

Heilbronn, June 16<sup>th</sup> 2020

## Information pertaining to the use of Xenios AG Extra Corporeal Life Support (ECLS) products in critically ill patients suffering from COVID-19

### SCOPE

This letter responds to ELSO's request and applies only to the following product lines and brands manufactured by Xenios AG for the use in ECLS of critically ill patients.

- External to the US, all tubing sets incorporating a HILITE 7000 LT oxygenator, branded either as Medos or Novalung
- In the US only, the X-Lung tubing set incorporating a HILITE 7000 LT oxygenator, branded as Novalung.

All products should be used according to the approved indications or instructions granted by the individual country. Any device not belonging to the above groups and/or not branded as LT is not covered by the following information. Gas exchangers not branded as LT are not suitable for long-term use common to ECLS therapies.

### DISCLAIMER

*This letter is for informational purposes only and is intended to provide a brief overview of the current scientific and medical information regarding the transmission of SARS-CoV-2 across the membrane of ECLS oxygenators. It is not medical advice and does not replace the judgment or experience of the attending physicians or nurses. The treatment of the patients and the decisions concerning specific patient treatments, including but not limited to the decision whether to use an oxygenator, are the sole responsibility of the attending physicians or healthcare providers.*

*It does also not replace the careful review of the relevant Instruction for Use (IFU) of the respective medical device. The IFU of the respective medical advice (including but not limited to the defined time utilization limit and unit maintenance), applicable guidelines and regulations of local authorities, as well as hygienic guidelines applicable in each country, hospital or other facility should always be complied with.*

Xenios AG is aware of the unprecedented surge on hospitals related to the global COVID-19 pandemic. During these uncertain and stressful times, we have been working to share relevant information that might be helpful in the care of patients with COVID-19 who need ECLS. Specifically, some in the medical community recently raised concerns regarding the safety of ECLS oxygenators with respect to COVID-19 transmission across the membrane and potential risk to providers or other patients. Therefore, the intent here is to present the current understanding on the topic, based on the limited information available. The data presented are exclusively derived from clinical assessments of patients done by physicians in hospitals, webinars presented and peer-reviewed publications. However, due also to limited numbers of samples and reports, they are by no means comprehensive. No internal lab assessment has been conducted by Xenios AG and is not planned. Yet, we believe that the available data combined with our technical expertise in oxygenators suggest that the likelihood of contamination would be very low.



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## Xenios AG oxygenator technical information

The oxygenator housing is made of polycarbonate. Internally, there are two modules, one for gas exchange and another for heat exchange. A non-porous, tubular polyethylene (PE) hollow fiber is used for the heat exchanger module in our oxygenators. The gas exchange module allows air flow from the external environment to course inside the hollow fibers, while blood flows outside the fibers. The membrane used to manufacture the gas exchange module is poly-4-methyl-pentene (PMP); some models are additionally coated with a biocompatible heparin and albumin multilayer. PMP membranes have an average pore size of less than 0.05 microns<sup>1</sup> and are integrally asymmetric; an even pore distribution throughout the whole wall thickness creates a dense outer skin (thickness  $\ll 1 \mu\text{m}$ )<sup>2</sup> that is designed to provide complete physical separation between blood and gas compartments<sup>2</sup>. This dense outer skin does not allow plasma and proteins to cross the membrane<sup>3</sup>, unless the fibers are damaged. Barring a technical defect (e.g., rupture or leakage), it is highly unlikely that the SARS-CoV-2 virus could pass across the oxygenator from the blood side to the water side.

## Available clinical data on the topic

Based on the technical features of the PMP membrane gas exchange module and our current understanding of SARS-CoV-2 transmission, theoretically, the probability that SARS-CoV-2 could pass from the bloodstream to the gas phase in a PMP oxygenator and extrude through the exhaust port is very low, unless fiber damage has occurred. In the literature, there are only two case reports of plasma leakage in PMP membranes<sup>4,5</sup>. The incidence of SARS-CoV-2 viremia is documented between 1-15%<sup>6</sup>. To date, there are only a limited number of studies performed under emergency conditions that investigated whether the SARS-CoV-2 virus might cross the gas exchanger membrane and be released through the gas outlet port of the oxygenator into the environment. As stated by Keibun Liu, during his presentation at an ELSO webinar, the diameter of the SARS-CoV-2 virus ranges between 0.06 and 0.14 microns<sup>7</sup>. Liu also speculated that surface-coating treatments might add an additional barrier to virus crossing<sup>7</sup>. This hypothesis is garnering traction with some experimental, but not definitive, positive confirmations in the last few weeks. La Pitié University Hospital, accounting for the majority of VV-ECMO runs performed in Europe so far<sup>8</sup>, performed mRNA measurements on the blood from 28 patients on ECMO, of whom 15 were positive and 13 were negative. SARS-CoV-2 was not detected on the oxygenator's gas outlet in any case<sup>8</sup>.

## Xenios AG position statement

Based on our current understanding of SARS-CoV-2 transmission, the concern that SARS-CoV-2 virus could cross the membrane in PMP oxygenators used in ECLS treatment is minimal, unless the fibers are damaged. We strongly recommend that clinicians closely survey the integrity of oxygenator's membrane in order to minimize any potential harms due to leakage. We also recommend that the de-airing oxygenator ports remain closed unless de-airing is temporarily needed to remove air bubbles (e.g., for patient safety or reducing device loss of efficiency). As an added precaution, salvaging of exhaust gas may be performed, based on local policies and practices or physician preferences. We are committed to communicating data that confirm or refute this current recommendation.



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