DE NOVO CLASSIFICATION REQUEST FOR HEMOLUNG RESPIRATORY ASSIST SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Extracorporeal system for carbon dioxide removal. An extracorporeal system for carbon dioxide removal is a system of devices and accessories that provides assisted extracorporeal carbon dioxide removal from the patient's blood in patients with acute respiratory failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent. The main devices and accessories of the system include, but are not limited to, the console (hardware), software, and disposables, including, but not limited to, a gas exchanger, blood pump, cannulae, tubing, filters, and other accessories (e.g., monitors, detectors, sensors, connectors).

NEW REGULATION NUMBER: 21 CFR 870.4150

CLASSIFICATION: Class II

PRODUCT CODE: QOH

BACKGROUND

DEVICE NAME: Hemolung Respiratory Assist System

SUBMISSION NUMBER: DEN210006

DATE DE NOVO RECEIVED: March 4, 2021

SPONSOR INFORMATION:

ALung Technologies, Inc.
2500 Jane Street, Suite 1
Pittsburgh, Pennsylvania 15203

INDICATIONS FOR USE

The Hemolung Respiratory Assist System is indicated for respiratory support that provides extracorporeal carbon dioxide (CO_2) removal from the patient's blood for up to 5 days in adults
with acute, reversible respiratory failure for whom ventilation of CO_2 cannot be adequately or safely achieved using other available treatment options and continued clinical deterioration is expected.

LIMITATIONS

The sale, distribution, and use of the Hemolung RAS are restricted to prescription use in accordance with 21 CFR 801.109.

Contraindications:

The Hemolung RAS is contraindicated for patients with known sensitivity to heparin (e.g., history of heparin-induced thrombocytopenia). The Hemolung Cartridge membranes are coated with heparin and systemic anticoagulation is required when using the device.

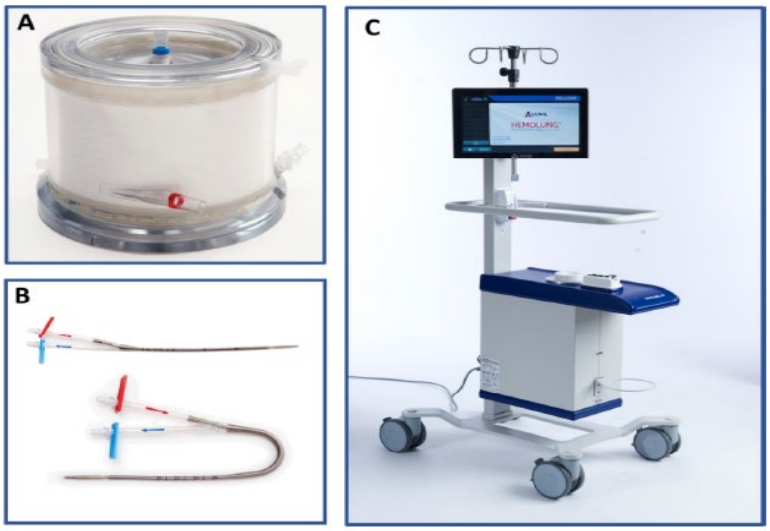
Use of the Hemolung 15.5 Fr Femoral Catheter is contraindicated for patients with an inferior vena cava filter.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Hemolung RAS provides low blood flow, veno-venous extracorporeal carbon dioxide removal (ECCO2R) using a single, 15.5 French dual lumen catheter inserted percutaneously in the femoral or jugular vein. The Hemolung RAS is not intended to provide therapeutic levels of oxygenation. During Hemolung therapy, blood passing through the circuit is oxygenated via room air sweep gas; however, at ultra-low extracorporeal blood flows, the limited oxygen carrying capacity of blood precludes meaningful oxygenation of mixed venous blood.

The Hemolung RAS consists of three main components:



C. Hemolung Controller is the mechanism for operating the Hemolung Respiratory Assist System. It controls the extracorporeal blood flow rate and the sweep gas flow rate.

A. Hemolung Cartridge is an integrated extracorporeal gas exchanger and blood pump. Blood is circulated around the outside of the Cartridge's hollow fiber membranes while a sweep gas flows through the inside of the membranes. Carbon dioxide diffuses out of the blood and is swept away by the sweep gas while oxygen diffuses from the sweep gas into the blood. Blood tubing and other accompanying disposable products are included in the Hemolung Cartridge Kit.

B. Hemolung Catheter is a dual lumen venous catheter designed specifically for use with the Hemolung RAS. It exhibits low resistance to flow while also resisting kinks. Individual femoral and jugular Hemolung Catheter Kits are available for use. Each kit includes a Catheter Insertion Kit.

SUMMARY OF NONCLINICAL/BENCH STUDIES

The following bench studies were performed to demonstrate that the technological characteristics of the Hemolung system are consistent with the device's indication for use:

Pump characterization	The Hemolung system was tested in a recirculation loop using a blood analogue at 37°C. Pressure-flow characteristics were measured for the system at various pump speeds when connected to Hemolung 15.5 Fr Femoral and Jugular Catheters	
Gas exchange	Gas exchange testing was performed to characterize gas exchange performance of the Hemolung system over the full range of blood and sweep gas flow rates. The system was tested in a recirculation loop using heparinized bovine blood at 37°C. At each blood flow rate (350 mL/min, 450 mL/min, 550 mL/min), gas exchange was measured at 1 L/min, 5.5 L/min and 10 L/min room air sweep gas flow rates. All results are normalized for an inlet pCO2 of 45mmHg.	
Heat loss/gain	Heat loss/gain testing was performed to simulate worst case conditions for heat loss or gain during normal operation of the Hemolung. The system was tested in a recirculation loop using heparinized bovine blood at 37°C and room air sweep gas. Temperatures were measured at the inlet and outlet of the 6' blood lines to account for heat loss/gain across the entire extracorporeal circuit.	
Reliability and Physical Integrity	Reliability testing evaluated physical integrity of the Hemolung system under worst case operating conditions. The test was performed in a recirculation loop of 40:60 glycerol: water, 0.9% NaCl solution at 37°C for a duration of 14 days. The Cartridges were operated at maximum pump speed (1400 RPM), maximum sweep gas flow (10 LPM), and 1.5X the maximum operating pressure. Following the 14-day simulated use, physical integrity of the blood and gas pathways were evaluated, and the Cartridge and Catheter were examined for any wear or corrosion	
Hemolysis	Hemolysis testing was performed to characterize blood damage within the system by measuring plasma free hemoglobin in a recirculation loop.	
Heparin coating leachability	Phosphate buffered saline (PBS) was recirculated through each Cartridge for a period of 7 days under worst case conditions (37°C, 1400 RPM, 550 mL/min). Eluted heparin was quantified in the PBS solution throughout the test, and fiber mat heparin activity was measured at the conclusion of the 7-day study.	
Catheter Performance Testing	Flow Test	Characterize flows and pressures through the catheter in both straight and bent configurations over a range of pump speeds in a recirculation loop using a blood analog at 37°C
	Physical Requirements	Ensure markings are present on catheters following a simulated soak for 2X the duration of use
	Kink Resistance	Distal top of the catheter was fixed to a 5cm radium wheel and bent around the wheel 25 times.
	Antiseptic Resistance	Antiseptics were placed on the catheter materials including glue joints and soaked for 24 hours at 37 ºC. The antiseptics used were: • 10% povidone-iodine solution in water (i.e.Betadine®), • 4% Chlorhexidine gluconate, • 2% chlorhexidine gluconate in 70% isopropyl alcohol (i.e. Chloraprep®), • Bacitracin zinc ointment (i.e. Polysporin®)
	Leak Test (Pressure and vacuum)	Catheters placed under vacuum and pressure representing 2X the maximum vacuum and pressure of the system for 10 min using DI water following simulated use.
	Force to Break Test	Measuring the force to break each distinct section of the Catheter using a tensile strain rate of 20mm/min/mm of gauge length.

	Corrosion Resistance	Catheters soaked in a sodium chloride solution for five hours, immersed in boiling distilled water for 30 min and then placed in an oven at 37°C for 48 hours and then inspected for corrosion.
	Ambulation-Dislodgement	Ensure suture ring can secure the catheter during simulated patient ambulation of axial, transverse, and upward forces of 15N and torque each applied for 15 seconds
	Ambulation-Weight on Catheter	Catheters placed in a water bath at 37°C and the extension tubes were bent in all four directions 25 times to simulate patient movement.
	Recirculation	Recirculation properties of the Catheter were tested in a vena cava simulated flow circuit using both SVC and IVC flow conditions at the minimum and maximum catheter flow rates, as compared to an FDA-approved dialysis catheter.
Biocompatibility Testing	Biocompatibility testing was performed on all patient contacting components as specified in ISO 10993-1 and Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" - Guidance for Industry and Food and Drug Administration Staff. All components of the system were tested in their final, finished, and sterilized (2X EtO) form.	
	Cytotoxicity (ISO-10993-5)	MEM Extraction Assay with L929 mammalian fibroblasts
	Sensitization (ISO 10993-10)	Guinea pig maximization test
	Irritation (ISO 109993-10)	Intracutaneous Reactivity
	Systemic Toxicity (ISO 10993-11)	Acute Systemic Injection Test Material mediated rabbit pyrogen test Sub Chronic Systemic Injection Test Leverage from functional large animal study
	Genotoxicity (ISO 10993-3)	Bacterial Mutagenicity Test - Ames Assay In Vitro Mouse Lymphoma Assay In Vivo Mouse Bone Marrow Micronucleus Assay
	Hemocompatibility (ISO 10993-4/A1 & ASTM F756 & ASTM F2382-18 & ASTM F2888-19)	Hemolysis; Saline Extract Hemolysis; Direct Contact Complement Activation - SC5b-9 Assay Partial Thromboplastin Time (PTT) with Comparison Article Heparinized Blood Platelet and Leukocyte Count with Comparison Article Surface Morphology Assessment In Vivo thrombogenicity; In Vivo animal study
	Implantation (ISO 10993-6)	In Vivo animal study
Shelf-Life Testing	Real-Time Aging	Device performance testing was completed using product following 2-year real time aging to characterize any impacts from aging on device performance or safety. The aged products were used to confirm that the device met all of the following product requirements: gas exchange, pump characterization, reliability, heparin stability, catheter performance.
	Accelerated Aging	Device performance testing was completed using 2-year accelerated aged product to support shelf-life where real time aging is not expected to impact device performance. The aged products were used to confirm that the device met all of the following product requirements: hemolysis, heat loss/gain, heparin/uniformity and leachability, verification by analysis, catheter recirculation, in vivo animal study.

Sterilization Validation	Sterilization validation was performed in accordance with ANSI/AAMI/ISO 11135-1:2014/ AMD1:2018 including two sublethal exposures, four half-cycle exposures, cold conditioning, and one full cycle exposure. An ethylene oxide (EO) sterilization validation study was performed for the Hemolung family of sterile products to confirm a 10-6 sterility assurance level (SAL) for the designated product load and acceptable levels of EO residuals. (ISO 11135:2014, ISO 11138-1:2017, ISO 11138-2:2017, ISO 11737-1:2018, ISO 117737-2: 2019, AAMI TIR No. 14 (2016), 15(2016), 16 (2017))
Packaging Validation	A packaging validation study was performed to evaluate the ability of each Hemolung product sterile packaging configuration to maintain strength and integrity of the sterile barriers' seals following simulated shipping and/or aging. Testing was conducted in accordance with ISO 11607-1 Packaging for Terminally Sterilized Medical Devices – Part 1: Requirements for materials, sterile barrier systems, and packaging systems. (ISTA 2A-2011, ISTA 3E:2017, ASTM D 4169-16, ASTM D 6653/D653M-13, ASTM F1980-16. ASTM F2096-11 (2019), ISO 11607-1: 2019, ASTM F 88/F 88M-15)
Hardware and Software Verification	The Hemolung CR4 Controller's hardware and software was tested to verify functionality and safety before clinical testing. The following functional areas were tested: interface with disposable components, power system, generation, control, and monitoring of sweep gas flow, CO2 monitoring, blood pump RPM control and monitoring, and blood flow monitoring. (ANSI/AMI/IEC 62304:2006 + AMDI: 2015)
Electrical Safety and Compliance Testing and other safety-related requirements	Electrical Safety and Compliance Testing was conducted for the Hemolung CR4 Controller to verify functionality and safety before clinical testing. This testing verified compliance with IEC 60601-1 electrical safety standard and IEC 60601-1-8 alarm system standard. This testing consisted of verifying short circuit protection of all off-board connections and operation of AC Power indicator. In addition, testing was conducted to verify detection of air in blood lines. In addition, the testing was used to verify the following functional areas: ventilation to prevent battery damage, measurement of enclosure temperature, and label resistance to bleach, soap and water. (IEC 60601-1:2015+ AMI: 2012, IEC 60601-1-2:2014, IEC 60601-1-6:2010+A1: 2013, IEC 60601-1-8: 2006 + AMD1:2012)
Electromagnetic Compatibility	Electromagnetic Compatibility Testing was conducted for the Hemolung CR4 Controller to verify conformance with IEC 60601-1-2 and collateral standards and conformance with AIM 7351731. (IEC 60601-1-2:2014, AIM 7351731, EN 55011:2009+A1:2010, IEC 61000-3-2:2014, IEC 61000-3-3: 2013. IEC 61000-4-2: 2008. IEC 61000-4-3:2010, IEC 61000-4-4:2012, IEC 61000-4-5:2014, IEC 61000-4-6:2013, IEC 61000-4-8:2019. IEC 61000-4-11:2010)
Environmental Verification	Environmental Verification Testing was conducted for the Hemolung CR4 Controller to verify fluid ingress rating of IPX1, test shipping to ISTA 3E, and that the Corner drop / Edge drop are in compliance with 60068-2-31. In addition, the following environmental conditions were verified in the testing: 1) operating temperature and humidity from 10C to 35C at 20% to 90% non-condensing humidity, 2) storage temperature and humidity from -20C to 50C at 15% to 95% non-condensing humidity, and 3) altitude requirements: maintain sweep gas for of 10.0 SLPM ±0.3 SLPM at simulated altitudes up to 8000 ft (2500 m).
Usability	Usability testing was conducted in accordance with IEC 62366-1:2015 to verify user interface components. In the testing, critical care nurses were trained in the use of the system and then after a decay period completed a summative test to validate all disposables-related tasks (unpacking disposables, system priming, recirculation, catheter unpackaging, patient connection, cartridge replacement, rinse back, and vacuum canister replacement).

PERFORMANCE TESTING - ANIMAL

The objective of the in vivo Animal Study was to perform a safety and performance evaluation of the Hemolung system under simulated clinical use.

Methods:	Eight (8) male calves were implanted with the Hemolung system. Calves were to be recovered and survived on therapy for 7 days. Blood chemistry, hematology, fibrinogen, plasma free hemoglobin, activated clotting time and hematocrit were regularly tested throughout the study. Calves were routinely observed by veterinary staff and Subjective Objective Assessment Plan examinations were performed by veterinarians. Clinical abnormalities were scored using an abnormality grading scale adapted from the Common Terminology Criteria for Adverse Events. At the end of the therapy, the Hemolung system was shut down and the circuit was thoroughly examined for clots/thrombi. The calves were humanely euthanized, and a detailed necropsy was performed to examine implant site and organs for gross abnormalities, excising representative samples for histopathology. Histopathology was performed on naïve and test catheter implanted sections of the right jugular vein, lungs, heart, lymph nodes, adrenal glands, liver, kidney, spleen and any other tissue with abnormal observations.
Results:	There were no major clinical events. Therapy was discontinued early on two (2) of the eight calves: one calf was taken off therapy on Day 1.7 post implant and terminated at Day 2 post implant, and one calf was taken off therapy on Day 6.2 post implant but terminated as planned on Day 7.
Conclusions:	There were no procedural complications directly related to the test article that put the calf's health at risk or created any significant clinical health concerns. There were adjustments required for the anticoagulation therapy as well as for routine maintenance and observation of the catheter. There were no significant health concerns to the calves resulting from these adjustments. Cartridge replacements were not required and cessation of therapy in two calves was due to decreases in blood flow through the test article. There was no clinical evidence of severe coagulation insufficiency in any of the calves. Based on the abnormality grading system, none of the calves were found to have any severe abnormalities that required a grade 3 or higher. The two calves that were taken off therapy were removed due the low blood flow alarms and were not removed for health reasons. Based on the daily PCV values none of the calves were clinically anemic. There was no clinical evidence of hemolysis. Plasma free hemoglobin (PFH) was increased in one calf but was found to be clinically insignificant as the calf did not have evidence of anemia, low hematocrit or hyperbilirubinemia. No obvious indications of excessive bleeding, inflammation, or infection were noted. No evidence of infection was observed at the test Catheter insertion site, and no gross thrombi were noted at the site of the insertion. Overall, the calves remained stable throughout the 7-day time point and did not have any clinical emergencies that threatened the life of the calf.

SUMMARY OF CLINICAL INFORMATION

Hemolung Clinical Performance

The clinical performance data provided to support the de novo request included data from 234 patients treated with Hemolung therapies from prospective clinical trials, real-world use, and the Hemolung Post-market Registry. Patients were systematically evaluated for inclusion in the effectiveness analysis if all 4 of the following criteria were met: 1) Original patient level efficacy data was available, 2) Pre-Hemolung pH and PaCO2 data was available, 3) Data coinciding with at least one additional time point during the first 35 hours after commencement of Hemolung therapy was available, and 4) the patient received Hemolung therapy for at least 6 hours. The two primary clinical outcomes used to evaluate effectiveness of Hemolung therapy were:

1) Correction of refractory hypercapnia and respiratory acidosis

OR

2) De-escalation of mechanical ventilatory support while preventing respiratory acidosis

Data was stratified based on baseline (Pre-Hemolung) pH as follows: Acidotic patients (pH < 7.35) were analyzed for correction of refractory hypercapnia and respiratory acidosis; Non-acidotic patients (pH ≥ 7.35) were analyzed for de-escalation of mechanical ventilatory support while preventing respiratory acidosis. An acute timepoint (first day of Hemolung therapy) was chosen to analyze Hemolung clinical effectiveness as the physiologic response from Hemolung therapy is observed within hours of initiating treatment. The acute time frame also eliminates longer-term confounding effects from underlying illness, additional critical care support technologies and patient-specific titration of Hemolung therapy.

The benefits of Hemolung therapy from this clinical data analysis are summarized as follows:

- Extra-corporeal carbon dioxide removal using the Hemolung demonstrated clinically and statistically significant correction of respiratory acidosis and de-escalation of mechanical ventilatory support in patients who have not been on ventilatory support and primarily received standard of care therapy until the Hemolung therapy was initiated
- 91% of Hemolung patients demonstrated a clinically beneficial response, where there was a correction in respiratory acidosis after one day of Hemolung therapy.
- 92% of non-invasively ventilated (NIV) patients avoided intubation and invasive mechanical ventilation (IMV) with Hemolung therapy. For acidotic patients failing NIV (n=43), Hemolung therapy resulted in correction of respiratory acidosis (pH =7.24 -> pH=7.36)

Hemolung Clinical Safety

Assessment of Hemolung safety was supported through analysis of clinical complication data from 1,034 patients that received Hemolung therapy Safety data was derived from four primary sources: 1) monitored and independently adjudicated adverse event data from prospective clinical trials, 2) US Expanded Access or Emergency Use Authorization data collection and surveillance, 3) the OUS post-market Hemolung Registry, and 4) OUS post-market surveillance. The Hemolung Registry Form was provided to treating physicians for all commercial therapies outside the US. For commercial therapies completed without a returned Registry Form, ALung post-market surveillance procedures were used to collect safety data directly from the treating physician where possible.

Therapy-Related Complications

A total of 172 therapy-related complications were reported as being definitely, probably, or possibly related to use of the Hemolung, or with unknown determination of causality (Table 1). The total number of patients who experienced therapy-related complications was 121 of the 1,034 treatments (i.e., 172 complications occurred in 121 patients). Of the 172-total therapy-related complications, 66 had no patient impact, 96 required medical intervention and 10 resulted in death. There were no reported unanticipated adverse device events.

Therapy-Related Complications	TOTAL (n=1034 pts)
Bleeding (n, incidence)	72 (7.0%)
Hemolysis (n, incidence)	27 (2.6%)
Thrombocytopenia (n, incidence)	22 (2.1%)
Thrombosis/coagulation disorder (n, incidence)	13 (1.3%)
Hemodynamic instability (n, incidence)	16 (1.6%)
Other (n, incidence)	22 (2.1%)
TOTAL # OF THERAPY-RELATED COMPLICATIONS	**172**
Required medical intervention	96
Resulted in death	10
No patient impact	66

Table 1. Summary of Hemolung therapy-related complications. Bleeding includes complications categorized as bleeding or anemia. Thrombosis/ coagulation disorder includes complications categorized as coagulation disorder, disseminated intravascular coagulopathy, pulmonary embolism, and vein thrombosis. Hemodynamic instability includes complications categorized as cardiac arrythmia, cardiac arrest, hemodynamic instability, hypovolemia, septic shock, and shock.

Procedural, Operational and Component-Related Complications

A total of 128 procedural, operational, and component-related complications were reported (Table 2). Of the 128 total complications, 116 had no patient impact, 8 required medical intervention and 4 resulted in death.

	TOTAL (n=1,034 pts)
Procedural-related complications (n, incidence)	62 (6.0%)
Required medical intervention	7
Resulted in death	4
No patient impact	51
Operational-related complications (n, incidence)	33 (3.2%)
Required medical intervention	0
Resulted in death	0
No patient impact	33
Component-related complications (n, incidence)	33 (3.2%)
Required medical intervention	1
Resulted in death	0
No patient impact	32

Table 2. Summary of Hemolung procedural-related, operational-related and component- related complications

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The Hemolung Respiratory Assist System labeling consists of Instructions for Use that includes a detailed summary of the non-clinical and in vivo evaluations pertinent to use of the device and accessories in the circuit. The Instructions for Use also includes adequate instructions with respect to circuit setup, performance characteristics with respect to compatibility among different devices and accessories in the circuit, and maintenance during a procedure.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of an extracorporeal system for carbon dioxide removal and the measures necessary to mitigate these risks.

Identified Risks to Health	Mitigation Measures
Bleeding, thrombocytopenia, hemolysis, thrombosis	In vivo evaluation Non-clinical performance testing Labeling
Infection	In vivo evaluation Sterility Shelf-life testing Labeling
Adverse tissue and/or hematologic reaction	In vivo evaluation Biocompatibility Labeling
Mechanical failure	In vivo evaluation Non-clinical performance testing Labeling Software validation, verification, and hazard analysis
Hemodynamic instability	In vivo evaluation Non-clinical performance testing Labeling
Hypothermia	In vivo evaluation Non-clinical performance testing Labeling
Mechanical injury to access vessels	In vivo evaluation Non-clinical performance testing Labeling

Inadequate gas exchange	In vivo evaluation Non-clinical performance testing Labeling
Hemodilution	In vivo evaluation Non-clinical performance testing Labeling
Gas embolism	In vivo evaluation Non-clinical performance testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the extracorporeal system for carbon dioxide removal is subject to the following special controls:

1) In vivo evaluation, which may include animal testing and clinical data, of the devices and accessories in the circuit must demonstrate their performance over the intended duration of use, including a detailed summary of the in vivo evaluation pertinent to the use of the devices and accessories to demonstrate their effectiveness
2) The technological characteristics of the device must ensure that the geometry and design parameters are consistent with the intended use, and that the devices and accessories in the circuit are compatible
3) Non-clinical performance testing of the devices and accessories in the circuit must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:
    a. Mechanical integrity;
    b. Durability; and
    c. Reliability.
4) All patient contacting components of the device must be demonstrated to be biocompatible.
5) Performance testing must demonstrate the electrical safety and electromagnetic compatibility (EMC) of any electrical components.
6) Software validation, verification, and hazard analysis must be performed.
7) Performance testing must demonstrate the sterility of all patient-contacting components.
8) Performance testing must support the shelf life of the device by demonstrating continued sterility and device functionality over the identified shelf life.
9) Labeling must include the following:
    a. A detailed summary of the non-clinical and in vivo evaluations pertinent to use of the device and accessories in the circuit; and
    b. adequate instructions with respect to circuit setup, performance characteristics with respect to compatibility among different devices and accessories in the circuit, and maintenance during a procedure; and
    c. A shelf life.

BENEFIT-RISK DETERMINATION

The benefits and risks of the device are based on nonclinical bench and animal studies as well as clinical data collected in clinical studies described above and real-world evidence.

Hemolung benefits were consistent across primary diagnoses and data sources, demonstrating generalizability of the clinical benefits for numerous acute respiratory failure etiologies. The two primary clinical benefits that were observed were 1) Correction of refractory hypercapnia and respiratory acidosis and 2) De-escalation of mechanical ventilatory support while preventing respiratory acidosis. 91% of Hemolung patients demonstrated a clinically beneficial response to Hemolung therapy. 92% of non-invasively ventilated (NIV) patients avoided intubation and invasive mechanical ventilation (IMV) with Hemolung therapy. The observed benefits are clinically meaningful enough to outweigh the potential complications related to device therapy.

Complications that were Hemolung therapy-related, procedural-related, operational-related, and component-related, occurred with low incidences, most often did not result in any patient harm, and rarely resulted in permanent patient harm or death. Complications from Hemolung therapy included bleeding, thrombosis/ coagulation disorder, and hemodynamic instability. Complications from procedures referred to insertion of the Hemolung Catheter, which is performed using a percutaneous technique. Complications during normal operational use of the Hemolung included circuit thrombosis, low blood flow due to patient/catheter positioning or hypovolemia, air in circuit, catheter dislodgement, and incorrect system setup. These complications are all expected risks of extracorporeal blood circulation. Complications related to Hemolung component failure or malfunction were primarily due to hardware/software issues with the Hemolung Controller, the majority of which have since been resolved through software bug fixes and hardware improvements. All risks from the Hemolung therapy are characterized and mitigated through non-clinical testing, including biocompatibility, in vivo animal studies, sterilization and packaging validation, mechanical reliability, and functional performance and safety testing. In addition, all risks from Hemolung therapy are characterized in ALung's Risk Management System and are appropriately mitigated through special controls. These risks are clinically acceptable and consistent with other technologically similar devices.
Overall, the clinical benefits of the Hemolung Respiratory Assist System outweigh the probable risks.

PATIENT PERSPECTIVES

This submission did not include specific information on patient perspectives for this device.

BENEFIT/RISK CONCLUSION

In conclusion, given the available information above, for the following indication statement:

> The Hemolung Respiratory Assist System is indicated for respiratory support that provides extracorporeal carbon dioxide (CO2) removal from the patient's blood for up to 5 days in adults with acute, reversible respiratory failure for whom ventilation of CO2 cannot be adequately or safely achieved using other available treatment options and continued clinical deterioration is expected.

The probable benefits outweigh the probable risks for the Hemolung Respiratory Assist System. The device provides benefits, and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Hemolung Respiratory Assist System is granted, and the device is classified as follows:

Product Code: QOH
Device Type: Cardiovascular Surgical Devices
Regulation Number: 21 CFR 870.4150
Class: II