

Coronavirus disease 2019 (COVID-19) and supply of substances of human origin in the EU/EEA – third update

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Executive summary

This document provides an update on the safety of substances of human origin (SoHO) in relation to COVID-19. It reassesses the risk and proposes revised mitigation measures for preventing transmission through SoHO. The report concludes that the risk of COVID-19 transmission via SoHO is negligible, except for lung and potentially intestine transplantation [1,2]. Mitigation measures should follow general guidelines for respiratory diseases. Specific criteria are outlined for SoHO donors, and non-standard donors require informed consent and monitoring. More stringent measures can be implemented based on local epidemiological conditions. General recommendations from public health authorities should be followed to protect personnel and donors against COVID-19.

Scope of the document

This third update of the document incorporates further experience gained during the COVID-19 pandemic regarding the safety of substances of human origin (SoHO) and recent scientific developments in understanding the evolution of the disease and its transmissibility through different types of SoHO. The document reassesses the risk posed by COVID-19 and revises options for mitigating the transmission risk of COVID-19 through SoHO.

Since the very beginning of the COVID-19 outbreak, the European Centre for Disease Prevention and Control (ECDC) has been publishing rapid risk assessments and technical reports to support the safety of the SoHO supply [3-5]. ECDC will update the document as and when new relevant information becomes available, or as required by the epidemiological situation, to avoid unnecessary barriers for SoHO donation.

What is new in this document?

- Reassessment of the risk of COVID-19 transmission via SoHO based on new evidence.
- Revised recommendations for mitigation measures in relation to SoHO.

Target institutions

National competent authorities for SoHO, SoHO establishments, organ procurement organisations and transplant centres in the European Union (EU)/European Economic Area (EEA).

Definitions

The definitions and the priority classification of SoHO remain the same as in the previous editions [3-5].

Abbreviations

SoHO	Substances of human origin
ECDC	European Centre for Disease Prevention and Control
COVID-19	Coronavirus disease-19
RT-PCR	real-time polymerase chain reaction
NAT	nucleic acid testing
BAL	bronchoalveolar lavage.

Background

Detailed information on the virus, disease epidemiology, COVID-19 case definition for EU surveillance, clinical manifestations and risk and prevention in the population is available on ECDC's website [6].

Laboratory testing

Information on the detection assays relevant to COVID-19 diagnostic testing and screening is available on ECDC's website [6].

Risk to the viral safety of SoHO

At the time of this update, with the exception of cases following lung transplantation [7-9], no transmission of COVID-19 via SoHO and plasma-derived medicinal products has been reported worldwide [10,11]. Studies published on the blood of asymptomatic patients with confirmed SARS-CoV-2 infection, or those with mild symptoms report the absence or low prevalence of samples positive for RNA [12-14]. In the field of organ transplantation, there is evidence of non-lung organs, and even lungs [15] being transplanted from individuals known to have tested positive for SARS-CoV-2 just prior to death, without reported transmissions [10,16].

For blood and blood components, the period during which donors should refrain from donating until after the resolution of clinical symptoms or clearance of test results, as recommended by various organisations, ranges from seven to 28 days [17-21]. No transmission of SARS-CoV-2 infection has been reported in association with the application of any of the existing recommendations [22].

A recent large study of 101 corneas from donors positive for SARS-CoV-2 in post-mortem nasopharyngeal swab tests showed no presence of SARS-CoV-2 virions in corneal specimens and storage media [23]. Similar results were obtained for other tissues [24,25]. In addition, a variety of procedures and reagents applied during tissue and cell procurement and processing, such as povidone iodine and polyvinylpyrrolidone solutions, reduce the potential bioburden of the SARS-CoV-2 virus in transplants [26,27].

Numerous recent studies in the field of organ donation have not demonstrated any transmission and show that use of SARS-CoV-2 NAT-positive non-lung donors resulted in similar recipient outcomes to SARS-CoV-2 NAT-negative donors [10,16,28-41] in terms of the quality of organs.

Furthermore, most recent large-scale studies showed that the incubation period differs among variants. For example, it was shorter (3.61 days) for the Omicron variant (with a range of 3.55–3.68 days) [42] compared to the previously-estimated five to six days (with a range of one to 14 days) [3] for the original strain. As a result of the significant improvement in the global epidemiological situation, the World Health Organization (WHO) declared that COVID-19 no longer constitutes a public health emergency of international concern [43].

Based on the current evidence and status of knowledge, the incidence of transmission of COVID-19 via SoHO seems negligible and, except for the lungs, and potentially intestine transplantation [1,2], there is no evidence of a risk.

Mitigation measures for SoHO transmission

Given that the risk of COVID-19 transmission via SoHO is only theoretical, except via lung and, potentially intestine transplantation, the recommended risk mitigation measures are precautionary and are based on ongoing donor assessment practices without transmission events and other evidence. Measures for preventing transmission of SARS-CoV-2 through SoHO should follow the general rules applied for the prevention of respiratory, influenza-like diseases. Living donors with active COVID-19 diseases at the time of donation, and deceased donors with COVID-19 as cause of death, are not eligible for the donation of SoHO. At the time of donation, living donors must be in good health and all donors must meet general eligibility criteria.

Specific criteria that SoHO donors should meet at the time of donation in relation to SARS-CoV-2 are specified in Table 1.

Table 1. Recommendations for donor eligibility criteria-standard donors

Donor	Eligibility criteria for donation according to the type of SoHO ¹			
	Blood	Non-reproductive tissues and cells	Non-lungs organs	Lungs and intestine
No history of COVID-19 and no contact with COVID-19 patients.	Standard donor selection procedures should be applied			<ul style="list-style-type: none"> Negative SARS-CoV-2 RT-PCR² test on respiratory secretions from BAL³ or deep bronchial aspirate. Test should be performed within 24 hours preferably, or max. 48 hours prior to procurement.
Donors with positive history of COVID-19, confirmed or unconfirmed.	<ul style="list-style-type: none"> >14 days after the complete resolution of symptoms. 	<ul style="list-style-type: none"> >7 days after clinical and virological recovery. 	<ul style="list-style-type: none"> >14 days after the onset of symptoms (or 7 days after documented virological recovery) >72 hours symptom free. 	<ul style="list-style-type: none"> >21 days after the onset of symptoms >72 hours symptom free.
			<p>Deceased donors</p> <ul style="list-style-type: none"> Negative SARS-CoV-2 RT-PCR test on respiratory secretions from BAL or deep bronchial aspirate. <p>Living donors</p> <ul style="list-style-type: none"> Negative SARS-CoV-2 RT-PCR test on respiratory secretions from a nasopharyngeal swab. Tests should be performed within 24 hours preferably, or max. 48 hours prior to procurement. 	
Donors with history of close contact with COVID-19 patients.	<ul style="list-style-type: none"> Standard donor selection procedures should be applied. 	<ul style="list-style-type: none"> Standard donor selection procedures should be applied. 	<p>Deceased donors</p> <ul style="list-style-type: none"> >7 days since contact. Negative SARS-CoV-2 RT-PCR test on respiratory secretions from BAL or deep bronchial aspirate. <p>Living donors</p> <ul style="list-style-type: none"> >7 days since contact negative SARS-CoV-2 RT-PCR test on respiratory secretions from a nasopharyngeal swab. Tests should be performed within 24 hours preferably, or max. 48 hours prior to procurement 	Not applicable
			<p>Deceased donors</p> <ul style="list-style-type: none"> Standard donor selection procedures should be applied. <p>Living donors</p> <ul style="list-style-type: none"> Standard procedure for donor vaccination should be followed. 	
Donors vaccinated with non-replicating, inactivated, or mRNA-based COVID-19 vaccine.	<ul style="list-style-type: none"> >48 hours since vaccination; without complications; this deferral period is recommended to prevent discarding and waste of resources due to the post donation notification of possible vaccine side effects [21,44]. 	<p>Deceased donors</p> <ul style="list-style-type: none"> Standard donor selection procedures should be applied. <p>Living donors</p> <ul style="list-style-type: none"> Standard procedure for donor vaccination should be followed. 	<p>Deceased donors</p> <ul style="list-style-type: none"> Standard donor selection procedures should be applied. 	Not applicable

¹ Donors eligible for donation should meet all the criteria listed in the corresponding column.

² RT-PCR = real-time polymerase chain reaction

³ BAL = bronchoalveolar lavage.

Non-standard deceased organ donors

Organs from deceased donors who are:

- SARS-CoV-2 real-time polymerase chain reaction (RT-PCR)-positive deceased organ donors where COVID-19 is NOT the cause of death;
- SARS-CoV-2 RT-PCR-negative deceased organ donors who were in close contact with a confirmed COVID-19 patient within seven days prior to donation;

can be considered for transplantation as coming from non-standard risk donors. Specific informed consent must be obtained from the recipient prior to transplantation. The outcomes of the transplantation should be monitored and reported through the national organ-vigilance system.

There is encouraging experience using lungs from donors with a history of SARS-CoV-2 infection and positive nasopharyngeal swab but negative BAL [33]. Until more evidence is obtained, the utilisation of lungs from such donors should be carefully evaluated on a case-by-case basis.

Non-standard donors of tissue and cells

In cases when the donor does not meet standard eligibility criteria in relation to SARS-CoV-2, tissues and cells can be accepted when a validated SARS-CoV-2 inactivation process is applied.

General considerations

This report represents minimal SoHO safety recommendations. Countries can decide to apply more stringent measures if/when justified by the local epidemiological situation.

To protect personnel and donors against COVID-19 infection in establishments and hospitals, the general recommendations of the relevant public health authorities must be applied.

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