MINISTERO DELLA SALUTE
Istituto Superiore di Sanità
Centro Nazionale Trapianti

WHO Collaborating Centre
On Vigilance and Surveillance for
Human Cells, Tissues and Organs

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Subject: update on the measures to prevent the transmission of the novel Coronavirus (SARS-CoV-2) infection through organ and tissue transplantation in Italy.

Dear All,
with respect to the epidemiologic evolution of the COVID-19 spread in our country, of the knowledge related to the transmission of the SARS-CoV-2 infection and of the new ministerial regulations, the following measures shall be adopted, in case of potential organ and tissue donor:

1. Donor with negative COVID-19 medical history or no contact with COVID-19 patients

1.1. All deceased donors shall be specifically tested for the search of SARS-CoV-2, on respiratory BAL secretions or deep bronchial suction, in case of organ and tissue donation; or from nasopharyngeal swab, in case of tissue donation only, on a sample collected 72 hours prior to retrieval;

1.2. All living donors shall be specifically tested for the search of SARS-CoV-2, on respiratory secretions collected through a nasopharyngeal swab, 72 hours prior to retrieval.

2. Donor with positive COVID-19 medical history, documented or undocumented, or contact with COVID-19 patients

2.1. **Deceased organ donor**

2.1.1. Donor with documented positive history for COVID-19: the donor's organs shall be used after 14 days from documented virological recovery (negative molecular or antigenic swab) with negative SARS-CoV-2 search on respiratory secretions from BAL or deep bronchial suction performed within 24, up to a maximum of 48 hours, prior to retrieval. In these cases, the risk level is to be considered standard.

2.1.2 Donor with undocumented COVID-19 medical history (symptoms compatible with COVID-19 but no swab or negative swab or anti-SARS-CoV-2 antibodies serological positivity): the donor's organs shall be used after 14 days from the disappearance of clinical symptoms with negative SARS-CoV-2 search on BAL respiratory secretions or deep bronchial suction performed within 24, up to a maximum of 48 hours prior to retrieval. In these cases, the risk level is to be considered standard.

2.1.3. Donor with a history of close contact with COVID-19 patients in the absence of clinical symptoms or with negative nasopharyngeal swab: the donor's organs shall be used after at least 14 days from last contact (high or low risk as defined by the Ministry of Health's circular letter 0060136-30/12/2021-DGPRE-DGPRE-P) with negative search for SARS-CoV-2 on BAL respiratory secretions or deep bronchial suction performed within 24, up to a maximum of 48 hours prior to retrieval. In these cases, the risk level is to be considered standard. The 14-day term can be reduced to 7 in the case of a subject vaccinated with at least 2 doses.

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2.2. **Living organ donor**

2.2.1. donor with a documented COVID-19 medical history: the donor may be prepared for donation after 14 days from their documented virological recovery (a negative molecular or antigenic swab) with a negative SARS-CoV-2 nasopharyngeal **molecular** swab performed upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval, given that the result is available before organ retrieval). In these cases, the risk level is to be considered standard.

2.2.2. Donor with undocumented COVID-19 medical history (symptoms compatible with COVID-19 but no swab or negative swab or anti-SARS-CoV-2 antibodies serological positivity): the donor shall be prepared for donation after 14 days from the disappearance of the clinical symptoms and with a negative SARS-CoV-2 nasopharyngeal **molecular** swab upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval, given that the result is available before organ retrieval). In these cases, the risk level is to be considered standard.

2.2.3. Donor with a medical history of contact with COVID-19 patients with no clinical symptoms or with a negative nasopharyngeal swab: the donor shall be prepared for donation after 14 days from last contact (high or low risk as defined by the Ministry of Health's circular letter 0060136-30/12/2021-DGPRE-DGPRE-P) and negative SARS-CoV-2 nasopharyngeal **molecular** swab upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval, given that the result is available before organ retrieval). In these cases, the level of risk is to be considered standard. The 14-day term can be reduced to 7, in the case of a subject vaccinated with at least 2 doses.

2.3. **Deceased tissue donor**

2.3.1. Donor with a documented COVID-19 medical history: the donor's tissues shall be retrieved 14 days after documented virological recovery (a negative molecular or antigenic swab) and with a negative SARS-CoV-2 nasopharyngeal molecular swab upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval, with results available before tissue distribution). For corneas retrieval, it is also recommended to use povidone iodine as a disinfectant of the ocular surface, which has been shown to be effective in the inactivation of SARS-CoV-2.

2.3.2. Donor with undocumented COVID-19 medical history (symptoms compatible with COVID-19 but no swab or negative swab or anti-SARS-CoV-2 antibodies serological positivity): donor's tissues can be retrieved after 14 days from the disappearance of clinical symptoms and with a negative SARS-CoV-2 nasopharyngeal molecular swab upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval and with results available before tissue distribution). For corneas retrieval, it is also recommended to use povidone iodine as a disinfectant of the ocular surface, which has been shown to be effective in the inactivation of SARS-CoV-2.

2.3.3. Donor with a medical history of contact with COVID-19 patients with no clinical symptoms or with negative nasopharyngeal swab: donor's tissues can be retrieved after 14 days from last contact (high or low risk as defined by the Ministry of Health's circular letter 0060136-30/12/2021-DGPRE-DGPRE-P) and negative SARS-CoV-2 nasopharyngeal **molecular** swab upon donation (performed within 24, up to a maximum of 48 hours prior to retrieval with results available before tissue distribution). For corneas retrieval, it is also recommended to use povidone iodine as a disinfectant of the ocular surface, which has been shown to be effective in the inactivation of SARS-CoV2. The 14-day term can be reduced to 7, in the case of a subject vaccinated with at least 2 doses.

2.4. **Living tissue donor**

2.4.1. Donor with documented COVID-19 positive medical history: the donor shall be prepared for donation after 14 days from their documented virological recovery (a negative molecular or antigenic swab) and with a SARS-CoV-2 negative nasopharyngeal molecular swab (performed within 24, up to a maximum of 48 hours prior to retrieval and with results available before tissue distribution).

2.4.2. Donor with undocumented COVID-19 medical history (symptoms compatible with COVID-19 but no swab or negative swab or anti-SARS-CoV-2 antibodies serological positivity): the donor can be prepared for donation after 14 days from the disappearance of the clinical symptoms and negative SARS-CoV-2 nasopharyngeal molecular swab (performed within 24 hours, up to a maximum of 48 hours prior to retrieval and with results available before tissue distribution);

2.4.3. Donor with a medical history of close contact with COVID-19 patients with no clinical symptoms or with a negative nasopharyngeal molecular swab: the donor shall be prepared for donation after 14 days from the last contact (high or low risk as defined by the Ministry of Health's circular letter 0060136-30/12/2021-DGPRE-DGPRE-P) and negative SARS-CoV-2 nasopharyngeal molecular swab (performed within 24, up to a maximum of 48 hours prior to retrieval and with results available before tissue distribution). The 14-day term can be reduced to 7, in the case of a subject vaccinated with at least 2 doses.

In all the above described cases, a shorter time interval than those indicated, means that the donor is considered positive to the SARS-CoV-2 virus. Therefore, in case of tissue donation from deceased donor, the donor shall be deemed unsuitable; in case of a living donor (organs and tissues) the donation shall be postponed. If the tissue retrieval surgery cannot be postponed, the donor shall be considered unsuitable. For organs from a deceased donor, the following measures shall be undertaken.

3. SARS-CoV-2 positive deceased donor

With reference to the definition of donor with active SARS-CoV-2 infection, the only donors who shall be considered for organ retrieval for transplantation purposes, are those who tested positive to the search of SARS-CoV-2 in a nasopharyngeal sample and/or BAL respiratory secretions or deep bronchial suction upon retrieval and/or within 14 days prior to retrieval, who died of other causes, with no clinical signs of the COVID-19 disease.

Organs from a deceased SARS-CoV-2 positive donor, **attributed with an acceptable level of risk**, can be offered, after consultation with the national second opinion expert for infectious diseases, to recipients who signed the informed consent for transplantation from acceptable non-standard risk donors, at the time of registration on the waiting list and, in any case, prior to the organ offer from a donor with active SARS-CoV-2 infection. Specific consent for transplantation of an organ from a SARS-CoV-2 positive donor must be acquired upon organ offer.

Specifically, such organs may be offered to:

3.1. Patients waitlisted for a **heart or liver** transplant for whom, according to the medical team responsible for the transplant, the risk of onset of further, serious complications connected to the patients' permanence on the waiting list, is far higher than those, so far known, arising from the potential transmission of COVID-19 from the donor, when at least one of the following conditions are met:

3.1.1. SARS-CoV-2 positive patients with no symptoms or with mild symptoms;

3.1.2. positive medical history of COVID-19 (to be evaluated case by case with the second opinion expert for infectious diseases);

3.1.3. patients who completed the vaccination cycle (3 doses) (the time interval from the last dose will be evaluated case by case with the second opinion expert for infectious diseases) and with documented response (antibody positivity and, if available, virus specific cell-mediated immunity). In case of unavailable antibody response, it is recommended not to increase the ischemia time while waiting for it and to consult with the second opinion expert for infectious diseases.

3.2. Patients waitlisted for **kidney** transplantation (see *Protocol for the use of kidneys retrieved for transplantation from SARS-CoV-2 positive donors_rev_1.0*) for whom, according to the medical team

responsible for the transplant, the risks of further worsening of the clinical conditions connected to the patients' permanence on the waiting list are higher than those, so far known, arising from the transmission of COVID-19 from the donor, when at least one of the following conditions are met:

3.2.1. positive medical history of COVID-19 (to be evaluated case by case with the second opinion expert for infectious diseases);
3.2.2. patients who completed the vaccination cycle (3 doses) (the time interval from the last dose will be evaluated case by case with the second opinion expert for infectious diseases) and with documented response (antibody positivity and, if available, virus specific cell-mediated immunity). In case of unavailable antibody response, it is recommended not to increase the ischemia time while waiting for it and to consult with the second opinion expert for infectious diseases.

These may include patients:
- in national urgency;
- included in the PNI program (National Hyperimmune Program);
- in regional urgency;
- with a long waiting period on dialysis;
- with such a hyperimmunization condition that a long waiting period on the list is to be expected.

The organs may also be offered to patients who do not fall into the above indicated categories according to the medical team responsible for the transplant.

In order to use monoclonal antibodies, the identification of the SARS-CoV-2 variant is not essential. Given the current spread of the Omicron variant, Sotrovimab is the only monoclonal that maintains a neutralizing activity against it. Therefore, in the event of clinical indications for the administration of monoclonal antibodies, the use of the aforementioned is recommended.

For livers and kidneys from a deceased donor with active SARS-CoV-2 infection, a biopsy to search for SARS-CoV-2 RNA and to bring out any other histopathological alterations, is recommended. It is also recommended to search for SARS-CoV-2 in the organs' perfusion fluid, and to share the results obtained from the aforementioned investigations with CNTO (the Italian National Transplant Centre's Operational Unit) and the second opinion expert for infectious diseases. As far as the heart is concerned, the biopsy is to be performed at the discretion of the transplant center. It is also made present that the results of such investigations do not need to be available prior to transplantation.

Those patients who meet the above described specific characteristics may start the transplant process procedures, prior to the signing of a specific informed consent (Annex 1 heart and liver and Annex 2 kidneys) and post-transplant monitoring (Annex 3).

The detection of the anti SARS-CoV-2 neutralizing antibodies in the recipients is recommended. The results may also be available once the transplant has already been performed.

Recipients who are candidates for kidney transplantation who test positive to SARS-CoV-2 must be suspended from the waiting list and can be re-admitted after 14 days from virological recovery. Contrarily, asymptomatic or paucisymptomatic candidates for heart and liver transplantation shall not be suspended from the list if tested positive for SARS-CoV-2. Heart and liver transplant candidates with symptoms shall, on the other hand, be suspended and re-admitted to the list after 14 days from virological recovery.

Asymptomatic or paucisymptomatic heart and liver transplant candidates who test positive to SARS-CoV-2 may also be offered SARS-CoV-2 negative deceased donors.
It is necessary to inform CNT Operational Unit in case of a waitlisted patient in national and/or macroarea

urgency who tested positive to SARS-CoV-2.

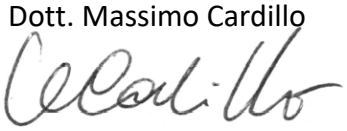
This note abrogates and replaces the previous ones listed below, with reference to preventive measures related to the transmission of SARS-CoV-2 infection through organ and tissue transplantation:

- May 31, 2021, Prot. 20696 / CNT 2021
- January 14, 2022, Prot. 1476 / CNT 2022
- January 19, 2022, Prot. 2042 / CNT 2022

The indications formulated in this note are subject to being updated with further scientific evidence.

The Coordinators of the Regional Transplant Centers are invited to promptly inform all structures, including the Transplant Centers and the Tissue Establishments, operating in the areas of competence.

The Italian National Transplant Center's General Director
Dott. Massimo Cardillo



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Annex 1

INFORMED CONSENT FORM FOR LIVER AND HEART TRANSPLANT CANDIDATE PATIENTS WITH ORGANS FROM SARS-CoV-2 POSITIVE DONORS

I, the undersigned …… born in …….. on ……. candidate for a …….. transplant at the …… Transplant Center hereby declare that I have been fully informed by Dr. …….. on the following:

In order to increase my chances of receiving a transplant, I have been offered, from the doctors at the Transplant Center, to receive an organ from a donor who has become infected with the SARS-CoV-2 virus, responsible for the disease called COVID-19.

I have been informed in detail of the criteria defined, drafted by the Italian National Transplant Center, and endorsed by the Italian Transplant Centers, which provide, in particular, the following:

- the SARS-CoV-2 virus has been found occasionally in the donor who donated the organ, and is not related to their cause of death;
- the organ is being offered to me because I tested positive for COVID-19 disease but show no symptoms or have mild ones, or I recovered from the infection at least 14 days ago or I have completed the vaccination cycle with 3 doses (therefore, it is assumed that I have protection from any new contact with the virus);
- the doctors of the Transplant Center also believe that, due to my clinical conditions, the risks of my further permanence on the list are higher than those, so far known, of the potential transmission of SARS-CoV-2 from the donor.

The preliminary experiences carried out in our country with the use of organs from donors with active SARS-CoV-2 infection did not result in any adverse consequences for the recipients.
I have been informed that this possibility cannot be excluded in the future. Furthermore, precisely due to the lack of reported case of transmission from the donor, the risks entailed for the recipient are unknown.
It was also confirmed that the suitability evaluation of both the donor and the organs, is always performed, in all Italian Centers, with the same criteria normally in use, i.e. collectively by all health professionals involved in the retrieval and transplant activities in collaboration with their respective Regional Transplant Center, with the Italian National Transplant Center Operational Unit and with the support of infectious diseases experts dedicated to this activity (National Second Opinion Expert for Infectious Diseases).

In order to verify the safety of the transplant, upon receiving it, I will undergo specific check-ups aimed at assessing my immune condition with regards to the SARS-CoV-2 infection, as well as the presence of an active infection. The same check-ups will be performed in the post-transplant period, to verify that the infection has not been transmitted.

Noted all of the above, I, the undersigned …….
Born in …….. on …….. candidate for a ……. Transplant, at the ……Transplant Center hereby declare that I have received the information and I have understood what Dr./Prof. …….. has explained to me.

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Therefore I hereby

□ **consent** □ **do not consent**

to receive the transplant of an organ retrieved from a donor with active SARS-CoV-2 infection and to undergo specific check-ups as provided by the Italian National Transplant Center.

Date …….

Transplant Candidate's Signature Doctor's signature

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Annex 2

INFORMED CONSENT FORM FOR KIDNEY TRANSPLANT CANDIDATE PATIENTS WITH ORGANS FROM SARS-CoV-2 POSITIVE DONORS

I, the undersigned …… born in …….. on ……. candidate for a kidney transplant at the …… Transplant Center hereby declare that I have been fully informed by Dr. …….. on the following:

In order to increase my chances of receiving a transplant, I have been offered, from the doctors at the Transplant Center, to receive an organ from a donor who has become infected with the SARS-CoV-2 virus, responsible for the disease called COVID-19.

I have been informed in detail of the criteria defined, drafted by the Italian National Transplant Center, and endorsed by the Italian Transplant Centers, which provide, in particular, the following:

- the SARS-CoV-2 virus has been found occasionally in the donor who donated the organ, and is not related to their cause of death;
- the organ is being offered to me because I recovered from the infection at least 14 days ago or I have completed the vaccination cycle with 3 doses (therefore, it is assumed that I have protection from any new contact with the virus);
- the doctors of the Transplant Center also believe that, due to my clinical conditions, the risks of my further permanence on the list are higher than those, so far known, of the potential transmission of SARS-CoV-2 from the donor.

The preliminary experiences carried out in our country with the use of organs from donors with active SARS-CoV-2 infection did not result in any adverse consequences for the recipients.
I have been informed that this possibility cannot be excluded in the future. Furthermore, precisely due to the lack of reported case of transmission from the donor, the risks entailed for the recipient are unknown.
It was also confirmed that the suitability evaluation of both the donor and the organs, is always performed, in all Italian Centers, with the same criteria normally in use, i.e. collectively by all health professionals involved in the retrieval and transplant activities in collaboration with their respective Regional Transplant Center, with the Italian National Transplant Center Operational Unit and with the support of infectious diseases experts dedicated to this activity (National Second Opinion Expert for Infectious Diseases).

In order to verify the safety of the transplant, upon receiving it, I will undergo specific check-ups aimed at assessing my immune condition with regards to the SARS-CoV-2 infection, as well as the presence of an active infection. The same check-ups will be performed in the post-transplant period, to verify that the infection has not been transmitted.

Noted all of the above, I, the undersigned ……
Born in …… on ……. candidate for a kidney transplant, at the……. Transplant Center hereby declare that I have received the information and I have understood what Dr./Prof. ……. has explained to me.

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Therefore I hereby

□ **consent** □ **do not consent**

to receive the transplant of an organ retrieved from a donor with active SARS-CoV-2 infection and to undergo specific check-ups as provided by the Italian National Transplant Center.

Date ----------

Transplant Candidate's Signature Doctor's signature

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MONITORING OF THE RECIPIENT OF ORGANS FROM SARS-CoV-2 POSITIVE DONOR

	PRE-TRANSPLANT	POST-TRANSPLANT			
		DAY 7	DAY 14	DAY 21	DAY 28
Nasopharyngeal swab for SARS-CoV-2	X	X	X	X	X
BAL if intubated patient		X	X	X	X
Serological test for SARS-CoV-2[*]	X		X		X
Search for SARS-CoV-2 in other biological specimen (biopsy, etc.)[#]		X	X	X	X
Search for SARS-CoV-2-RNA in biopsy of retrieved organ from donor and on perfusion fluid[&]	X				

[*] It is necessary to acquire the result before transplant. Specify the type of serological test used and ideally always search for specific neutralizing antibodies

[#] if indicated and if validated diagnostic tests are available

[&] The result will be acquired *a posteriori* and does not affect the transplant. It is essential to report to CNT any adverse event that may occur in the recipients of these organs and to monitor the recipient even after the first month after transplantation in order to assess any possible negative impact in the medium and long term.

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