

**SPECIAL SUPPLEMENT TO DIRECTIONS FOR USE: INSPIRE OXYGENATORS**  
**TEMPORARY MODIFICATION TO INDICATIONS FOR USE TO ADDRESS COVID-19**

**BACKGROUND**

The United States Food and Drug Administration issued a guidance document *Enforcement Policy for Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency* (Monday, April 6, 2020) to expand the availability of devices used in extracorporeal membrane oxygenation (ECMO) therapy to address the Coronavirus Disease 2019 (COVID-19) Pandemic. This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), including any renewals made by the HHS Secretary.

COVID-19 can trigger acute respiratory failure and/or acute cardiopulmonary failure. Under such conditions, long-term extracorporeal oxygenation (i.e., extracorporeal oxygenation for greater than 6 hours) can be an important tool for treating patients and FDA recognizes the importance and utility of increased availability of extracorporeal oxygenation devices for patients during the COVID-19 public health emergency. Cardiopulmonary bypass devices, cleared or approved by FDA, are technologically capable of being used for ECMO therapy, providing extracorporeal oxygenation for longer than 6 hours. Therefore, to facilitate expanded availability of devices to perform ECMO therapy to treat COVID-19 patients, FDA is permitting manufacturers of cardiopulmonary bypass devices to modify the indications for use of their devices to include ECMO greater than 6 hours, without prior submission of a premarket notification to FDA (i.e. FDA clearance).

| Device model | Catalogue Number |
|--------------|------------------|
| Inspire 6 M  | 050700           |
| Inspire 7 M  | 050725           |
| Inspire 8 M  | 050701           |

**INDICATIONS FOR USE**

FDA-Cleared Indications for Use

The devices in the scope of this document are intended for use in adult and small adult surgical procedures requiring cardio-pulmonary bypass. It provides gas exchange support and blood temperature control. The devices in the scope of this document are intended for use for six hours or less.

Special Indications for Use permitted by FDA on a temporary basis to address the COVID-19 pandemic

The device can be used in an ECMO circuit to treat patients who are experiencing acute respiratory failure and/or acute cardiopulmonary failure. The device can be used in an ECMO circuit greater than 6 hours. When used longer than 6 hours, continuous monitoring is required to ensure correct device operation.

**ADDITIONAL INFORMATION RELATED TO SPECIAL INDICATIONS FOR USE**

**The following information provides an addendum to the existing FDA-Cleared Directions for Use (DFU) about the device related to the Special Indications for Use.**

011680-20 SUPPLEMENT IFU FOR INSPIRE USE IN ECMO DURING COVID-19 – US ONLY

## Device Performance

See DFU at paragraph “**B. TECHNICAL FEATURES**” and “**SYSTEM SPECIFICATIONS AND PERFORMANCE GRAPHS**”

### Summary of Durability Testing

Available data confirm declared performance of the device up to 6 hours, according to ISO 7199:2016 *Cardiovascular implants and artificial organs – Blood-gas exchangers (oxygenators)*. When used for longer than 6 hours, continuous monitoring is required to ensure correct device operation (refer to section ***Clinical Signs and Observations that suggest device change-out is required***).

### Summary of Animal Testing

There is no additional animal testing related to use for ECMO greater than 6 hours.

### Summary of Clinical Performance

Device performance in terms of gas transfer and thermoregulation were confirmed for all Inspire models in CPB procedures. When used longer than 6 hours, continuous monitoring is required to ensure correct device operation (refer to section ***Clinical Signs and Observations that suggest device change-out is required***).

### Potential Risk

The following hazardous situations may arise during the use of the device in an ECMO circuit:

- Gas Exchange Failure
- Plasma leakage
- Clotting
- Pressure drop increase
- Increased occurrence of device change-out

In patients with viremia there is the theoretical possibility of passage of virus from blood through the fiber membrane into the exhaled gas from the oxygenator, particularly in the presence of plasma leakage across the membrane. No specific testing has been performed to evaluate the likelihood of this occurrence and clinical evidence is insufficient to quantify any associated risks. Use of polymethylpentene (PMP) membrane oxygenators may mitigate the risk of virus passage across the oxygenator membrane. Local Standard Operating Procedure (SOP) of the institution for dealing with infectious patients should be followed throughout device operation.

### Clinical Signs and Observations that suggest device change-out is required

General indications are provided in the DFU at paragraph “**N. DEVICE CHANGE-OUT**”. For specific change-out clinical signs and observations refer to “**Extracorporeal Life Support Organization (ELSO) General Guidelines for all ECLS Cases - August, 2017 – version 1\_4**”:

- Per the Extracorporeal Life Support Organization (ELSO) Guidelines for Adult Respiratory Failure, a membrane oxygenator will be selected for goal rated flow based on gas transfer and surface area. ((ELSO), 2017, p. 8) These factors will contribute to maximal oxygen delivery and carbon dioxide clearance. If a membrane oxygenator is failing to provide rated flow or minimal gas transfer, or the upsaturation of inlet blood of 65% to exit saturation of 95% or less, and blood and gas flow goals are met, it may be advisable



to exchange the membrane oxygenator component due to failing gas exchange. Failure blood or gas flow goals may indicate a phase obstruction, and also warrant exchange.

- ELSO Guidelines also support the use of multiple membrane oxygenators in parallel in the event of inadequate gas exchange achieved by a single membrane. Further, water vapor can condense in the membrane lung resulting in poor CO<sub>2</sub> clearance, and may be cleared by intermittently increasing sweep gas flow to a higher flow. ((ELSO), 2017, p. 9).
- Clotting in the circuit is detected by careful examination, using a flashlight to go over all the extracorporeal circuit. Clots are seen as very dark nonmoving areas on the surfaces. Every circuit will have some small clots at the site of connectors, infusion lines, or in areas of low flow in the pre-pump or the membrane lung. These clots are in the range of 1 to 5 mm, do not require circuit changes, and are simply observed. Clots larger than 5 mm or enlarging clots on the infusion side of the circuit (post membrane lung) should be removed by removing that section of the circuit or by changing the entire circuit if there are many such clots. Platelet/fibrin thrombi appear as white areas on the circuit at connectors and stagnant sections. These are clots which have not accumulated red cells, usually because they are in areas of very high flow. As with dark clots, no intervention is necessary unless the white thrombi are greater than 5 mm or growing. ((ELSO), 2017, p. 18).
- Pre and post membrane lung pressure and alarms. These measurements will determine the transmembrane lung pressure gradient. Clotting in the oxygenator is represented by increasing membrane lung pressure gradient. ((ELSO), 2017, p. 10).

In addition, the following phenomena should be monitored:

- Plasma leakage: Polypropylene microporous membrane allows plasma leak for procedures exceeding 6 hours of use and results in fluid or foamy plasma exiting gas outlet. When a plasma leak occurs, performance may become impaired.
- Oxygenating fiber leaks
- Pressure drop increase and/or inability to guarantee sufficient blood flow

If any of the above conditions are observed, consider change-out of the oxygenator.

### Use Conditions

The extracorporeal circulation is intended to temporarily bypass the heart and lungs function by an external circuit, where single components work independently but in synergy with each other.

When using the device in ECMO procedures, do not use in conjunction a venous reservoir and an arterial filter.

In the absence of an integrated reservoir, care must be taken to monitor inflow conditions to the pumping mechanism that will feed the oxygenator. Air ingress and reduced preload conditions may impact therapeutic goals of flow delivery.

Microporous membrane does allow blood compartment air embolization in case blood path pressure becomes lower in respect to gas path pressure. The pressure in the blood compartment must always exceed that of the gas compartment to prevent gas emboli from appearing in the blood compartment.

See DFU at paragraph “**C. INTENDED USE**” and “**D. CONTRAINDICATIONS**”

((ELSO), E. L. (2017). *Adult Respiratory Failure Guidelines, Ven 1.4*. Extracorporeal Life Support Organization.

