

Identification Code MCP 0477
Valid from 2020-03-27

Use of Getinge oxygenators and cardiopulmonary products in COVID-19 / SARS-CoV-2 patients

Dear valued business partners and colleagues,

Getinge endeavors to support you and our customers during the corona virus (COVID-19/SARS-CoV-2) pandemic.

Due to the current situation with person-to-person spread of corona virus (COVID-19/SARS-CoV-2) we have received frequent inquiries about the usage of our oxygenators and cardiopulmonary products with COVID-19 patients. The following Q&A provides an overview about the current situation.

Getinge points out that it has no test data specific to this topic. The Q&A is mainly based on technical and theoretical considerations of which Getinge is aware.

DISCLAIMER: This is NOT medical advice, the information contained herein is intended for informational purposes ONLY, and should NOT be used as a substitute for the advice of an appropriately qualified and licensed physician or healthcare provider. The responsibility for deciding whether to use an oxygenator rests solely with the attending physician or healthcare provider. Getinge Group urges to strictly follow the instructions for use (IFU) provided with each medical device unit as approved or cleared by the FDA, or country specific regulatory authority. Including, the device specific time utilization limit and adequate unit maintenance. Please, check with a physician or healthcare provider if you have health questions or concerns about medical device interactions, or contact the FDA/other local authorities for a comprehensive list of warnings. Although we attempt to provide accurate and up-to-date information related to our products and COVID-19/SARS-CoV-2, Getinge makes no representation or warranty of any kind, express or implied, of any information or medical device use not contained or described in the approved medical device instruction for use.

Q&A

Has COVID-19 been identified in blood specimen of patients?

We are currently only aware of a few publications from China^{1,2} in which the COVID-19 virus has been detected in patient blood. Nevertheless, the existing publications show that this scenario is possible.

Can the COVID-19 virus, if present in patient's blood, migrate to the gas side of the Getinge oxygenator?

We address this concern in parts. See below.

How do we assess the likelihood of a virus transmission in Getinge oxygenators with microporous gas exchange fibers?

Microporous membranes by definition have micropores. Getinge is using microporous fibers with a technically specified pore size of up to 200 nm ($\leq 0.2\mu\text{m}$). Based on the reported diameter of the virus³ ($\approx 60 - 140$ nanometers) there is a (theoretical) risk of virus transmission across the gas exchange membrane. In simple words, the virus could leave patients' blood, enter the inner lumen of gas fibers and leave the oxygenator through the gas outlet passing from the blood to the gas side of such oxygenators. The virus could potentially reach the gas fiber inner lumen if plasma leakage occurs. We currently believe that the corona virus will probably not be able to migrate to the gas side without a liquid medium (due to the lack of driving force causing it to leave the blood).

If a Getinge microporous membrane oxygenator is used beyond the recommended duration limit of 6 hours, blood plasma could leak through the microporous of gas exchange fibers from blood to the gas containing inner lumen of such oxygenators. This is a well-known limitation of oxygenators with microporous gas exchange fibers and it is not specific to Getinge oxygenators.

During the process of plasma leakage, corona virus could potentially escape patient's blood and spread into the environment via the gas outlet of a microporous membrane oxygenator. However, as of today, Getinge has not received any report of actual or suspected virus release through the mechanism as described above. Nevertheless, based on currently available information it cannot be ruled out whether corona virus can transmit across microporous gas exchange fibers.

¹ Wang W, Xu Y, Gao R, Lu R, Han K, Wu G, Tan W: Detection of SARS-CoV-2 in Different Types of Clinical Specimens. JAMA 2020.

² Chang L, Yan Y, Wang L: Coronavirus Disease 2019: Coronaviruses and Blood Safety. Transfus Med Rev 2020.

³ Na Zhu, Dingyu Zhang, Wenling Wang, Xingwang Li, Bo Yang, Jingdong Song, Xiang Zhao, Baoying Huang, Weifeng Shi, Roujian Lu, Peihua Niu, Faxian Zhan, Xuejun Ma, Dayan Wang, Wenbo Xu, Guizhen Wu, George F. Gao, Wenjie Tan for the China Novel Coronavirus Investigating and Research Team: A Novel Coronavirus from Patients with Pneumonia in China, 2019. In: The New England Journal of Medicine. 24. January 2020, doi:10.1056/NEJMoa2001017

Consequently, while Getinge has no evidence that the corona virus migrates through the microporous membrane of its microporous membrane oxygenators, judicious use of such Getinge oxygenators within the recommended guidelines should be strictly followed to minimize risk of corona virus spread from these oxygenators.

Is the use of a Getinge oxygenator with microporous gas exchange fibers in cardiac surgery on a patient with confirmed or suspected corona virus infection a risk for the customer

As described above there is a potential infection transmission risk in case of plasma leakage. If the Getinge microporous membrane oxygenator is used according to its recommended use, then we currently believe there is no increased risk resulting from the use of our microporous oxygenators.

How do we assess the likelihood of a corona virus transmission in Getinge oxygenators with Polymethylpentene (PMP) diffusion membrane fibers?

Oxygenators with PMP fibers by design has its barriers which may prevent leakage, however, testing to that end has not been performed. Getinge produces oxygenators with PMP fibers that are typically used in hospitals for extracorporeal life support. If a fully functional Getinge PMP membrane oxygenator is used for prolonged ECLS / ECMO in accordance with well-established recommendations, there is a possibility that the corona virus would not pass from the blood to the gas side of the membrane due to the use of such a plasma tight diffusion membrane oxygenator. As of today, Getinge has no evidence that the corona virus penetrates or diffuses through the PMP membrane used in such oxygenators manufactured by Getinge.

Summary:

Assuming an intact Getinge oxygenator and membrane, it is highly unlikely for a Getinge PMP membrane oxygenator to permit corona virus migration into the gas stream from the blood stream of an infected patient. For a Getinge microporous membrane oxygenator there is a potential risk for corona virus to migrate in the case of plasma leakage. Based on the facts known to Getinge at this time, the use of a Getinge PMP membrane oxygenator is preferable, wherever possible, to mitigate risk of corona virus transmission even though any viral transmission risk when using a Getinge microporous membrane oxygenator is believed to be hypothetical when such an oxygenator is used for no more than six hours.

What happens in the case of a pass over from the corona virus from the blood side into the gas stream?

If a plasma leakage in a microporous oxygenator occurs, there is a potential risk that a contaminated aerosol can exit the oxygenator via the gas outlet.

The user should not use microporous oxygenators for applications over 6 hours. This significantly reduces the risk of plasma leakage.

Getinge assumes that patients with SARS-CoV-2 will only undergo a surgery in an emergency and that a corresponding infection diagnosis has already been made.

Local Standard Operating Procedure (SOP) of the institution for dealing with infectious patients must be followed.

If a plasma leakage occurs within the 6 hours of use of a microporous oxygenator, it must be individually decided how to proceed with a given situation (e.g. change out of the tubing set or oxygenator, finalizing the surgery, etc.).

In any case, the Standard Operating Procedures (SOP) for contaminated environment and material respectively of the local institution must be followed.

For medical devices used outside the USA, **information only available in non-US IFU.**

- It can be considered to connect the gas outlet of the oxygenator to a suction device. The user must ensure that the suction system used is an effective measure for the intended purpose.
 - Make sure that the suction flow volume is greater than the gas feed flow volume.
 - Ensure that the suction device does not create a negative pressure on the gas side, even in the case of a complete interruption of the fresh gas supply.

If there is a potential contamination risk, the affected staff should be tested for COVID-19 as a precautionary measure in accordance with the local Standard Operating Procedure (SOP) of the institution.

All further steps such as quarantine, etc. should be derived from the local guidelines.

Can the corona virus, if present in patient's blood, migrate to the water side of the oxygenator?

A liquid and particle-tight TPU fiber is used as water fiber. Unless there is a technical defect (e.g. rupture or leakage), it is believed that the corona virus cannot pass from the blood side to the water side.

Can viruses pass through the hydrophobic membrane at the de-airing port of the microporous and/or the PMP membrane oxygenator?

As long as the de-airing port of the oxygenator is closed, no aerosol or liquid may exit from the de-airing membrane, therefore, reducing risk of contamination from a virus. We also believe that there is no risk of an open de-airing port during the priming procedure as there is no blood contact at this time.

Getinge recommends to keep the de-airing port closed during use and monitor it closely.

If an active de-airing is required during use, a virus may potentially exit through the membrane since this membrane also contains micropores. It must be individually decided how to proceed with a given situation (e.g. change out of the tubing set or oxygenator, finalizing the surgery, etc.).

In any case, the Standard Operating Procedures (SOP) for contaminated environment and material respectively of the local institution must be followed.

Which disinfectants can be used against corona viruses for surface disinfection of medical devices manufactured by Getinge, for example, such as the Cardiohelp-i?

For surface disinfection of cardiopulmonary devices the corresponding sections of the respective instruction for use (IFU) have to be followed.

Human corona viruses such as SARS, MERS, HCoV can be efficiently inactivated by surface disinfection procedures with 62-71% ethanol within 1 min exposure time. A similar effect is expected against the SARS-CoV-2. Also 70% isopropanol efficiently inactivated coronavirus infectivity within 30 seconds exposure time in suspension tests (Kampf et al 2020).

Please note that Ethanol and/or Isopropanol at a concentration of 70% are referenced in all Instructions of Use for surface disinfection of Cardiohelp-i, the Rotaflow Console and Heater Unit HU 35.

The alcohol based disinfectant Bacillo® AF listed in the IFU for surface disinfection of Cardiohelp-i and HU 35 is officially declared as effective against enveloped viruses including 2019-nCoV by the manufacturer BODE Chemie GmbH.

For further information related to device usage, surface cleaning and disinfection refer to the corresponding instruction for use, and where appropriate the user manual.

An Express Letter with more details will be published shortly.

Will Getinge perform specific tests with the COVID-19 virus in the context of using its oxygenators in corona virus infected patients?

Our current assessment of the situation is based on scientific publications, expert assessments and technical considerations. Due to the novelty and rapid global spread of corona virus laboratory testing with this virus to empirically evaluate the risk of corona virus transmission from Getinge oxygenators is not available. Should such empirical data become available to Getinge, then Getinge will pass such information on to you and our customers.

Getinge has contacted several experts in- and outside of our company in order to better understand the current situation with respect to COVID-19 patients who have used our oxygenators. Furthermore, Getinge monitors the development of the corona virus pandemic situation on a regular basis and will continuously update this Q&A based on any new information obtained by Getinge through the worldwide medical community.

Are there already reported cases in which a transmission of COVID-19 viruses has taken place between an infected patient and another person via any Getinge oxygenator?

Getinge currently is not aware of any reported cases of such transmission with our products.