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Subject: Measures to prevent the transmission of the Monkeypox virus (MPXV) infection through organ, tissue, hematopoietic stem cells and reproductive cells transplantation.

In relation to recent national and international reports of human cases of Monkeypox (MPX) and to reports by the European Centre for Disease Prevention and Control (ECDC)ⁱ, and to the internal regulation of the General Directorate for Health Prevention of the Ministry of Health of 25/05/2022 (Prot. DGPREV 0026837)ⁱⁱ, it is noted that, to date:

- There are no documented cases of transmission of the MPXV through organs, tissues, hematopoietic stem cells and reproductive cells;
- There are reports on cases of transmission of the virus from mother to child during pregnancy and some studies show the presence of the virus in the blood, tissues and organs of infected animals;
- viraemia has been demonstrated, although its duration is unclear and there are no data in asymptomatic patients or during the incubation period.

However, although information is limited, the transmission of MPXV through organ, tissue, hematopoietic stem cells and reproductive cells transplantation cannot be ruled out, even if the overall risk for the recipients in the EU/EEA is low. Therefore, in light of the above and based on the definition of caseⁱⁱⁱ, it is deemed necessary to introduce the following preventive measures:

1. Strengthen investigations on the deceased organ and tissue donors' medical history regarding their close contacts^{iv} with human cases (confirmed^v or suspect^{vi} or probable^{vii}) or contact with infected animals or in case of recent travel to areas affected by confirmed indigenous MPX^{viii} cases (i.e. Canary Islands) or to countries where MPXV is endemic. In case of positive medical history, it is required to contact the Operational National Transplant Coordination (CNTo) or the second opinion expert on infectious diseases in order to evaluate further measures. Should the donor present symptoms and signs consistent with MPXV infection, it is necessary to perform, before organ or tissue retrieval, the following diagnostic investigations aimed to rule out the presence of the virus:
 - 1.1 Real Time PCR on a swab from a vesicle after its opening;
 - 1.2 Real Time PCR on an oropharyngeal swab or saliva swab (test tube with virus specific transport medium);

In addition, it is recommended to send a blood sample (test tube with separator gel) for further investigations. The samples will have to be sent to reference laboratories identified by the Regions. If the samples are sent on the same day or the day after, they can be preserved at 4°C and they can be sent at room temperature. If the transport is postponed, biological samples such as oropharyngeal swab, saliva swab, vesicle swab shall be frozen at -20°C; the serum (after centrifugation of the stock test tube and possible transfer to a sterile tube) may be preserved at 4°C. At this point, the

shipping shall be refrigerated with ice. (All transported samples must have appropriate triple packaging, labeling and documentation and must be shipped in accordance with applicable national and/or international regulations. The shipping requires a certified carrier for dangerous goods. For information on shipping requirements for infectious substances, read WHO's Guidance on regulations for the transport of infectious substances 2021-2022, available at the link: <https://www.who.int/publications/i/item/9789240019720>). **In case of documented diagnosis of MPX, the donor must be considered at unacceptable risk;**

2. As far as the donation of organs, tissues, hematopoietic stem cells and reproductive cells from living donors is concerned, in addition to strengthening the anamnestic and diagnostic investigations at point 1., it is recommended as follows:
 - 2.1 apply the temporary 21 day suspension criterion, from the last day of exposure, for donors with a medical history of close contact with confirmed or suspect or probable MPX cases, or in case of recent travel to areas affected by confirmed indigenous cases of MPX (i.e. Canary Islands) or to countries where MPXV is endemic;
 - 2.2 since the prodromal stage of MPX varies in duration (1–4 days) and the symptoms may be non-specific and mild or absent, perform a careful examination for any signs of infection even after the deferral period's expiry date (at least 21 days from the last day of exposure). The examination should not overlook mild and non-specific signs such as headache or fatigue or anogenital skin lesions;
 - 2.3 in case of MPXV infection, the donation of organs, tissues, hematopoietic stem cells and reproductive cells can be carried out 21 days after the diagnosis and in the absence of symptoms.

The Regional Transplant Centres' coordinators are encouraged to promptly implement the actions foreseen, keeping all structures well informed, including the Transplant Centres and the Tissues Establishments operating in the field.

The indications formulated in this note are subject to update in relation to the acquisition of further information about the pathogen agent in question and to the evolution of the national and international epidemiological situation.

ⁱEuropean Centre for Disease Prevention and Control – Monkeypox multi-country outbreak, 23 May 2022 and 31 May 2022 update

ⁱⁱInternal regulation of the General Directorate for Health Prevention of the Ministry of Health of 25/5/2022 (Prot. DGPREV 0026837)

ⁱⁱⁱWHO of 21/05/2022 <https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON385>

^{iv}**Close contact:**

- Sexual partner
- Person living in the same house or similar environment (i.e. camping, hotel room, etc)
- Person who shared clothes, linens, utensils etc during the case's rash phase
- Person who shared for a long period of time the same work environment (indoors)
- A symptomatic MPX's case caregiver
- Healthcare professional who had contact with MPX cases (lesions or prolonged face-to-face contact) without adequate PPE
- Healthcare professional or other person who suffered a cut or was exposed to body fluids of the MPX case or was exposed to a procedure which generates aerosols without PPE
- Laboratory staff exposed to specimen containing the virus on their workplace by accident (squirts, cuts or aerosols exposure etc.)
- Sitting passenger (plane/bus/train/other means of transport) within two seats of distance from the MPX case during a ≥ 8 hour long trip



^vConfirmed contact:

A case that meets the suspect or probable case definition and is confirmed in the laboratory for MPXV through the detection of single viral DNA sequences by real time polymerase chain reaction testing (PCR) or sequencing.

^{vi}Suspect case:

A person of any age who has an acute rash of unknown cause in a country where MPX is non-endemic and one or more of the following signs or symptoms, from March 15, 2022:

- headache, acute onset of fever ($> 38.5^{\circ} \text{C}$), lymphadenopathy, myalgia, back pain, asthenia and for which the following causes of common acute rashes do not explain the clinical picture: varicella zoster, herpes zoster, measles, herpes simplex, bacterial skin infection, diffuse gonococcal infection, primary or secondary syphilis, gangrene, venereal lymphogranuloma, inguinal granuloma, molluscum contagiosum, allergic reaction (for example, to plants); and any other locally relevant common cause of papular or vesicular rashes.

Please, note: in the presence of a clinical picture consistent with MPX it is not necessary to wait for negative laboratory results for the diseases listed as common causes of rashes, in order to classify the case as suspect.

Excluded case:

A suspect or probable case with MPX negative PCR and/or sequencing laboratory tests.

^{vii}Probable case:

A person who meets the suspect case definition and one or more of the following elements:

- has an epidemiological link (direct exposure, including healthcare professionals without eye and respiratory protection); direct physical contact with skin or lesions, including sexual contact; or contact with contaminated material such as linens or utensils with a probable or confirmed MPX case within 21 days of illness onset
- has declared to have traveled to countries where MPX is endemic within 21 days of illness onset
- has had multiple or anonymous sexual partners within 21 days of illness onset
- has a positive orthopoxvirus serological test, in the absence of smallpox vaccination or other known orthopoxvirus exposure
- has been hospitalized because of the disease

^{viii}The countries where Monkeypox is endemic are: Benin, Cameroon, Central African Republic, Democratic Republic of Congo, Gabon, Ghana (identified in animals only), Ivory Coast, Liberia, Nigeria, Republic of Congo, Sierra Leone and South Sudan.