your left hand and disengage it with your right hand.
   c. Rotate and angle the (b) (4) Module (b) (4) toward you to disengage it from the pump slots.
   d. Lift the (b) (4) Module up and out of the OCS™ Lung Console.
2. Dispose of the entire (b) (4) Module using your institution's protocol for handling and dis- posing of blood-contaminated materials.

6.11. Preparing the OCS™ Lung System for Storage

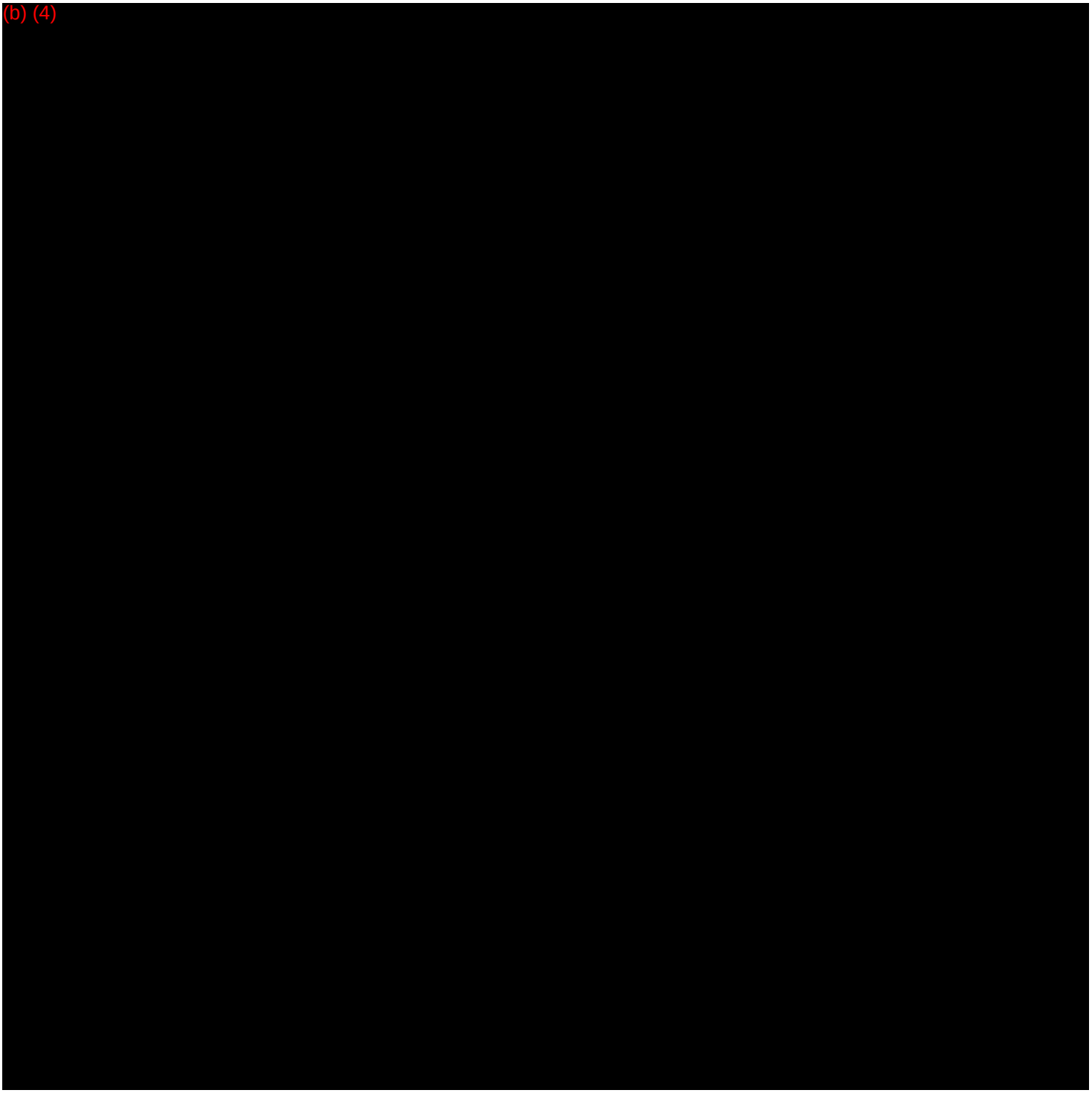
1. Disconnect the system from AC power.
2. Clean the system by following the instructions in the *TransMedics Technical User Guide: OCS™ Lung System*.
3. Reinstall the top cover.
4. Transport the system to the storage area and connect it to an AC outlet with the Monitor docked in its cradle, ensuring the power switch remains in the ON position and that the system is stored in STANDBY MODE.

(b) (4)

(b) (4)



(b) (4)



APPENDIX A. OCS™ LUNG SYSTEM INSPIRE STUDY

1. Study Objectives and Endpoints

The primary objective of the INSPIRE study is to compare the safety and effectiveness of the OCS Lung System with the current cold storage standard of care for the preservation of standard criteria donor lungs. The study is a prospective, multi-center, randomized, controlled investigation of 320 subjects conducted at 21 sites in the United States, Europe, Canada and Australia. Subjects were assigned to either the standard cold static organ preservation (control) or to the OCS Lung System warm, perfused and ventilated preservation (treatment).

The primary effectiveness endpoint is a composite of all cause patient survival post-transplantation at day 30, and absence of PGD Grade 3 within the first 72 hours post-transplant.

INSPIRE was designed as non-inferiority study, with a non-inferiority margin of 4.0%, however, it was pre-specified that in the event non-inferiority is demonstrated, superiority will be tested using Chi-square test or, in the case of one or more cells of contingency table having an expected frequency of five or less, Fisher's exact test (two-sided). This conservative 4% non-inferiority is smaller than the non-inferiority margin (delta) of 10 to 15% that is typically used in clinical studies of cardiovascular and thoracic devices (e.g., ENDURANCE Trial, PROCEED II Trial, Celsior Trial).

An additional clinical endpoint was calculated as an adjunct to the primary effectiveness endpoint. This additional endpoint is a composite of patient survival at day 30 and survival at initial hospital discharge and absence of PGD3 within the first 72 hours post-transplantation. This adjunct composite endpoint analysis evaluates the same fundamental clinical components as the primary effectiveness endpoint (short term survival and freedom from PGD 3 in the first 72 hours); however, it assesses survival throughout the initial hospital post-transplant course instead of limiting to 30-days post-transplant to capture the full initial transplant mortality component.

2. Secondary Effectiveness Endpoints

The secondary effectiveness endpoints were:

- Incidence of ISHLT PGD 3 at T72 hours post-lung transplantation
- Incidence of ISHLT PGD 2 or 3 at T72 hours post-lung transplantation
- Patient survival at day 30

3. Safety Endpoint

The primary safety endpoint is the mean number of lung-graft-related serious adverse events (SAE) through the 30 days post-transplantation per subject. A lung-graft-related serious adverse event is defined as the occurrence of any of the following four categories of adverse events that are also serious. In calculating the primary safety endpoint, multiple occurrences of SAE of the same category on the same subject within 30 days is counted as one lung-graft-related SAE.

- Acute rejection
- Respiratory failure
- Bronchial anastomotic complication

- Major pulmonary-related infection

4. Study Population

Subjects were lung transplant recipients who met inclusion/exclusion criteria as outlined below. Inclusion/exclusion criteria were also defined for the donor organs as described below.

Inclusion Criteria:

Donor Inclusion Criteria

- Age <65 years old
- Normal gas exchange, i.e., PaO2/FiO2 ≥300, at the time of final acceptance of donor lungs
- No active primary pulmonary disease
- Donor lungs suitable for preservation with either OCS™ or Standard of Care

Recipient Inclusion Criteria:

- Registered male or female primary double-lung transplant candidate
- Age ≥ 18 years old
- Signed: 1) written informed consent document and 2) authorization to use and disclose protected health information

Exclusion Criteria:

Donor Exclusion Criteria

- Positive serology for Hepatitis B, Hepatitis C, or HIV
- Presence of moderate to severe traumatic lung injury presenting as moderate or massive pneumothorax, hemothorax or lung contusion as evidenced by chest X-ray, CT-Scan, visual inspection or bronchoscopy
- Presence of confirmed active pneumonia

Recipient Exclusion Criteria

- Prior solid organ or bone marrow transplant
- Single lung recipient
- Multiple organ transplant recipient
- Chronic use of hemodialysis or diagnosis of chronic renal insufficiency

5. Study Treatments

The donor organs in the OCS Arm were perfused with the OCS™ Lung System. The Control Arm utilized an FDA-cleared, commercially available solution for lung flushing and preservation. The solution was used according to its instructions for use.

Follow-up data collection was conducted at 7 days, hospital discharge, 30 days, and 6 months post-transplant, with additional long-term data collection at 12 and 24 months.

6. Analysis Populations

The OCS™ Lung System requires the use of a high-oncotic perfusion solution supplemented with matched packed red blood cells (pRBCs) as part of the perfusate. The initial INSPIRE Trial IDE was approved to allow for either OCS™ Lung Solution or a commercially available solution (due to their similar chemical composition).

TransMedics is approved to use only the OCS™ Lung Solution with its OCS™ Lung System. Therefore, the data are presented for both the OCS Arm, which includes subjects perfused with

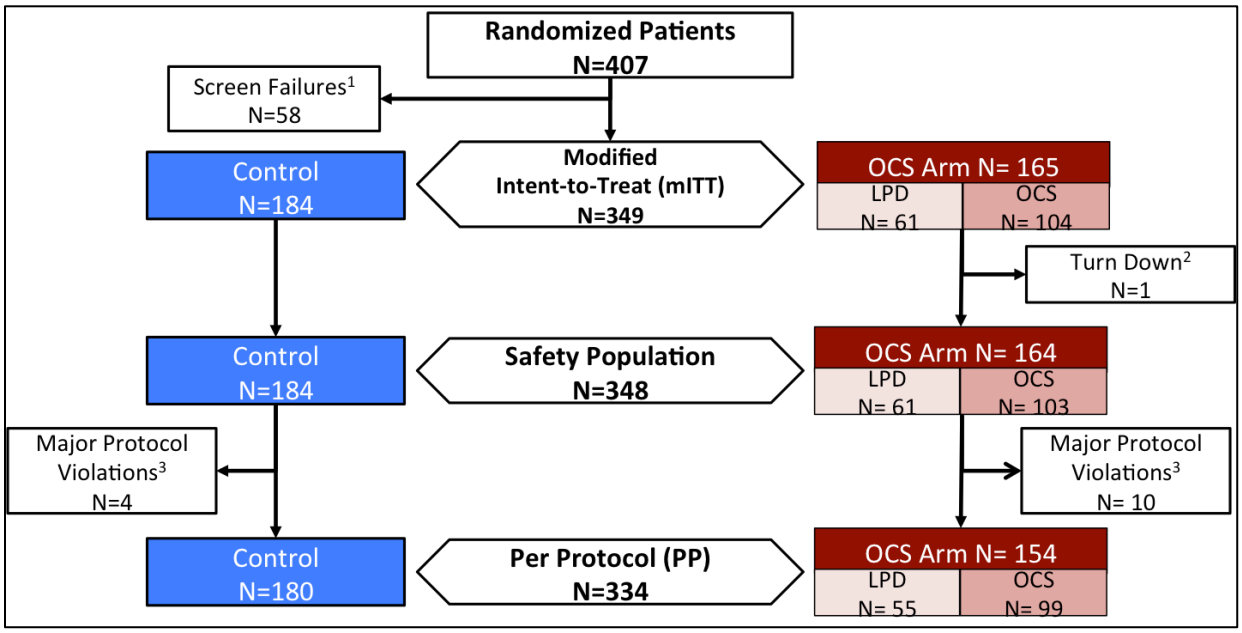
both OCS™ Lung Solution and the commercially available solution, as well as for subjects perfused with the OCS™ Lung Solution only (i.e., the OCS Lung Solution subgroup).

The following are the Analysis Populations that were pre-specified in the protocol and the statistical analysis plan:

- Per Protocol Population (PP) (N= 334)
- Modified Intent to Treat Population (mITT) (N = 349)
- As Treated Population (AT) (N = 319)
- Safety Population (SP) (N = 348)

The subject consort diagram is shown in Figure 44 along with an explanation of the Protocol Deviations and Screen Failures.

Figure 44: INSPIRE Trial Enrollment Detailed Consort Diagram



Screen Failures

- Donor screen failure= 33
- Recipient screen failure= 6

(b) (4)

[redacted]

[3] OCS Major Protocol Violations N=9:

- n=1: Donor lung eligibility for the study was not confirmed given that no final donor PaO_2/FiO_2 ratio was obtained during final assessment of the donor prior to retrieval
- n=1: Donor lung did not meet eligibility criteria due to presence of left lower lobe pneumonia, consolidation and mucopurulent secretions at time of lung retrieval
- n=1: Donor lung did not meet eligibility criteria due to presence of severe emphysema/COPD with blebs and large ruptured bullae on donor lungs
- n=1: Failure to follow the study protocol for using ABO compatible pRBCs. The donor lungs were perfused using ABO incompatible pRBCs
- n=1: Failure to follow the IFU by exceeding recommended range of OCS pump flow during perfusion of donor lungs, which may have resulted in air being introduced to the perfusion line.

- n=1: Failure to follow the IFU and protocol by failing to connect the OCS ventilator air-line to the OCS ventilator circuit to ventilate the donor lungs on the device. Lung was immediately removed from OCS and transplanted using cold storage
- n=1: Failure to follow IFU and protocol for connecting the OCS perfusion module to engage with the ventilator arm, resulting in interruption of ventilation to the donor lung. Lung was immediately removed from OCS and transplanted using cold storage
- n=1: Failure to follow IFU and protocol for management of donor lung on OCS:
    - Staff at investigational site initiated OCS procurement against instructions from sponsor due to his lack of knowledge on how to operate the OCS. The operator was unable to locate the on-button for the OCS device;
    - Did not apply the OCS lung wrap to protect against barotrauma;
    - Did not perform any blood gas measurements on the OCS to assess the donor lung management
- n=1: Failure to follow IFU for management of donor lung on OCS:
    - Used only 1 liter of perfusion solution instead of minimum of 1.5 liters to prime OCS
    - Did not apply the OCS lung wrap to protect against barotrauma while ventilating donor lungs on OCS

[4] ***Control Arm Protocol Violations N=4:***

- n= 3: The donor lungs were flushed and preserved using a different preservation solution than the pre-specified solution in the protocol.
- n=1: Donor lung did not meet eligibility criteria due to presence of active pneumonia/aspiration with mucopurulent secretions in the right and left bronchi at time of harvest.

7. Demographic and Baseline Information

Recipient characteristics are shown in Table 9 below. The two groups were similar in all categories and no significant differences were noted.

Table 9: Recipient Demographic and Baseline Characteristics (mITT Population)

Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Age (years)			
N	184	165	104
Mean ± SD	50.34 ± 13.43	50.45 ± 12.82	49.63 ± 13.21
Median	55.0	54.0	52.5
Minimum - Maximum	18.0 - 72.0	18.0 - 72.0	18.0 - 71.0
Gender			
Female	35.9% (66/184)	47.9% (79/165)	51.0% (53/104)
Male	64.1% (118/184)	52.1% (86/165)	49.0% (51/104)
Ethnicity			
Hispanic or Latino	9.2% (17/184)	13.3% (22/165)	12.5% (13/104)
Not Hispanic or Latino	70.7% (130/184)	66.7% (110/165)	68.3% (71/104)
Not Applicable	20.1% (37/184)	20.0% (33/165)	19.2% (20/104)
Race			
American Indian or Alaskan Native	0.0% (0/183)	0.0% (0/162)	0.0% (0/102)
Asian	1.6% (3/183)	1.9% (3/162)	1.0% (1/102)
Black or African American	2.7% (5/183)	4.3% (7/162)	4.9% (5/102)
Hispanic	3.3% (6/183)	7.4% (12/162)	5.9% (6/102)
Native Hawaiian or Other Pacific Islander	0.5% (1/183)	0.0% (0/162)	0.0% (0/102)
White	88.0% (161/183)	84.6% (137/162)	87.3% (89/102)

Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Other	3.8% (7/183)	1.9% (3/162)	1.0% (1/102)
Weight (kg)			
N	184	165	104
Mean ± SD	68.78 ± 15.30	67.13 ± 16.65	65.20 ± 17.35
Median	68.0	66.0	63.0
Minimum - Maximum	37.0 - 112.5	32.0 - 128.0	32.0 - 128.0
Type of Status			
Urgent	84.3% (43/51)	82.7% (43/52)	82.4% (28/34)
High-Urgent	15.7% (8/51)	17.3% (9/52)	17.6% (6/34)
Lung Allocation Score			
N	125	107	66
Mean ± SD	47.57 ± 18.34	50.54 ± 20.10	48.32 ± 17.75
Median	40.0	41.0	40.0
Minimum - Maximum	29.0 - 95.0	29.0 - 95.0	31.0 - 94.0
Primary Cause of Lung Failure			
Chronic Obstructive Pulmonary Disease	28.8% (53/184)	28.5% (47/165)	29.8% (31/104)
Cystic Fibrosis	23.4% (43/184)	20.6% (34/165)	23.1% (24/104)
Idiopathic Pulmonary Arterial Hypertension	4.3% (8/184)	8.5% (14/165)	9.6% (10/104)
Bronchiectasis	4.9% (9/184)	4.8% (8/165)	4.8% (5/104)
Idiopathic Pulmonary Fibrosis	34.8% (64/184)	35.2% (58/165)	32.7% (34/104)
Sarcoidosis	4.9% (9/184)	2.4% (4/165)	1.9% (2/104)
Other	3.3% (6/184)	4.8% (8/165)	2.9% (3/104)
Additional Risk Factors			
Diagnosis of Secondary Pulmonary Hypertension	32.2% (59/183)	40.2% (66/164)	39.8% (41/103)
Diagnosis of Heart Failure	7.2% (13/180)	8.5% (14/164)	11.7% (12/103)

Donor demographic baseline characteristics and risk factors are shown in Table 10 below. The donor characteristics were generally similar between the arms, although there was a trend towards slightly more males than females in the control group. Also, the OCS group had a higher percentage of abnormal findings on final physical examination of the donor lungs prior to retrieval and a higher percentage of surgical complications during retrieval prior to preservation (e.g., adhesions tears, COPD blebs resections).

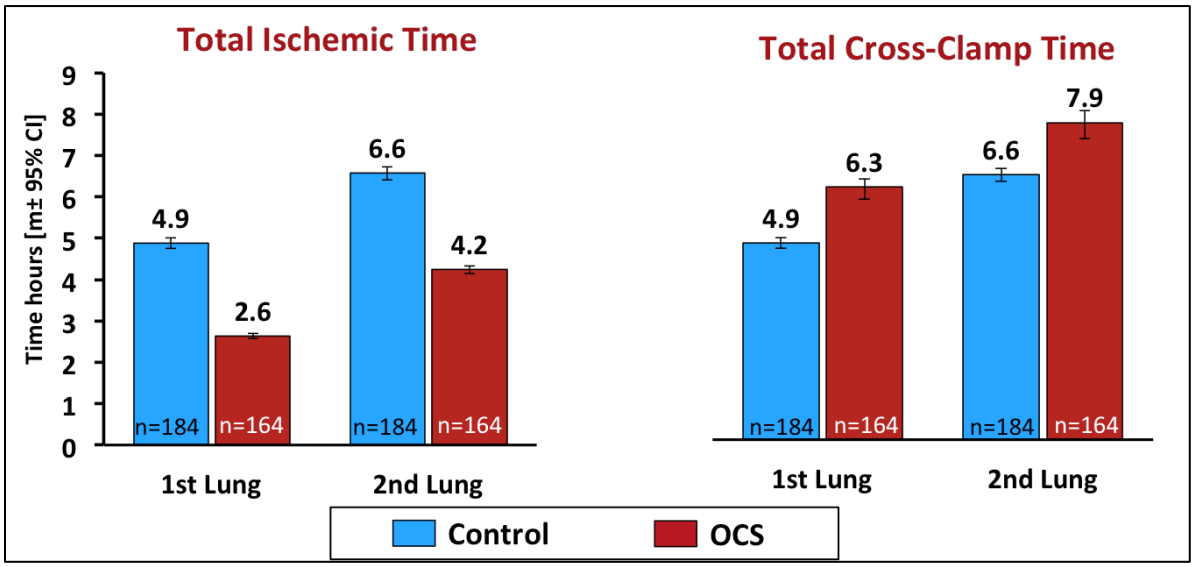
Table 10: Donor Demographic and Baseline Characteristics (ITT Population, N=349, Combined Cohort)

Parameter	Control (N=184)	OCS Arm (N=165)	OCS Solution Subgroup (N=104)
Donor Age (years)	n=183	n=163	n=103
Mean ± SD	40.15 ± 13.70	41.52 ± 14.40	41.00 ± 14.53
Median	42.0	44.0	43.0
Min.-Max.	14.0 - 63.0	13.0 - 64.0	13.0 - 63.0
Gender	n=184	N=165	N=104
Female	39.7% (73/184)	47.3% (78/165)	51.0% (53/104)
Male	60.3% (111/184)	52.7% (87/165)	49.0% (51/104)
Donor Final PaO_2/FiO_2 Ratio	n=184	n=163	n=103
Mean ± SD	431.73 ± 73.34	441.37 ± 78.89	445.83 ± 78.61
Median	427.1	435.0	443.1
Min.-Max.	301.0 - 642.0	304.0 - 689.0	315.0 - 689.0
Abnormal Findings on Physical Examination of Donor Lungs Prior to Retrieval	25.5% (47/184)	36.4% (60/165)	41.3% (43/104)
Any Surgical Complications/Tears during Retrieval?	1.4% (2/148)	6.0% (9/151)	6.3% (6/95)
Cigarette use (>20 pack years) Continued in Last 6 months	n=183	n=165	n=104
Yes	17.5% (32/183)	18.3%(30/164)	18.3% (19/104)
No	71.6% (131/183)	69.5% (114/164)	71.2% (74/104)
Unknown	10.9% (20/183)	12.2% (20/164)	10.6% (11/104)

8. Donor (b) (4) Characteristics & Critical Times

The use of OCS significantly reduced the injurious ischemic time on the donor lungs ($p<0.0001$) while allowing donor lungs to be preserved with a significantly longer total cross clamp time ($p<0.0001$). See Figure 45 below.

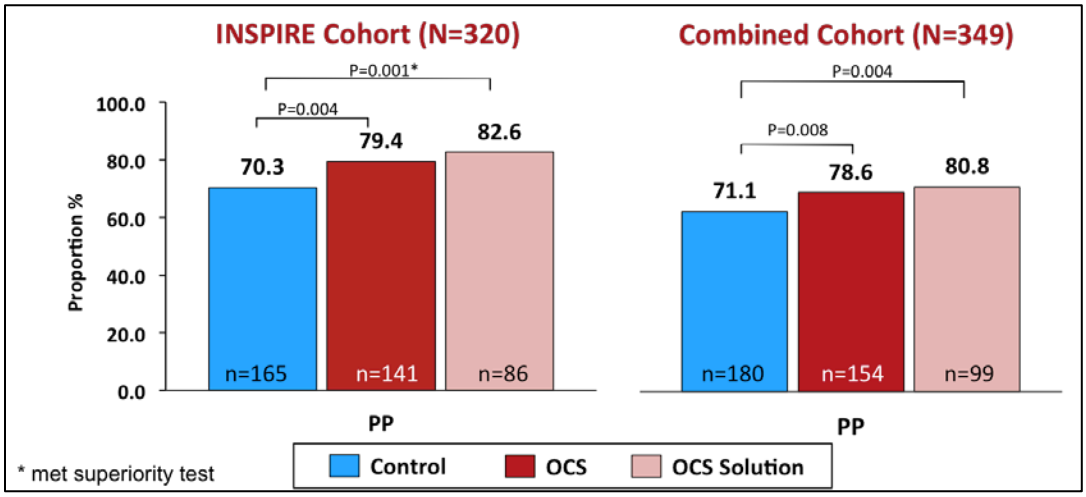
Figure 45: Total Cross Clamp and Ischemic Times on Transplanted Lungs (As Treated Population)



9. Primary Effectiveness Endpoint & Related Analyses

The INSPIRE Trial primary effectiveness endpoint assessed the impact of the OCS Lung System on 30-day patient survival and incidence of PGD3 within 72 hours post-transplantation. As shown in Figure 46 below, the primary effectiveness objective was met in the INSPIRE Cohort (N=320) as well as in the Combined Cohort (N=349), which includes patients from the Administrative Extension. The rate of the primary endpoint in the OCS arm was non-inferior to Control arm at the 4% non-inferiority margin in the PP population, the primary analysis population for the INSPIRE Trial ($p=0.008$ and $p=0.004$ for the Combined and INSPIRE Cohorts, respectively). The primary effectiveness objective was also met in the OCS Solution subgroup in both populations, which reflects results of the OCS Lung System under review in this PMA, as well as the to-be-marketed product. In the mITT population, the OCS arm did not meet the non-inferiority margin for both Cohorts ($p=0.06$ and $p=0.10$), while the OCS Solution subgroup was shown to be statistically non-inferior in both Cohorts ($p=0.012$ and $p=0.033$ for the INSPIRE and Combined Cohorts, respectively). Interpretation of the mITT population results should take into consideration the confounding clinical variables stated above (outcomes for non-transplanted patients, major protocol violations and treatment cross over to use cold storage and analyzed in the OCS arm).

Figure 46: Composite of All Cause Patient Survival at 30 days Post-Transplant and Absence of PGD grade 3 in The First 72 Hours (Primary Effectiveness Endpoint) (PP Population)



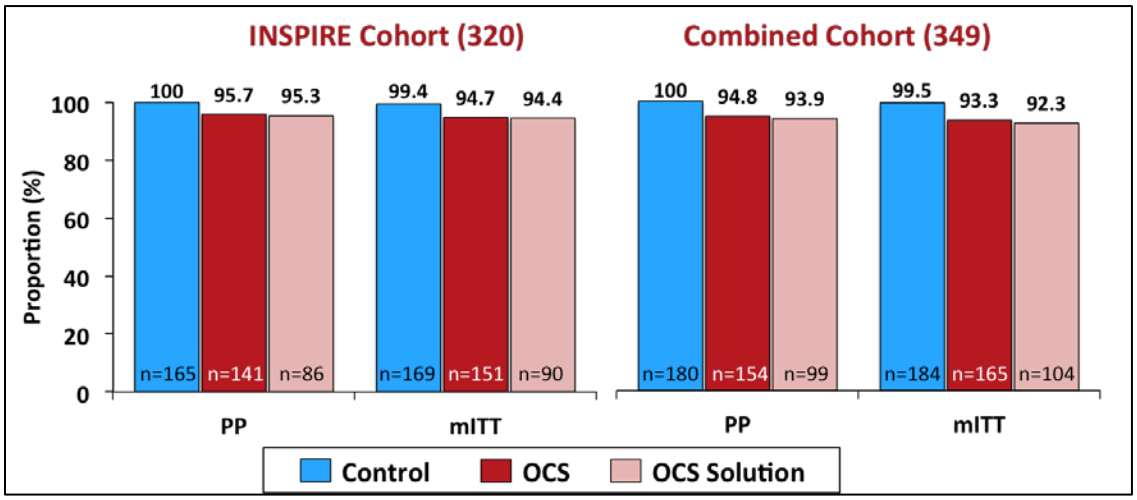
* Non Inferiority Test P value

In summary, the results of the INSPIRE Trial demonstrate that the primary effectiveness endpoint was met.

10. Patient Survival at Day 30

As shown in Figure 47 below, patient survival at 30 days was lower in the OCS arm in comparison to control. There were 11 deaths in the OCS group and 1 death in the Control group within 30 days in the Combined Cohort (n=349). Of the 11 deaths in the OCS arm, 6 were due to cardiac or vascular causes adjudicated as unrelated to the lung transplanted graft, 4 were lung graft failure or infection and one was due to generalized sepsis. The death in the control group was due to metabolic coma. Note that the 30-day all-cause mortality reported for lung transplant recipients in the 2012 OPTN/SRTR annual report was 4.1% [OPTN/SRTR 2014]. The rate reported for the OCS group (6.7%) is similar to the national average while the control group mortality is lower (0.5%). Additional analysis in early survival trends demonstrated that 30-day and in-hospital mortality were similar between the OCS and Control arms.

Figure 47: Survival at 30 Days in INSPIRE Trial (INSPIRE and Combined Cohorts, mITT and PP populations)



11. OCS Lung System Reduces the Incidence of PGD3

Figure 48 and Figure 49 below provide the results for one of the components of the composite primary endpoint, i.e., of the incidence of PGD3 within the initial 72 hours post-transplantation. Results are shown for both the INSPIRE Cohort and the Combined Cohort, respectively.

In the Combined Cohort, the OCS arm and the OCS Solution subgroup were shown to be statistically superior in reducing PGD3 within the initial 72 hours as compared to the Control arm in the PP population (OCS arm p=0.033, OCS Solution subgroup p=0.018). In the PP population, the incidence of PGD3 was reduced by about a third for the overall OCS arm compared to Control, and by nearly half for OCS patients who were transplanted using OCS Lung Solution.

In the mITT population, the incidence of PGD3 was numerically lower in the OCS arm and the OCS Solution subgroup; however, the differences were not statistically significant. The attenuation of the treatment effect in the mITT analysis was expected as the mITT population includes randomized OCS patients who were never transplanted in the study or were transplanted using cold storage yet analyzed in the OCS arm, as well as patients who were transplanted with donor lungs that did not meet eligibility criteria of the trial protocol.

Figure 48: Incidence of PGD3 within 72 hours (INSPIRE and Combined Cohorts, PP Population)

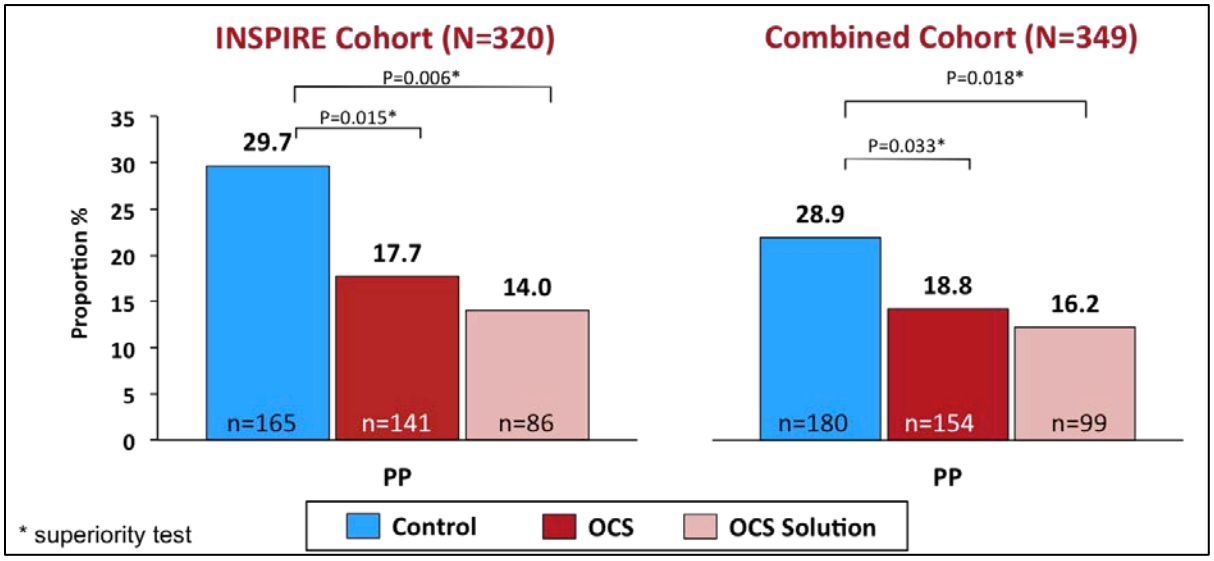
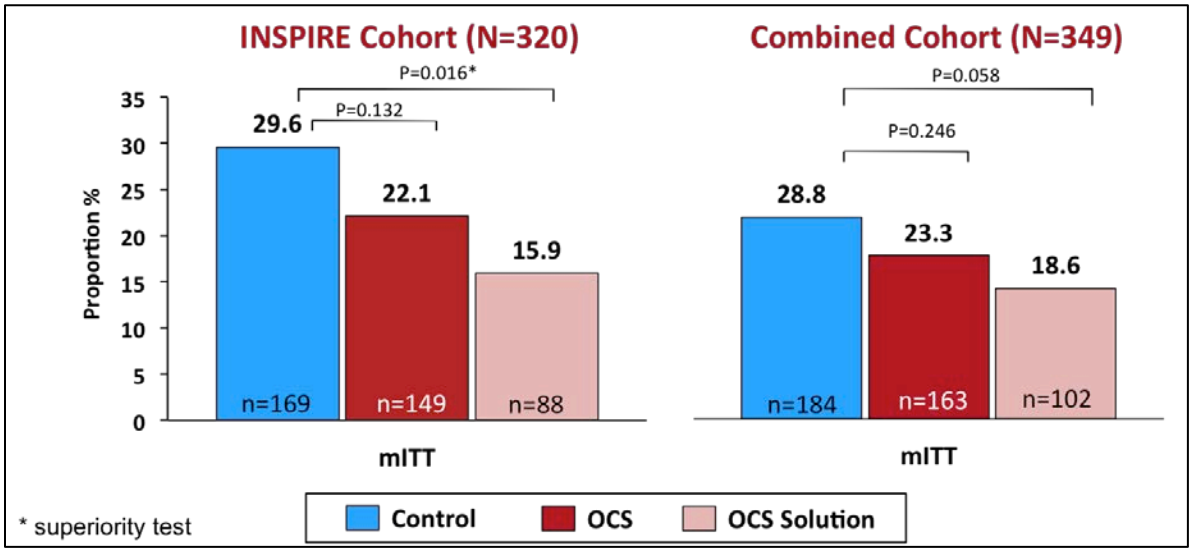


Figure 49: Incidence of PGD3 within 72 hours (ITT Population, INSPIRE and Combined Cohorts)



12. Safety Endpoint was Met

The results for the safety endpoint (i.e., the average number of Lung Graft-Related Serious Adverse Events (LGRSAEs) through 30 days post-transplant) for the Combined Cohort Safety Population are shown in Table 11. The safety endpoint was met, providing substantial evidence for the safety of the OCS Lung System for the proposed use.

Table 11: Safety Endpoint Analysis – (Average Number of LGRSAEs through the 30 days post-transplantation per patient) in Combined Cohort Safety Population

INSPIRE Combined Cohort (n=349)	Control N=184	OCS N=164	OCS Solution N=103
Lung-graft related SAEs, n (%)	45 (24.5)	40 (24.4)	28 (27.2)
Mean ± SD	0.29 ± 0.54	0.26 ± 0.48	0.30 ± 0.52
Non-Inferiority p-value		0.042	0.193
Type of Lung-graft related SAEs, n (%)			
Acute Rejection	4 (2)	2 (1)	2 (2)
Respiratory Failure	16 (9)	23 (14)	15 (15)
Bronchial Anastomotic Complication	4 (2)	0	0
Major Pulmonary-Related Infection	29 (16)	18 (11)	14 (14)

13. In-Hospital and Longer-Term Survival

As previously shown, survival at Day 30 was lower in the OCS arm compared to Control. However, as shown in Figure 50 below, when considering mortality at both 30-day and at initial hospital discharge (if greater than 30 days), survival is similar in both arms. Mortality at Day 30 **and** at initial hospital discharge post-lung transplantation (if greater than 30 days) provides a more comprehensive assessment of early post-transplant mortality since some patients suffering from transplant-related complications may live past 30 days post-transplant, but die prior to discharge (i.e., surgical mortality). This analysis also provides another perspective on clinical benefit, since living through day 30 but dying in the hospital – with or without PGD3 – is clearly not a favorable patient outcome.

Figure 51 shows the cause of death for patients who died at 30 days or In Hospital. Note that 8 of 12 (66.7%) deaths in the Control arm were lung graft failure or infection compared to 4 of 12 (33.3%) deaths in the OCS arm.

This finding underscores the importance of assessing early mortality throughout the initial hospitalization period after transplantation to capture the full clinical picture for patients who were suffering from transplant-related complications that resulted in their mortality after the 30-day timepoint but before being discharged from the hospital.

Figure 50: 30-Day and In-Hospital Survival for OCS and Control Groups (INSPIRE Cohort and Combined Cohort)

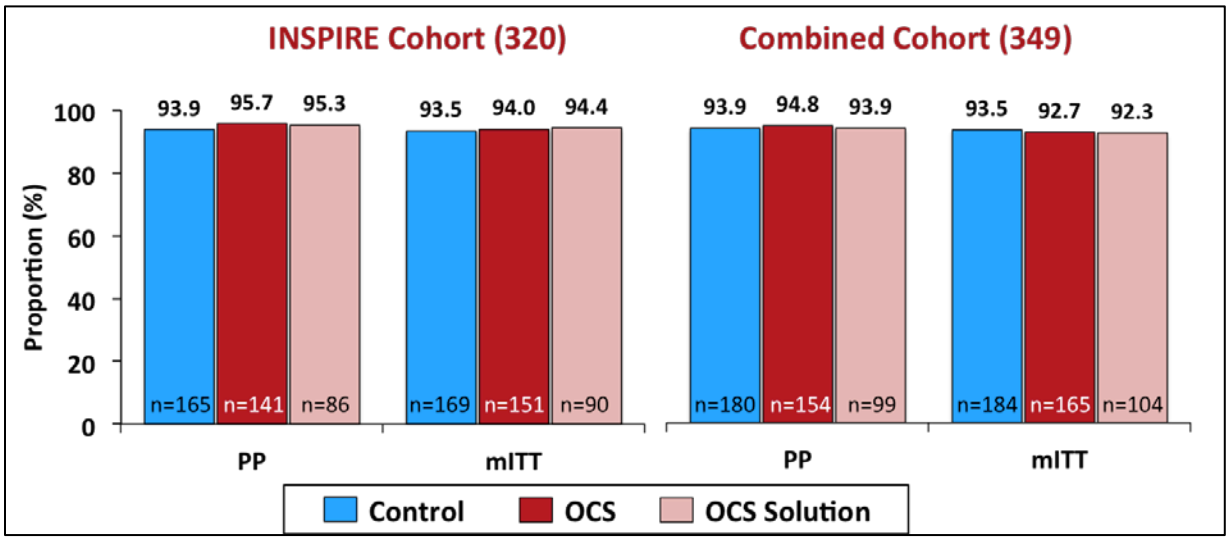


Figure 51: Causes of Death for OCS and Control Groups (30-Day and In-hospital) – mITT Population, Combined Cohort

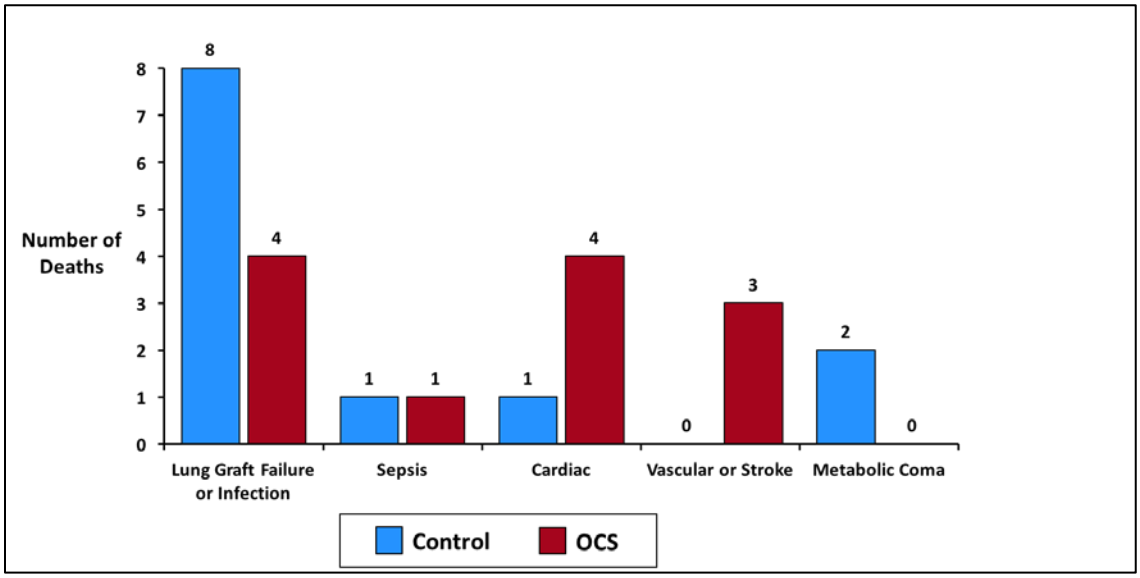
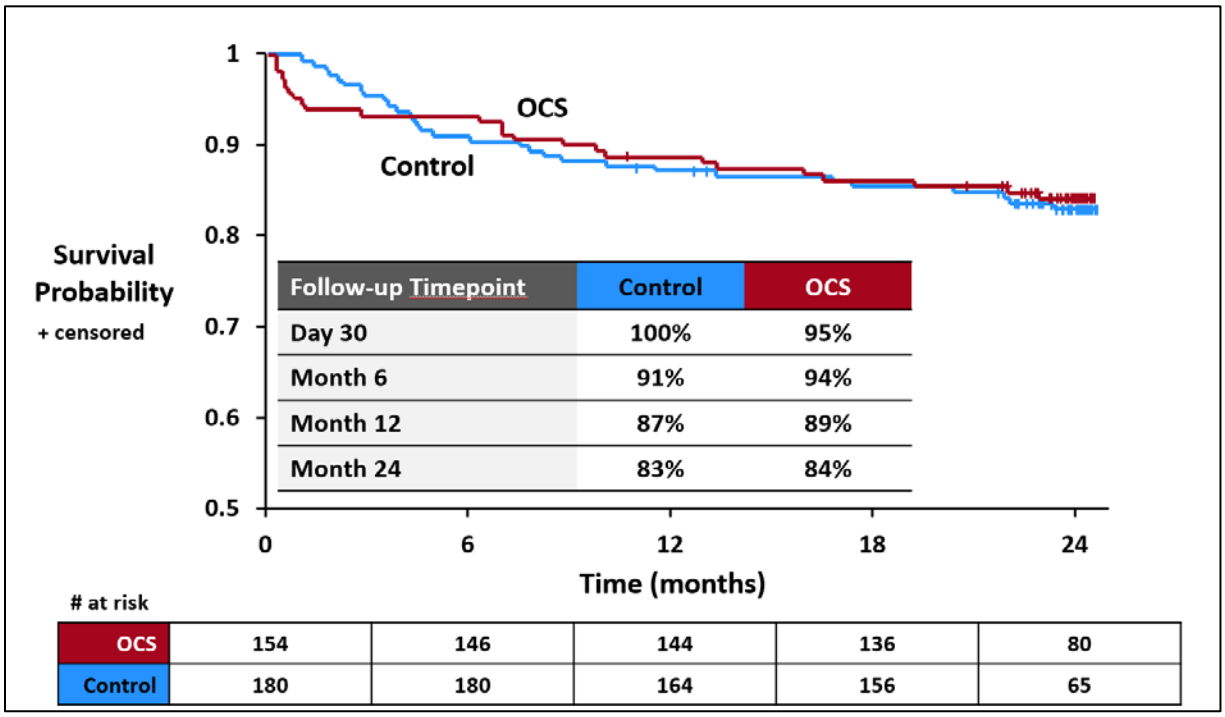


Figure 52 below demonstrates the results of the Kaplan-Meier (K-M) survival analyses through 24 months for the Combined Cohort (PP Population), with the point estimates for each of the assessment timepoints below the graph. The long-term survival of the OCS and Control arms were similar after 24 months of follow-up.

Figure 52: K-M Survival for OCS and Control groups at 24 Months (Combined Cohort PP Population)

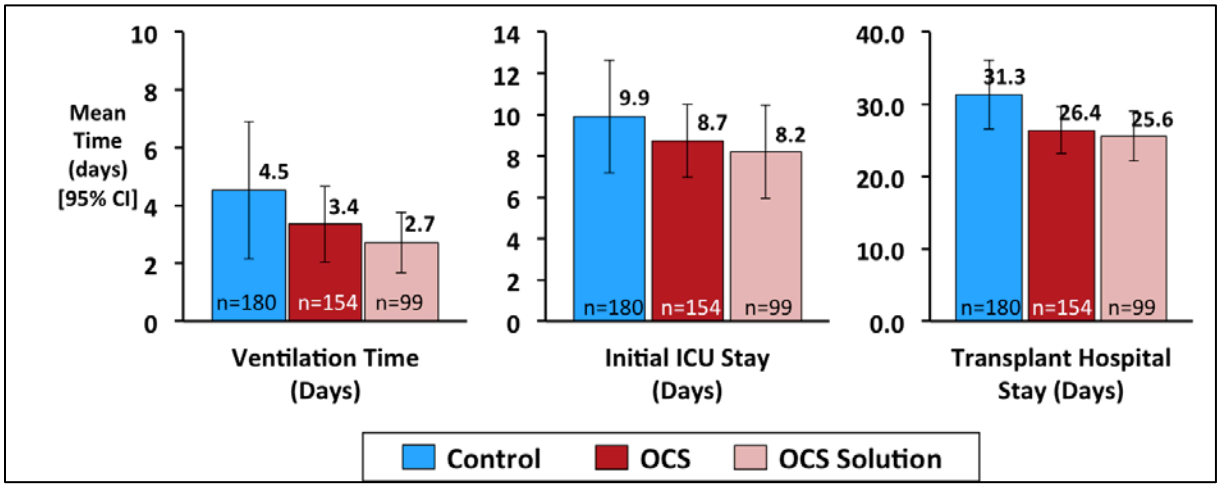


Follow-up Timepoint	Control	OCS
Day 30	100%	95%
Month 6	91%	94%
Month 12	87%	89%
Month 24	83%	84%

14. Reduction in Mechanical Ventilation, ICU Stay and Hospital Stay

The OCS Lung System had numerically favorable procedural outcomes compared to cold storage. Compared to the control arm, the duration of mechanical ventilation was approximately a day shorter overall for the OCS arm and nearly two days shorter for the OCS patients treated with OCS Lung Solution. The duration of post-transplant ICU stay was reduced from an average of about 10 days in the Control group to 8.7 days in the OCS arm and 8.2 days in the OCS Solution Subgroup. The overall length of hospital stay was approximately 5 days shorter in the OCS arm.

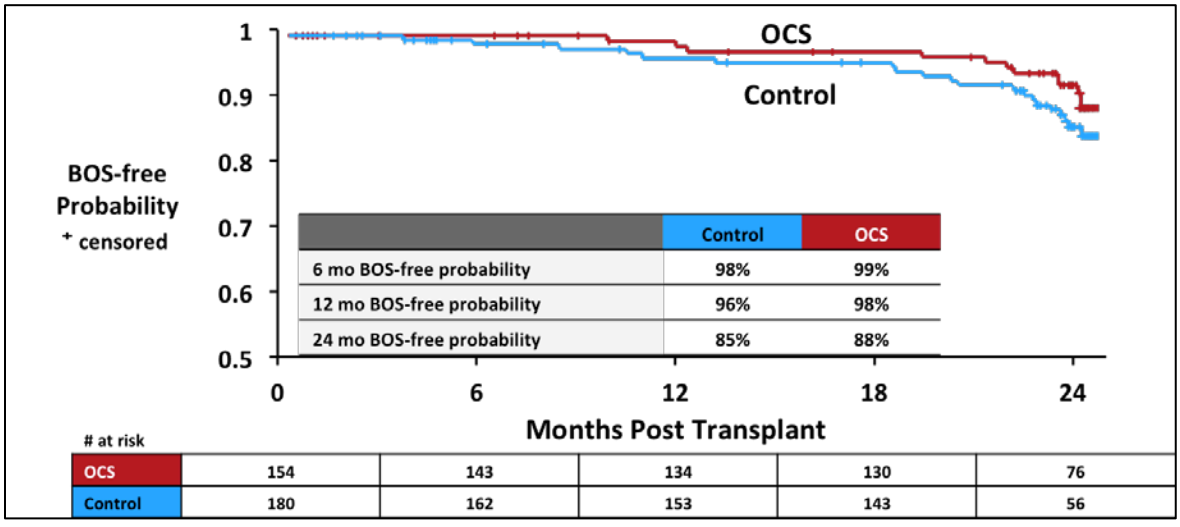
Figure 53: Improvements in Ventilation Time, ICU Time and Hospitalization (PP, Combined Cohort)



15. Freedom from BOS through 24 Months

BOS is the most common long-term complication after lung transplantation and is the leading cause of long-term graft failure in lung transplantation. Figure 54 below demonstrates the results of the overall 24-month KM freedom from BOS analysis. The OCS arm showed a numerically higher percentage of patients who were free from BOS as compared to the Control arm at 24 months (88% for OCS compared to 85% for the control group).

Figure 54: BOS-Free Probability through 24 Months (PP, Combined Cohort)



16. Summary of Benefits and Risks of OCS Lung System

The data from the INSPIRE Trial provides considerable prospective evidence demonstrating the safety and effectiveness of the OCS Lung System. The trial demonstrated the clinical benefit of the OCS Lung System without increasing the risk as compared to standard of care. The INSPIRE Trial met its primary effectiveness and safety non-inferiority endpoints and the data provide strong evidence for the reasonable assurance of safety and effectiveness required for approval of the marketing application. In addition, there are several other findings from the INSPIRE trial that support a positive benefit-risk.

- The OCS Lung System reduces the incidence of PGD3 in the initial 72-hour period following lung transplantation. This is the first (b) (4) technology to demonstrate a reduction in PGD3, one of the most severe complications in lung transplantation and a critical indicator of short-term and long-term patient outcomes. The long-term impact of reducing the incidence of PGD3 within 72 hours will be evaluated in our post-market study
- The OCS Lung System significantly reduced injurious ischemic time on donor lungs compared to the Standard of Care cold storage, despite the fact that the cross-clamp time was significantly longer. This is another first in (b) (4). The ability to reduce injurious ischemic time for the donor lung graft would provide the potential for better logistical management of the donor lung retrieval process that is currently driven by the constraints of ischemia time.
- Patients treated with the OCS Lung System demonstrate similar mortality in the initial post-transplant hospitalization period and at 12 and 24 months compared to cold storage standard of care. Although the mortality at 30 days is higher in the OCS group, early mortality in the OCS arm was associated with iatrogenic surgical and medical causes that were unrelated to the transplanted organ.
- The OCS Lung System had a higher percentage of patients who were BOS free through 24 months after transplantation compared to the cold storage standard of care. BOS is a chronic condition that develops between 2 and 5 years following lung transplantation. TransMedics plans to evaluate this encouraging trend for an additional 3 years (up to 5 years post-transplant) in our proposed post-market study.
- The OCS Lung System had a lower duration of mechanical ventilation, reduced ICU stay and reduced hospital stay compared to the Control Arm.

The OCS Lung System offers a new paradigm in lung transplantation with the potential to improve outcomes and expand the utilization of donor lungs in the U.S.

FDA approval of the OCS Lung System based on the INSPIRE Trial results would be an important first step for further development to advance the field of lung transplantation.

Once approved, the use of OCS Lung System will continue to be evaluated in post-approval Study for routine lung transplantation as well as premarket trials for other indications.

In summary, the OCS Lung System represents a novel technology that overcomes several limitations of cold ischemic storage in lung transplantation. The INSPIRE Trial met its primary non-inferiority endpoints, and the data meet the FDA requirements for approval by demonstrating reasonable assurance of safety and effectiveness in preservation of standard criteria donor lungs for transplantation.

17. Summary of Adverse Events

An overall summary of adverse events is presented in Table 12 below and the serious adverse events (SAEs) are shown in Table 13, presented by MEDRA preferred term. Both analyses are for the safety population (N=319). There were no differences noted between Standard of Care control and OCS Subjects.

Table 12: Adverse Events by Type of Event; Safety Population (N=319)

Parameter	Control (N=169)	OCS (N=150)	OCS Solution (N=89)
Subjects with Any Type of Adverse Events	141 (83.4%)	125 (83.3%)	75 (84.3%)
Subjects with Adverse Events Definitely Related to OCS or Control	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects with Adverse Events Probably Related to OCS or Control	0 (0.0%)	1 (0.7%)	1 (1.1%)
Subjects with Adverse Events Possibly Related to OCS or Control	5 (3.0%)	5 (3.3%)	2 (2.2%)
Subjects with Adverse Events Unlikely Related to OCS or Control	53 (31.4%)	52 (34.7%)	28 (31.5%)
Subjects with Adverse Events Unrelated to OCS or Control	121 (71.6%)	105 (70.0%)	62 (69.7%)
Subjects with Unanticipated adverse Device Effect (UADE)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Subjects with Any Serious Adverse Events	107 (63.3%)	83 (55.3%)	49 (55.1%)
Deaths up to 24 months[1]	26 (15.4%)	23 (15.3%)	14 (15.7%)

[1]OCS arm death count includes Subjec(b) (6) who was withdrawn from study first, then followed by re-transplantation and died afterwards.
All Adverse Events were up to 30 days post-transplantation or initial hospital discharge, LGR SAEs were up to 6 months post-transplantation.

Table 13: Adjudicated Serious Adverse Events by Preferred Term that occurred in ≥1% of Subjects; Safety Population (N=319)

AE Category	AE Term	Control Subjects (N=169)	Control Events (N=224)	OCS Subjects (N=150)	OCS Events (N=175)	OCS Solution Subjects (N=89)	OCS Solution Events (N=101)
Total		**107 (63.3%)**	**224 (100.0%)**	**83 (55.3%)**	**175 (100.0%)**	**49 (55.1%)**	**101 (100.0%)**
Respiratory, thoracic and mediastinal disorders							
	Respiratory failure	15 (8.9%)	16 (7.1%)	17 (11.3%)	19 (10.9%)	10 (11.2%)	12 (11.9%)
	Pleural effusion	12 (7.1%)	12 (5.4%)	6 (4.0%)	7 (4.0%)	3 (3.4%)	4 (4.0%)
	Pneumothorax	12 (7.1%)	12 (5.4%)	5 (3.3%)	6 (3.4%)	3 (3.4%)	4 (4.0%)
	Haemothorax	6 (3.6%)	6 (2.7%)	7 (4.7%)	8 (4.6%)	2 (2.2%)	3 (3.0%)
	Bronchostenosis	3 (1.8%)	4 (1.8%)	5 (3.3%)	5 (2.9%)	3 (3.4%)	3 (3.0%)
	Pulmonary embolism	3 (1.8%)	3 (1.3%)	2 (1.3%)	2 (1.1%)	1 (1.1%)	1 (1.0%)
	Bronchial disorder	3 (1.8%)	4 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Bronchial secretion retention	2 (1.2%)	2 (0.9%)	2 (1.3%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
	Chylothorax	2 (1.2%)	2 (0.9%)	1 (0.7%)	1 (0.6%)	1 (1.1%)	1 (1.0%)
	Bronchopleural fistula	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Infections and infestations							
	Pneumonia	18 (10.7%)	18 (8.0%)	13 (8.7%)	14 (8.0%)	9 (10.1%)	10 (9.9%)
	Lung infection	7 (4.1%)	8 (3.6%)	2 (1.3%)	2 (1.1%)	1 (1.1%)	1 (1.0%)
	Bronchopneumonia	3 (1.8%)	3 (1.3%)	4 (2.7%)	4 (2.3%)	2 (2.2%)	2 (2.0%)
	Infection	4 (2.4%)	4 (1.8%)	2 (1.3%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
	Bronchitis	4 (2.4%)	4 (1.8%)	1 (0.7%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
	Bronchopulmonary aspergillosis	4 (2.4%)	4 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

AE Category	AE Term	Control Subjects (N=169)	Control Events (N=224)	OCS Subjects (N=150)	OCS Events (N=175)	OCS Solution Subjects (N=89)	OCS Solution Events (N=101)
	Lung infection pseudomonal	1 (0.6%)	1 (0.4%)	3 (2.0%)	3 (1.7%)	2 (2.2%)	2 (2.0%)
	Respiratory tract infection	2 (1.2%)	2 (0.9%)	2 (1.3%)	2 (1.1%)	2 (2.2%)	2 (2.0%)
	Sepsis	4 (2.4%)	4 (1.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Diverticulitis	2 (1.2%)	2 (0.9%)	1 (0.7%)	1 (0.6%)	1 (1.1%)	1 (1.0%)
	Wound infection	3 (1.8%)	3 (1.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Aspergillosis	0 (0.0%)	0 (0.0%)	2 (1.3%)	2 (1.1%)	1 (1.1%)	1 (1.0%)
	Clostridium difficile colitis	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Cytomegalovirus infection	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Septic shock	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Staphylococcal infection	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Cardiac disorders							
	Atrial fibrillation	6 (3.6%)	7 (3.1%)	7 (4.7%)	7 (4.0%)	5 (5.6%)	5 (5.0%)
	Cardiac arrest	0 (0.0%)	0 (0.0%)	5 (3.3%)	6 (3.4%)	4 (4.5%)	4 (4.0%)
	Arrhythmia	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Atrial flutter	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Cardiac failure congestive	0 (0.0%)	0 (0.0%)	2 (1.3%)	2 (1.1%)	1 (1.1%)	1 (1.0%)
	Cardiac tamponade	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Renal and urinary disorders							
	Renal failure acute	6 (3.6%)	6 (2.7%)	9 (6.0%)	9 (5.1%)	5 (5.6%)	5 (5.0%)
	Renal failure	6 (3.6%)	6 (2.7%)	2 (1.3%)	2 (1.1%)	0 (0.0%)	0 (0.0%)
Vascular disorders							

AE Category	AE Term	Control Subjects (N=169)	Control Events (N=224)	OCS Subjects (N=150)	OCS Events (N=175)	OCS Solution Subjects (N=89)	OCS Solution Events (N=101)
	Haemorrhage	3 (1.8%)	3 (1.3%)	5 (3.3%)	5 (2.9%)	3 (3.4%)	3 (3.0%)
	Deep vein thrombosis	0 (0.0%)	0 (0.0%)	4 (2.7%)	4 (2.3%)	2 (2.2%)	2 (2.0%)
	Ischaemia	0 (0.0%)	0 (0.0%)	2 (1.3%)	2 (1.1%)	1 (1.1%)	1 (1.0%)
Injury, poisoning and procedural complications							
	Post procedural haemorrhage	1 (0.6%)	1 (0.4%)	6 (4.0%)	6 (3.4%)	3 (3.4%)	3 (3.0%)
	Wound dehiscence	2 (1.2%)	2 (0.9%)	3 (2.0%)	3 (1.7%)	3 (3.4%)	3 (3.0%)
Gastrointestinal disorders							
	Impaired gastric emptying	2 (1.2%)	2 (0.9%)	1 (0.7%)	1 (0.6%)	1 (1.1%)	1 (1.0%)
	Gastrointestinal haemorrhage	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Large intestine perforation	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Immune system disorders							
	Lung transplant rejection	12 (7.1%)	12 (5.4%)	5 (3.3%)	5 (2.9%)	4 (4.5%)	4 (4.0%)
Nervous system disorders							
	Cerebrovascular accident	0 (0.0%)	0 (0.0%)	4 (2.7%)	4 (2.3%)	1 (1.1%)	1 (1.0%)
	Encephalopathy	2 (1.2%)	2 (0.9%)	1 (0.7%)	1 (0.6%)	0 (0.0%)	0 (0.0%)
	Brain oedema	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Convulsion	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
	Delirium	2 (1.2%)	2 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Potential AEs that may occur but that were not observed in the INSPIRE study include: anemia; cough; gastroesophageal reflux disease; malignancy (post-transplant lymph proliferative disorder (PTLD)); mucus plug; neurological dysfunction; pleural bleeding; and pulmonary infarction

18. Summary of INSPIRE Clinical Study

The data from the INSPIRE Trial provide strong support for favorable benefit-risk for the OCS Lung System. The INSPIRE Trial met its primary effectiveness and safety endpoints and provide evidence for the reasonable assurance of safety and effectiveness required for approval of the marketing application. In addition, there are several other findings from the INSPIRE study that support a positive benefit-risk.

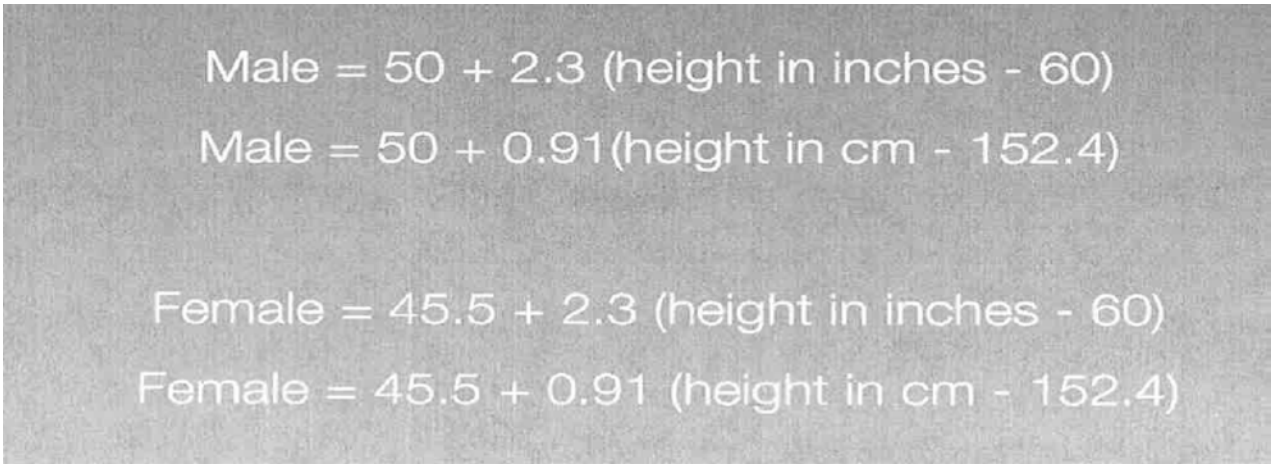
- The OCS Lung System reduces the incidence of PGD3 in the initial 72-hour period following lung transplantation. This is the first (b) (4) technology to demonstrate a reduction in PGD3, one of the most severe complications in lung transplantation and a critical indicator of short-term and long-term patient outcomes.
- The OCS Lung System significantly reduced injurious ischemic time on donor lungs compared to the Standard of Care cold storage, despite the fact that the cross-clamp time was significantly longer. This is another first in (b) (4). The ability to reduce injurious ischemic time for the donor lung graft would provide the potential for better logistical management of the donor lung retrieval process that is currently driven by the constraints of ischemia time.
- Although the mortality at 30 days is higher in the OCS group, patients treated with the OCS Lung System demonstrate similar mortality in the initial post-transplant hospitalization period and at 12 and 24 months compared to cold storage standard of care. Early mortality in the OCS arm was associated with iatrogenic surgical and medical causes that were unrelated to the transplanted organ.
- The OCS Arm in the INSPIRE Trial has shown numerically lower incidence of BOS through 24 months after transplant compared to cold storage. BOS is a chronic condition that develops between 2 and 5 years following lung transplantation. TransMedics plans to evaluate this encouraging trend for an additional 3 years (up to 5 years post-transplant) in our proposed post-market study.
- The OCS Lung System is associated with reductions in mechanical ventilation, ICU stay, and hospital stay. These results are relevant given the clinical and economic benefits that result from a reduction in ventilation support time, ICU, and hospital stay.
- As with any new technology, there are risks posed by the introduction of the OCS Lung System into standard clinical practice for transplantation. The risk of device malfunction or user error that could lead to a potential loss in an organ has been mitigated by careful product design and testing, incorporation of an extensive, hands on training program.

FDA approval of the OCS Lung System based on the INSPIRE Trial results would represent an important first step for further development and expansion of the clinical knowledge base of the OCS System, and would lead to additional research to advance the field of lung transplantation. Once approved, the use of OCS Lung System will continue to be evaluated in post-approval Study for routine lung transplantation as well as premarket trials for other indications.

In conclusion, the OCS Lung System represents a novel technology that overcomes several limitations of cold ischemic storage. The INSPIRE trial data provide strong evidence for the safety, effectiveness and clinical benefit of the OCS Lung System and support its approval for use in standard criteria(b) (4) for transplantation.

APPENDIX B. BODY WEIGHT FORMULA

*Devine's formula for a suggested ideal body weight calculation for person's height over 5 feet (150 Cms) is provided below:



* Paul L. Marino. (1998). *The ICU Book. (Second edition)*. Maryland: Lippincott Williams & Wilkins. p 872

*Devine, Ben J (1974). "Gentamicin therapy". Drug Intell Clin Pharm 8 (11): 650–5.

TransMedics

200 Minuteman Rd., Suite 302, Andover, MA 01810, USA

(b) (4)

Web: www.transmedics.com

Software Version 3.1.1
PN 100004071, Rev 2
REF 2102