Selection criteria for donors are based on an analysis of the risks related to the application of the specific cells/tissues

**Indicators:**

- review of the medical and behavioural history,
- physical examination,
- biological testing,
- post-mortem examination (for deceased donors),
- any other appropriate investigation.
Selection criteria for donors

- Procurement of human tissues and cells shall be carried out by persons who have successfully completed a training programme specified by a clinical team specialising in the tissues and cells to be procured or a tissue establishment authorised for procurement.

- The tissue establishment or procurement organisation shall have written agreements with the staff or clinical teams responsible for donor selection, unless they are employed by the same organisation or establishment.
Responsible person?
Deceased Donors

General criteria for exclusion

- Cause of death unknown, unless autopsy provides information on the cause of death after procurement and none of the general criteria for exclusion set out in the present section applies.

- History of a disease of unknown aetiology.

- Presence, or previous history, of malignant disease, except for primary basal cell carcinoma, carcinoma in situ of the uterine cervix, and some primary tumours of the central nervous system that have to be evaluated according to scientific evidence. Donors with malignant diseases can be evaluated and considered for cornea donation, except for those with retinoblastoma, haematological neoplasm, and malignant tumours of the anterior segment of the eye.
Deceased Donors

General criteria for exclusion

- Risk of transmission of diseases caused by prions. This risk applies, for example, to:
  - people diagnosed with Creutzfeldt–Jakob disease, or variant Creutzfeldt-Jacob disease, or having a family history of non-iatrogenic Creutzfeldt-Jakob disease;
  - people with a history of rapid progressive dementia or degenerative neurological disease, including those of unknown origin;
  - recipients of hormones derived from the human pituitary gland (such as growth hormones) and recipients of grafts of cornea, sclera and dura mater, and persons that have undergone undocumented neurosurgery (where dura mater may have been used).
Deceased Donors

General criteria for exclusion

- Systemic infection which is not controlled at the time of donation, including bacterial diseases, systemic viral, fungal or parasitic infections, or significant local infection in the tissues and cells to be donated. Donors with bacterial septicaemia may be evaluated and considered for eye donation but only where the corneas are to be stored by organ culture to allow detection of any bacterial contamination of the tissue.

- Prolonged corticosteroid therapy.

- Donor with more than 20% total surface area burn.

- Person with haemophilia or related clotting disorders who have received human-derived clotting factor concentrates.
Deceased Donors

General criteria for exclusion

- History, clinical evidence, or laboratory evidence of HIV, acute or chronic hepatitis B (except in the case of persons with a proven immune status), hepatitis C and HTLV I/II, transmission risk or evidence of risk factors for these infections:
  - persons who have had sex in the preceding 12 months with any person known or suspected to have HIV infection,
  - persons who have been exposed in the preceding 12 months to known or suspected HIV infected blood through percutaneous inoculation or through contact with an open wound, non-intact skin, or mucous membrane,
  - past history of blood transfusion,
  - men who have had sex with another man in the preceding 5 years,
  - persons who report non-medical intravenous, intra-muscular, or subcutaneous injection of drugs in the preceding 5 years,
  - men and women who have engaged in sex exchange for money or drugs in the preceding 5 years,
  - persons that have undergone tattooing, acupuncture, ear or body piercing preceding 12 months,
  - intravenous drug use.
Deceased Donors

General criteria for exclusion

- History of chronic, systemic autoimmune disease that could have a detrimental effect on the quality of the tissue to be retrieved.

- Indications that test results of donor blood samples will be invalid due to:
  - the occurrence of haemodilution, where a pre-transfusion sample is not available;
  - treatment with immunosuppressive agents.

- Evidence of any other risk factors for transmissible diseases on the basis of a risk assessment, taking into consideration donor travel and exposure history and local infectious disease prevalence.
Deceased Donors

General criteria for exclusion

- Ingestion of, or exposure to, a substance (such as cyanide, lead, mercury, gold) that may be transmitted to recipients in a dose that could endanger their health.
- Recent history of vaccination with a live attenuated virus where a risk of transmission is considered to exist.
- Transplantation with xenografts.
Deceased Donors
General criteria for exclusion
Additional exclusion criteria for deceased child donors

- Any children born from mothers with HIV infection or that meet any of the exclusion criteria described above must be excluded as donors until the risk of transmission of infection can be definitely ruled out.
  - Children aged less than 18 months born from mothers with HIV, hepatitis B, hepatitis C or HTLV infection, or at risk of such infection, and who have been breastfed by their mothers during the previous 12 months, cannot be considered as donors regardless of the results of the analytical tests.
  - Children of mothers with HIV, hepatitis B, hepatitis C or HTLV infection, or at risk of such infection, and who have not been breastfed by their mothers during the previous 12 months and for whom analytical tests, physical examinations, and reviews of medical records do not provide evidence of HIV, hepatitis B, hepatitis C or HTLV infection, can be accepted as donors.
<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>*26. Male Donors: Has the deceased had sex with another male in the Past 5 years?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*27. In the past 5 years has the deceased used a needle to inject drugs into their veins, muscle, or under their skin for nonmedical use?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*28. Has the deceased received human-derived clotting factor concentrates for hemophilia or related clotting disorders?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*29. Has the deceased engaged in sex in exchange for money or drugs in the past 5 years?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*30. Was the deceased exposed to known or suspected viral Hepatitis or HIV-infected blood through accidental needlestick or through contact with an open wound, non-intact skin, or mucous membrane in the past 12 months?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*31. Was the deceased an inmate of a correctional system or jail, or released from a correctional system or jail in the past 12 months?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>*32. Has the deceased had sex in the past 12 months with any person known or suspected to have viral Hepatitis or HIV infection, or any person described in above questions #26-31?</td>
<td>□ Yes □ No □ Other</td>
</tr>
</tbody>
</table>

**PEDIATRIC DONORS**

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>*33. A. Was the child born to a mother with, or at risk for HIV infection, or who responded “yes” to question 26-32?</td>
<td>□ Yes □ No □ Other</td>
</tr>
<tr>
<td>B. If “yes”, was the child breast fed in the past 12 months?</td>
<td>□ Yes □ No □ Other</td>
</tr>
</tbody>
</table>
Autologus Living Donors

General criteria for exclusion

- If the removed tissues and cells are to be stored or cultured, the same minimum set of biological testing requirements must apply as for an allogeneic living donor. Positive test results will not necessarily prevent the tissues or cells or any product derived from them being stored, processed and reimplanted, if appropriate isolated storage facilities are available to ensure no risk of cross-contamination with other grafts and/or no risk of contamination with adventitious agents and/or mix-ups.
Alogeneic Living Donors

General criteria for exclusion

- The assessment must include relevant factors that may assist in identifying and screening out persons whose donation could present a health risk to others, such as the possibility of transmitting diseases or health risks to themselves. For any donation, the collection process must not interfere with or compromise the health or care of the donor. In the case of cord blood or amniotic membrane donation, this applies to both mother and baby.
Alogeneic Living Donors

General criteria for exclusion

- The same exclusion criteria must be applied as for deceased donors. Depending on the tissue or cell to be donated, other specific exclusion criteria may need to be added, such as:

  - pregnancy (except for donors of umbilical cord blood cells and amniotic membrane and sibling donors of haematopoietic progenitors);

  - breastfeeding;

  - in the case of haematopoietic progenitor cells, the potential for transmission of inherited conditions.
Tissue Specific criteria for exclusion

Ocular Tissue

Contraindications for tissues used for penetrating keratoplasty, lamellar or patch grafts, epikeratoplasty, and for scleral tissues include, but are not limited to:
- congenital rubella;
- Reye's syndrome;
- active viral encephalitis or encephalitis of unknown origin or progressive encephalopathy;
- active bacterial or fungal endocarditis;
- active viral hepatitis;
Tissue Specific criteria for exclusion

Ocular Tissue

- intrinsic eye disease such as:
  - retinoblastoma;
  - malignant tumours of the anterior ocular segment, of primary or metastatic origin (e.g., adenocarcinoma);
- active ocular or intraocular inflammation;
- congenital or acquired disorders of the eye that would preclude successful outcome for the intended use; or pterygia or other superficial disorders of the conjunctiva or corneal surface involving the central optical area of the corneal button;
- active disseminated lymphomas;
- prior intraocular or anterior segment surgery such as:
  - refractive corneal procedures;
  - laser photoablation surgery.
Tissue Specific criteria for exclusion

Bone:
- age: < 50 F, < 60 M,
- no osteoporosis, no arthrosis, no other bone diseases
  (Paget disease, osteopetrosis).

Rib cartilage:
- age: 14- 22,
- no osteoporosis, no arthrosis, no other bone diseases
  (Paget disease, osteopetrosis).

Skin:
- age: < 70
- no skin diseases

Amnion:
- no intrautheral infection
Use the appropriate gender drawing of the External Physical Examination Form for documentation of physical assessment performed at recovery. If the posterior view of the body shows no signs of any of the following items or others, indicate by statement that the "Posterior view of body is unremarkable." to document viewing of this side of the body.

- At the time of recovery inspect both anterior and posterior views of the body for abrasions. Circle Y = Yes, N = No, for the presence of abrasions and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for burns. Circle Y = Yes, N = No, for the presence of abrasions and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for fractures. Circle Y = Yes, N = No, for the presence of fractures and indicate location on the drawing. If fractures are discovered during the recovery, indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for gun shot wounds. Circle Y = Yes, N = No, for the presence of gun shot wounds and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for lacerations. Circle Y = Yes, N = No, for the presence of lacerations and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for penetrating wounds. Circle Y = Yes, N = No, for the presence of penetrating wounds and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for tattoos. Circle Y = Yes, N = No, for the presence of tattoos and indicate location on the drawing. Donors exhibiting tattoos that are less than 12 months old are not acceptable for recovery. This information is gleaned both from the medical/social interview and the appearance of the tattoo. Donors exhibiting tattoos that appear irritated and new are not acceptable for recovery. While noting location tattoos inspect the tattoo for signs of needle marks as an indication for drug abuse.

- At the time of recovery inspect both anterior and posterior views of the body for scars. Circle Y = Yes, N = No, for the presence of scars and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for sutures. Circle Y = Yes, N = No, for the presence of sutures and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for nasal gastric tube. Circle Y = Yes, N = No, for the presence of nasal gastric tube and indicate location on the drawing.
- At the time of recovery inspect both anterior and posterior views of the body for endotracheal tube. Circle Y = Yes, N = No, for the presence of endotracheal tube and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for chest tube. Circle Y = Yes, N = No, for the presence of chest tube and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for central venous pressure line. Circle Y = Yes, N = No, for the presence of central venous pressure line and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for intravenous line. Circle Y = Yes, N = No, for the presence of intravenous line and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for arterial lines. Circle Y = Yes, N = No, for the presence of arterial lines and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for needle punctures. Circle Y = Yes, N = No, for the presence of needle punctures and indicate location on the drawing.

  If there are needle punctures they have to be explained as "pharmaceutical" or as "drug abuse". If no explanation is given the donor is automatically excluded.

- At the time of recovery inspect both anterior and posterior views of the body for body piercing. Circle Y = Yes, N = No, for the presence of body piercing and indicate location on the drawing.

  Donors exhibiting body piercing less than 12 months is not acceptable for recovery. Donors exhibiting recent body piercing with signs of irritation indicate recent or infected site of piercing are not acceptable for recovery. Donors with body piercing greater than 12 months of age are acceptable for recovery.

- At the time of recovery inspect both anterior and posterior views of the body for Foley catheter. Circle Y = Yes, N = No, for the presence of Foley catheter and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for lividity. Circle Y = Yes, N = No, for the presence of lividity and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for bruising. Circle Y = Yes, N = No, for the presence of bruising and indicate location on the drawing.

- At the time of recovery inspect both anterior and posterior views of the body for blood draw sites. Circle Y = Yes, N = No, for the presence of blood draw sites and indicate location on the drawing.

  BDS is not identical to Needle Punctures. BDS is only used to indicate the place of drawing blood for serum test of the donor.
EXTERNAL PHYSICAL EXAMINATION

Circle Y for Yes or N for No, and note the location of any YES answer on the anatomical drawing. This form must be completed before the recovery is initiated.

- Abrasions Y N
- Burns Y N
- Contusions Y N
- Fractures Y N
- Gun shot wounds Y N
- Lacerations Y N
- Penetrating wound Y N
- Tatoos ≥ 1 year Y N
- Scars Y N
- Sutures Y N
- Nasal gastric tube Y N
- Endotracheal tube Y N
- Chest tube Y N
- Central venous pressure line Y N
- Intravenous line Y N
- Arterial line Y N
- Needle punctures Y N
- Piercing ≥ 1 year Y N
- < 1 year Y N
- Foley catheter Y N
- Lividity Y N
- Bruising Y N
- Blood draw sites Y N

Date / Time of blood draw. Indicate as BDS on anatomical drawing.
Donor Initials: ______________________

Age: _______ (Years)

Sex: _______ (f = female / m = male) Weight of donor: _______

Note anomalies and physical condition: ________________________________

Note all blood draw sites on the anatomical drawing. Comments about blood draw:

I have examined the body for the following signs and symptoms of HIV and Hepatitis and have noted any findings below: 

- Blue or purple spots on the skin or mucous membranes typical of Kaposi's Sarcoma, yellowing of the eyes or skin, and enlarged liver.
- Genital area for signs of sexually transmitted diseases, needle tracks on arms, legs, trunk, between toes and fingers, under nails, in the mouth and gums, and in tattoos (if any were present).

Date of examination

Name of person performing assessment/title

Signature
EXTERNAL PHYSICAL EXAMINATION

Donor No:............

Circle Y for Yes or N for No, and note the location of any YES answer on the anatomical drawing. This form must be completed before the recovery is initiated.

A  Abrasions          Y  N
B  Burns              Y  N
C  Confusions         Y  N
Fz Fractures          Y  N
Gs Gun shot wounds    Y  N
L  Lacerations        Y  N
PW Penetrating wound  Y  N
T  Tattoos
   ≥1 year           Y  N
   < 1 year          Y  N
Sc Scars             Y  N
S  Sutures           Y  N
NG Nasal gastric tube Y  N
ET Endotracheal tube Y  N
CT Chest tube        Y  N
CVP Central venous pressure line Y N
IV Intravenous line  Y  N
AL Arterial line     Y  N
NP Needle punctures   Y  N
BP Piercing
   ≥1 year           Y  N
   < 1 year          Y  N
F  Foley catheter    Y  N
LJ Lividity          Y  N
Br Bruising          Y  N
BDS Blood draw sites Y  N

Date_/_/_  Time__ of blood draw. Indicate as BDS on anatomical drawing

Donor Initials:__________________

Age:______________ (Years)
Sex:_______________ (f = female / m = male) Weight of donor:__________

Note anomalies and physical condition:______________________________

Note all blood draw sites on the anatomical drawing. Comments about blood draw

I have examined the body for the following signs and symptoms of HIV and Hepatitis and have noted any findings below. Blue or purple spots on the skin or mucous membranes typical of Kaposi's Sarcoma, yellowing of the eyes or skin, and enlarged liver. Genital area for signs of sexually transmitted diseases. Needle tracks on arms, legs, trunk, between toes and fingers, under nails, in the mouth and gums, and in tattoos (if any were present). Signs and Symptoms:__________________________

Date__________________________ Name of person performing assessment/title ____________ Signature____________________


Rabies
Rabies is a preventable viral disease of mammals most often transmitted through the bite of a rabid animal. The vast majority of rabies cases occur in wild animals like raccoons, skunks, bats, and foxes. Domestic animals account for less than 10% of the reported rabies cases, with cats, cattle, and dogs most often reported rabid.

Rabies virus infects the central nervous system, causing encephalopathy and ultimately death. Early symptoms of rabies in humans are nonspecific, consisting of fever, headache, and general malaise. As the disease progresses, neurological symptoms appear and may include insomnia, anxiety, confusion, slight or partial paralysis, excitation, hallucinations, agitation, hypersalivation, difficulty swallowing, and hydrophobia (fear of water).

Death usually occurs within days of the onset of symptoms.
Rabies virus belongs to the order *Mononegavirales*, viruses with a nonsegmented, negative-stranded RNA genomes. Within this group, viruses with a distinct "bullet" shape are classified in the *Rhabdoviridae* family, which includes at least three genera of animal viruses, *Lyssavirus*, *Ephemerovirus*, and *Vesiculovirus*. The genus *Lyssavirus* includes rabies virus, Lagos bat, Mokola virus, Duvenhage virus, European bat virus 1 & 2 and Australian bat virus.
Rabies

Rhabdoviruses are approximately 180 nm long and 75 nm wide. The rabies genome encodes five proteins: nucleoprotein (N), phosphoprotein (P), matrix protein (M), glycoprotein (G) and polymerase (L).

All rhabdoviruses are have two major structural components: a helical ribonucleoprotein core (RNP) and a surrounding envelope. In the RNP, genomic RNA is tightly encased by the nucleoprotein. Two other viral proteins, the phosphoprotein and the large protein (L-protein or polymerase) are associated with the RNP. The glycoprotein forms approximately 400 trimeric spikes which are tightly arranged on the surface of the virus. The M protein is associated both with the envelope and the RNP and may be the central protein of rhabdovirus assembly.
Transmission of rabies virus usually begins when infected saliva of a host is passed to an uninfected animal. Various routes of transmission have been documented and include contamination of mucous membranes (i.e., eyes, nose, mouth), aerosol transmission, and corneal transplantations. The most common mode of rabies virus transmission is through the bite and virus-containing saliva of an infected host.
Rabies

The host immune defenses may confer cell-mediated immunity against viral infection because rabies virus is a good antigen. The uptake of virus into peripheral nerves is important for progression of the infection.

Rabies virus is transported to the central nervous system (CNS) via retrograde axoplasmic flow. Typically this occurs via sensory and motor nerves at the initial site of infection. The incubation period is the time from exposure to onset of clinical signs of disease. The incubation period may vary from a few days to several years, but is typically 1 to 3 months.

Dissemination of virus within the CNS is rapid, and includes early involvement of limbic system neurons. Active cerebral infection is followed by passive centrifugal spread of virus to peripheral nerves.

Centrifugal spread of virus may lead to the invasion of highly innervated sites of various tissues, including the salivary glands. During this period of cerebral infection, the classic behavioral changes associated with rabies develop.
Rabies

The first symptoms of rabies may be nonspecific flu-like signs — malaise, fever, or headache, which may last for days. There may be discomfort or paresthesia at the site of exposure (bite), progressing within days to symptoms of cerebral dysfunction, anxiety, confusion, agitation, progressing to delirium, abnormal behavior, hallucinations, and insomnia. The acute period of disease typically ends after 2 to 10 days. **Once clinical signs of rabies appear, the disease is nearly always fatal, and treatment is typically supportive.** Disease prevention is entirely prophylactic and includes both passive antibody (immune globulin) and vaccine. Non-lethal exceptions are extremely rare. To date only six documented cases of human survival from clinical rabies have been reported and each included a history of either pre- or postexposure prophylaxis.
Rabies

Several tests are necessary to diagnose rabies ante-mortem (before death) in humans; no single test is sufficient. Tests are performed on samples of saliva, serum, spinal fluid, and skin biopsies of hair follicles at the nape of the neck.

- Saliva can be tested by virus isolation or reverse transcription followed by polymerase chain reaction (RT-PCR).
- Serum and spinal fluid are tested for antibodies to rabies virus.
- Skin biopsy specimens are examined for rabies antigen in the cutaneous nerves at the base of hair follicles.
- Histopathologic evidence of rabies encephalomyelitis (inflammation) in brain tissue and meninges.
Bird flu

acchhoo!

very funny Dave!
Bird flu

- Avian influenza - commonly called "bird flu" - is an infection caused by influenza viruses that occur naturally in birds.
- Wild birds can carry the viruses, but usually do not get sick from them. However, some domesticated birds, including chickens, ducks, and turkeys, can become infected, often fatally.
- One strain of avian influenza, the H5N1 virus, is endemic in much of Asia and has recently spread into Europe. Avian H5N1 infections have recently killed poultry and other birds in a number of countries.
- Strains of avian H5N1 influenza may infect various types of animals, including wild birds, pigs, and tigers.
- Symptoms in birds and other animals vary, but virulent strains can cause death within a few days.
**Influenza A H5**
Nine potential subtypes of H5 are known. H5 infections, such as HPAI H5N1 viruses currently circulating in Asia and Europe, have been documented among humans and sometimes cause severe illness or death.

**Influenza A H7**
Nine potential subtypes of H7 are known. H7 infection in humans is rare but can occur among persons who have direct contact with infected birds. Symptoms may include conjunctivitis and/or upper respiratory symptoms. H7 viruses have been associated with both LPAI (e.g., H7N2, H7N7) and HPAI (e.g., H7N3, H7N7), and have caused mild to severe and fatal illness in humans.

**Influenza A H9**
Nine potential subtypes of H9 are known; influenza A H9 has rarely been reported to infect humans. However, this subtype has been documented only in a low pathogenic form.
**Influenza Type B**

Influenza B viruses are usually found only in humans. Unlike influenza A viruses, these viruses are not classified according to subtype. Influenza B viruses can cause morbidity and mortality among humans, but in general are associated with less severe epidemics than influenza A viruses. Although influenza type B viruses can cause human epidemics, they have not caused pandemics.

**Influenza Type C**

Influenza type C viruses cause mild illness in humans and do not cause epidemics or pandemics. These viruses are not classified according to subtype.
Bird flu

- Human H5N1 influenza infection was first recognized in 1997 when this virus infected 18 people in Hong Kong, causing 6 deaths.
- The World Health Organization is tracking the number of human cases of the H5N1 virus.
- Currently, close contact with infected poultry has been the primary source for human infection. Though rare, there have been isolated reports of human-to-human transmission of the virus.
- Genetic studies confirm that the influenza A virus H5N1 mutates rapidly. Should it adapt to allow easy human-to-human transmission, a pandemic could ensue — it has not done so to date.
- At this time, it is uncertain whether the currently circulating H5N1 virus will lead to a global disease outbreak in humans — a pandemic.
- The reported symptoms of avian influenza in humans have ranged from typical influenza-like symptoms (e.g. fever, cough, sore throat, and muscle aches) to eye infections (conjunctivitis), acute respiratory distress, viral pneumonia and other severe, life-threatening complications.
Bird flu

Avian influenza A viruses may be transmitted from animals to humans in two main ways:

- Directly from birds or from avian virus-contaminated environments to people.
- Through an intermediate host, such as a pig.
Bird flu
SARS

- Severe acute respiratory syndrome (SARS) is a viral respiratory illness caused by a coronavirus, called SARS-associated coronavirus (SARS-CoV). SARS was first reported in Asia in February 2003. Over the next few months, the illness spread to more than two dozen countries in North America, South America, Europe, and Asia.

- According to the World Health Organization (WHO), a total of 8,098 people worldwide became sick with SARS during the 2003 outbreak. Of these, 774 died. In the United States, only eight people had laboratory evidence of SARS-CoV infection. All of these people had traveled to other parts of the world with SARS. SARS did not spread more widely in the community in the United States.
The name coronavirus derives from the halo/corona appearance of viral particles when viewed under a microscope, which is a result of the protruding spike proteins that coat the surface of the virus. The enveloped viral particle is 60-130 nm in diameter and contains a single-stranded positive RNA strand. The SARS-CoV genome is 29,272 nucleotides in length with 41% being G/C residues. Large genome size is characteristic of coronaviruses, which actually exhibit the largest genomes of all RNA viruses. There are 11 open reading frames (ORFs) in SARS-CoV, and genome organization of the major structural proteins: [5'- replicase (rep), spike (S), envelope (E), membrane (M), nucleocapsid (N)-3']
SARS

- Virus loses infectivity after exposure to different commonly used disinfectants and fixatives.
- Only minimal reduction in virus concentration after 21 days at 4°C and -80°C.
- Reduction in virus concentration by one log only at stable room temperature for 2 days. This would indicate that the virus is more stable than the known human coronaviruses under these conditions.
- Heat at 56°C kills the SARS coronavirus at around 10000 units per 15 min (quick reduction).
SARS

Diagnostics

RT-PCR

Although studies to date have not definitively determined the best specimens for SARS RT-PCR diagnostics, it is reasonable to collect:

- During the first week of illness: Nasopharyngeal (NP) swab plus oropharyngeal (OP) swab and a serum or plasma specimen
- After the first week of illness: NP swab plus OP swab and a stool specimen

Serologic Diagnostics

Serum specimens for SARS-CoV antibody testing should be collected when the diagnosis is first suspected and at later times if indicated. An antibody response is occasionally detected during the first week of illness, likely to be detected by the end of the second week of illness, and sometimes may not be detected until > 28 days after onset of symptoms.
SARS

Key Clinical Features of SARS-CoV Disease

- Incubation period of 2-10 days
- Begins with a high fever (>100.4°F, >38.0°C)
- After 3-7 days, onset of lower respiratory symptoms occurs including a dry, nonproductive cough or dyspnea which may be accompanied by or progress to hypoxemia
- Most patients develop pneumonia by day 7-10 of illness
- Diarrhea is typically absent but may occur in some cases
- Severity of illness is highly variable ranging from mild illness to death
- Lymphopenia in most cases
Case Detection
Severe respiratory illness in the context of a documented exposure risk is the key to diagnosing SARS-CoV disease. Providers should therefore consider SARS-CoV disease in patients requiring hospitalization for:

- Radiographically confirmed pneumonia or acute respiratory distress syndrome of unknown etiology,
- One of the following risk factors in the 10 days before illness onset:
  - *Travel* to mainland China, Hong Kong, or Taiwan, or close contact with an ill person with a history of recent travel to one of these areas,
  - *Employment* in an occupation associated with a risk for SARS-CoV exposure (e.g., healthcare worker with direct patient contact; worker in a laboratory that contains live SARS-CoV),
  - Part of a *cluster* of cases of atypical pneumonia without an alternative diagnosis
Creutzfeldt-Jakob disease
Creutzfeldt-Jakob disease symptoms

- vague feelings of fatigue, disordered sleep, decreased appetite
- neurologic symptoms (memory loss, confusion, uncharacteristic behavior)
- focal signs (ataxia, aphasia, visual loss, hemiparesis, amyotrophy)
- muscle wasting in the spinal cord (may simulate motor neuron disease) aphasia, hemianopia
Prions

PrP$^\text{Sc}$ are formed by posttranslational modifications of PrP$^\text{c}$ presented in the cells.

PrP$^\text{c}$ is composed of four α-helixes, while PrP$^\text{Sc}$ of four β-sheets.

It seems, that exogenous PrP$^\text{Sc}$ can stimulate modifications of PrP$^\text{c}$ to PrP$^\text{Sc}$.

Newly synthetised prion PrP$^\text{c}$ is transported to the cell surface and forms „scrapie associated filaments”, which together with PrP$^\text{Sc}$ can form amyloid plaques.
Prions

PrP<sup>Sc</sup>  PrP<sup>c</sup>
Prions
PrPs\textsuperscript{Sc} are resistant to:

a/ standars steam sterilisation

b/ chemical sterilisation (alcohol, formaldehyde, fenol),

c/ radiation-sterilisation - even doses of 50 - 200 kGy (5 - 20 Mrads) do not inactivate infectious prion proteins.

Inactivation of PrPs\textsuperscript{Sc}

a/ 1-2 N NaOH in 20\degree C for 1 hour,

b/ 2,5 % NaOCl in 20\degree C for 1 hour,

c/ autoclaving in temp. 138\degree C for 1 hour.
West Nile virus
West Nile virus (WNV)

WNV was first isolated and identified in 1937 in a febrile person in the West Nile district of Uganda. Prior to 1999, the virus was found only in the Eastern Hemisphere, with wide distribution in Africa, Asia, the Middle East, and Europe. There were infrequent reports of human outbreaks, mainly associated with mild febrile illnesses, in Israel and Africa. These were mostly in groups of soldiers, children, and healthy adults. One notable outbreak in Israeli nursing homes in 1957 was associated with severe neurologic disease and death.

Since the mid-1990s, the frequency and apparent clinical severity of WNV outbreaks have increased. Outbreaks in Romania (1996), Russia (1999), and Israel (2000) involved hundreds of persons with severe neurologic disease. It is unclear if this apparent change in disease severity and frequency is due to differences in the circulating virus's virulence or to changes in the age structure, background immunity, or prevalence of other predisposing chronic conditions in the affected populations.
West Nile virus (WNV)

Infectious Agent
West Nile virus (WNV) is a single-stranded RNA virus of the family Flaviviridae, genus Flavivirus. Flaviviruses share a common size (40-60 nm), symmetry (enveloped, icosahedral nucleocapsid), nucleic acid (positive-sense, single stranded RNA approximately 10,000-11,000 bases), and appearance in the electron microscope.

WNV is a member of the Japanese encephalitis virus antigenic complex, which includes several medically important viruses associated with human encephalitis: Japanese encephalitis, St. Louis encephalitis, Murray Valley encephalitis, and Kunjin, an Australian subtype of WNV.

For unknown reasons, deaths among birds from WNV infection have occurred only in the United States, Israel, Canada, and Mexico. Since 1999, very few genetic changes have occurred in the WNV strains circulating in the United States.
West Nile virus (WNV)

The main route of human infection is through the bite of an infected mosquito.

Mosquitoes become infected when they feed on infected birds, which may circulate the virus in their blood for a few days. Infectious mosquitoes carry virus particles in their salivary glands and infect susceptible bird species during blood-meal feeding. Bird reservoirs will sustain an infectious viremia for 1 to 4 days after exposure after which the hosts that survive develop life-long immunity.

People, horses, and most other mammals are not known to commonly develop infectious-level viremias and thus are probably "dead-end" or incidental hosts.

There is no documented evidence of animal-to-person transmission of WNV apart from mosquitoes.
West Nile virus (WNV)

Clinical Features of Severe Disease

- Fever
- Gastrointestinal symptoms
- Ataxia and extrapyramidal signs
- Optic neuritis
- Seizures
- Weakness
- Change in mental status
- Myelitis
- Polyradiculitis
- A minority of patients with severe disease develop a maculopapular or morbilliform rash involving the neck, trunk, arms, or legs.
- Flaccid paralysis is sometimes seen.
- Although not observed in recent outbreaks, myocarditis, pancreatitis, and fulminant hepatitis have been described.

Severe Disease: West Nile Meningitis, West Nile Encephalitis and West Nile Poliomyelitis
West Nile virus (WNV)

Clinical Suspicion

- The diagnosis of WNV infection relies on a high index of clinical suspicion and on results of specific laboratory tests.

- WNV or other arboviral diseases, such as St. Louis encephalitis, should be seriously considered in adults 50 years of age or older who have onset of unexplained encephalitis or meningitis in late summer or early fall.

- The local presence of WNV enzootic activity or other human cases of WNV infection should further raise the index of suspicion.

- Severe neurologic disease due to WNV infection has occurred in persons of all ages, and because year-round transmission is possible in southern states.

- WNV should always be considered in persons with unexplained encephalitis and meningitis.
West Nile virus (WNV)

Treatment

- No specific treatment is available.
- In severe cases treatment consists of supportive care that often involves hospitalization, intravenous fluids, respiratory support, and prevention of secondary infections.
Porcine Viruses

PERV  - porcine endogenous retrovirus - endogenous genetic elements with potential to produce infectious virions

HEV    - swine hepatitis E virus - does not cause clinical symptoms in swine, but might be zoonotic agent infecting humans and causing hepatitis

PCMV   - porcine cytomegalovirus - latent infection

PCV1   - porcine circovirus type 1 - ?

PCV2   - porcine circovirus type 2 - causes post-weaning multi-systemic wasting syndrome

PLHV1/2 - porcine lymphotropic herpes virus type 1 and 2 - can potentially be reactivated in human recipient
PERV

- persists in donor animal
- is present in organs and tissues destined for donation
- enters human cells
- replicates in human cells
- persists in human recipient
- disseminates from donation site
- interacts with human viruses
Biological tests required for donors

The following biological tests must be performed for all donors as a minimum requirement:

- HIV 1 and 2 - Anti-HIV-1,2
- Hepatitis B - HBsAg, Anti HBc
- Hepatitis C - Anti-HCV-Ab
- Syphilis
Biological tests required for donors

- When anti-HBc is positive and HBsAg is negative, further investigations are necessary with a risk assessment to determine eligibility for clinical use.

- A validated testing algorithm must be applied to exclude the presence of active infection with Treponema pallidum. A non-reactive test, specific or non-specific, can allow tissues and cells to be released. When a non-specific test is performed, a reactive result will not prevent procurement or release if a specific Treponema confirmatory test is non-reactive. A donor whose specimen tests reactive on a Treponema-specific test will require a thorough risk assessment to determine eligibility for clinical use.
**Biological tests required for donors**

- HTLV-I antibody testing must be performed for donors living in, or originating from, high-incidence areas or with sexual partners originating from those areas or where the donor’s parents originate from those areas.

- In certain circumstances, additional testing may be required depending on the donor’s history and the characteristics of the tissue or cells donated (e.g. RhD, HLA, malaria, CMV, toxoplasma, EBV, Trypanosoma cruzi).
Biological tests required for donors

- The tests must be carried out by a qualified laboratory, authorised as a testing centre by the competent authority in the Member State, using EC-marked testing kits where appropriate. The type of test used must be validated for the purpose in accordance with current scientific knowledge.

- The biological tests will be carried out on the donor’s serum or plasma; they must not be performed on other fluids or secretions such as the aqueous or vitreous humour unless specifically justified clinically using a validated test for such a fluid.
Biological tests required for donors

- When potential donors have lost blood and have recently received donated blood, blood components, colloids or crystalloids, blood testing may not be valid due to haemodilution of the sample.

- An algorithm must be applied to assess the degree of haemodilution in the following circumstances:

  - ante-mortem blood sampling: if blood, blood components and/or colloids were infused in the 48 hours preceding blood sampling or if crystalloids were infused in the hour preceding blood sampling;

  - post-mortem blood sampling: if blood, blood components and/or colloids were infused in the 48 hours preceding death or if crystalloids were infused in the hour preceding death.
Biological tests required for donors

- Tissue establishments may accept tissues and cells from donors with plasma dilution of more than 50% only if the testing procedures used are validated for such plasma or if a pre-transfusion sample is available.

- In the case of a deceased donor, blood samples must have been obtained just prior to death or, if not possible, the time of sampling must be as soon as possible after death and in any case within 24 hours after death.
Biological tests required for donors

- In the case of living donors (except allogeneic bone marrow stem-cell and peripheral blood stem-cell donors, for practical reasons), blood samples must be obtained at the time of donation or, if not possible, within seven days post donation (this is the "donation sample").

- Where tissues and cells of allogeneic living donors can be stored for long periods, repeat sampling and testing is required after an interval of 180 days. In these circumstances of repeat testing, the donation sample can be taken up to 30 days prior to and 7 days post donation.

- Where tissues and cells of allogeneic living donors cannot be stored for long periods and repeat sampling is therefore not possible blood samples must be obtained at the time of donation or, if not possible, within seven days post donation (this is the "donation sample").
Biological tests required for donors

- If in a living donor (except bone marrow stem-cell and peripheral blood stem-cell donors) the "donation sample", as defined above, is additionally tested by the nucleic acid amplification technique (NAT) for HIV, HBV and HCV, testing of a repeat blood sample is not required. Retesting is also not required if the processing includes an inactivation step that has been validated for the viruses concerned.

- In the case of bone marrow and peripheral blood stem-cell collection, blood samples must be taken for testing within 30 days prior to donation.

- In the case of neonatal donors, the biological tests may be carried out on the donor’s mother to avoid medically unnecessary procedures upon the infant.
Lab determinations
Lab determinations

Tissue establishment laboratories should be suitably designed so that there is adequate space for receiving, processing, packaging/labeling, storage, etc., to: minimize contaminants; assure orderly handling procedures; and prevent mixups.
When tissue bank activities include processing of tissues and cells, this shall take place in an environment with specified air quality and cleanliness in order to minimise the risk of contamination, particularly cross-contamination between samples.

The effectiveness of these measures shall be validated and monitored.
Lab determinations

- Floors, walls and ceilings of non porous smooth surfaces,
- Temperature control,
- For sterile processing air filtered (HEPA),
- Documented system for enviromental monitoring temperature, air supply conditionns, particle number, CFU),
- Documented system for clining and disinfection, (rooms, equipment and instruments),
- Documented system for gowning and laundry,
- Adequate space for staff, processing and storage,
- Access limited to authorised personnel.
Lab determinations

- When tissues or cells are exposed to the environment during processing, without a subsequent microbial inactivation process, an air quality of Grade A as defined in the current European Guide to Good Manufacturing Practice, is required, usually achieved by using a laminar air flow (LAF) cabinet. The background environment must be demonstrated to guarantee the maintenance of Grade A in the tissue/cell manipulation area while in use and unmanned.
Lab determinations

A less stringent environment may be acceptable where:

- a validated microbial inactivation or terminal sterilisation process is applied after final packaging;
- where it is demonstrated that exposure in a Grade A environment has a detrimental effect on the required properties of the tissue or cell concerned;
- where it is demonstrated that the mode and route of application of the tissue or cell to the recipient implies a significantly lower risk of bacterial or fungal infection than cell and tissue transplantation (e.g. insemination);
- where it is not technically possible to carry out the required process in a Grade A environment (e.g., due to requirements for specific equipment in the processing area that is not fully compatible with Grade A).

In above, an environment of at least Grade D shall be provided.
Lab determinations

- Appropriate garments and equipment for personal protection and hygiene shall be provided in each relevant department of the tissue establishment along with written hygiene and gowning instructions.

- When the activities for which accreditation / designation / authorisation or licensing is sought involve storage of tissues and cells, the storage conditions necessary to maintain the required tissue and cell properties, including relevant parameters such as temperature, must be defined.
Lab determinations

- Critical parameters (e.g. temperature, humidity, potential contamination) must be controlled, monitored, and recorded to demonstrate compliance with the specified storage conditions.

- Physically separate areas should be provided for the storage of tissues and cells prior to release / quarantine, and for released and for rejected tissues and cells. A separate area should be allocated in both quarantine and released storage locations for certain tissues and cells collected in compliance with special criteria (e.g., Autologous or Directed Donations and known infected materials).

- The areas in which cells/tissues are stored shall be accessible only to authorized persons.
Lab determinations

**Grade A:** The local zone for high risk operations, e.g. filling zone, stopper bowls, open ampoules and vials, making aseptic connections, cell cultures. Normally such operations are protected by a laminar unidirectional air flow work station (Laminar Flow work stations). Laminar Unidirectional air flow systems shall provide a homogeneous air speed in a range of 0.36 – 0.54 m/s at the working position in open clean room applications flow at a defined working plane. The air velocity shall be specified and measured 150-300 mm from the filter face and close to the working plane. In open cleanroom applications the air flow velocity would typically be 0.45 m/s +/-20% (guidance value) 150-300 mm from the filter face.
Lab determinations

**Grade B:** For aseptic preparation and filling, this is the **background environment for grade A zones** when conventional cleanroom technology is employed.

**Grade C** and **D:** Clean areas for carrying out less critical stages in the manufacture of sterile products.
## Lab determinations

<table>
<thead>
<tr>
<th>Class</th>
<th></th>
<th>Max. number of particles/m³ in size no bigger than:</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Standby</td>
<td>Operating</td>
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<tr>
<td></td>
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<td>5µm</td>
</tr>
<tr>
<td>A</td>
<td>3 500</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>3 500</td>
<td>0</td>
</tr>
<tr>
<td>C</td>
<td>350 000</td>
<td>2 000</td>
</tr>
<tr>
<td>D</td>
<td>3 500 000</td>
<td>20 000</td>
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# Lab determinations

<table>
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<tr>
<th>Class</th>
<th>Limits for microbiological contamination</th>
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<tr>
<td></td>
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</tr>
<tr>
<td>C</td>
<td>100</td>
</tr>
<tr>
<td>D</td>
<td>200</td>
</tr>
</tbody>
</table>
Lab determinations

Characteristics such as temperature and relative humidity depend on the product and nature of the operations carried out. The parameter settings should be such not to interfere with the defined cleanliness standard.

For temperature and relative humidity, the general accepted guidance values are $18 \pm 2^\circ\text{C}$ and $40\%$ to $60\%$, respectively.

When selecting the environmental temperature and relative humidity limits the requirements for the product, process, operative comfort and area Grade shall be taken into account.

Typical operating ranges would be $17 - 21^\circ\text{C}$ and $35$ to $55\%$ relative humidity (guidance values).
Lab determinations

Outdoor clothing should not be brought into changing rooms leading to grade B and C rooms.

For every worker in a Grade A/B area, clean sterile (sterilised or adequately sanitised) protective garments should be provided at each work session, or at least once a day if monitoring results justify it. Gloves should be regularly disinfected during operations.

Masks and gloves should be changed at least at every working session.
Lab determinations

Design
Laboratories should prevent errors and cross-contamination.

Security
Access to restricted areas limited to authorised personnel.

Environmental monitoring
Control temperature, humidity, temperature, air supply conditions, particle number, CFU.

Sanitisation
Facilities used for retrieval, processing and preservation should be subjected to routine, scheduled and documented cleaning and disinfection procedures.

Waste Disposal
Handling and disposal of wastes should include appropriate collection, storage, and transportation procedures before utilisation.
Equipment and instruments should of appropriate quality to their intended functions.

Equipment and non-disposable supplies that come into contact with tissues or cells should be constructed so surfaces do not alter the safety or quality of the biological material.

Equipment should be designed, manufactured and qualified for appropriate cleaning and should be sterilised or decontaminated after each use.

A separate set of clean, sterile instruments should be used for each donor.

There should be SOPs for monitoring, inspection, maintenance, calibration and cleaning procedures for all equipment.

Refrigerators, freezers and other equipment required to maintain a specific temperature, should be inspected on a regularly scheduled basis.

Appropriate certification and maintenance records should be maintained for instruments and equipment.
Lab determinations

General Requirements

- No eating, drinking, smoking, or chewing gum.
- Specified garments must be worn when entering and inside the clean area. These shall be stored in the anteroom and not worn in non-clean areas.
- Only approved clean room paper shall be allowed in the area.
- Use only ballpoint pens (fine point preferred).
- Rouge, lipstick, eye shadow, eyebrow pencil, mascara, and false eyelashes shall not be worn by any worker while in any clean area.
- No cosmetics of any kind are to be applied or removed in the clean area.
- Skin lotions or lanolin-base soaps are in the restrooms for employees to use to guard against flaking due to dry skin.
Lab determinations

General Requirements

- Solvent contact with the bare skin should be avoided, as most solvents will remove the natural skin oils and cause excessive skin flaking.
- The use of paper or fabric towels is not recommended - washrooms should have electrically powered, warm-air dryers.
- Approved pliers, tweezers or lint-free gloves must be used to handle manufacturing materials, components, or finished devices.
- Do not touch with gloves or finger cots any covered or uncovered part of the body, or any item or surface that has not been thoroughly cleaned.
- All containers, racks, jigs, fixtures, and tools should be cleaned to the same level of cleanliness specified for the device being processed.
Lab determinations

Non-laminar Airflow Clean rooms

➢ Garments shall be pocket-less, lint-free coveralls, with snug fitting fasteners at the neck, wrist, and ankles.

➢ Lint-free caps must be worn and must completely cover the hair and head except for the eyes, nose, mouth, and chin.

➢ Shoes shall be cleaned and covered with a non-shedding boot-type cover or changed to approved clean room footwear. If special footwear is provided, it shall not be worn outside the clean room and dressing room.

➢ Janitorial services shall be performed only by adequately trained and supervised personnel, each of whom must be properly garbed.

➢ All equipment to be brought into the clean room shall be qualified for clean room use and first be thoroughly cleaned. Use only equipment that will minimize the generation of contaminants.

➢ Traffic into and within the clean room shall be restricted to authorized and properly garbed personnel, and unnecessary movements by these personnel shall be minimized.
Lab determinations

Laminar Airflow Clean Rooms

- Garments may vary with the operation being performed, but the minimum garment shall be a pocket-less, lint-free smock which extends to at least 15 inches below the work surface. The collar and cuffs shall have fasteners.

- Head covering shall be worn, and shall completely cover the hair. If the operation requires the wearer to lean over the work, or move into the airstream between the filter bank and the work piece, the front, sides, and rear neck areas of the head shall also be covered.

- Shoe covers are not necessary for vertical or horizontal laminar airflow facilities except when the work is being performed less than 24 inches from the floor.

- A face mask may be needed if an operator has a cold, or if the nose and mouth must be brought very close to the work piece for work on miniature components or devices.
Lab determinations

Clean Room Personnel Rules
Personnel should be asked to cooperate in maintaining a low contaminant emission rate by observing the following rules.

- Bath at night, instead of in the morning, to allow the build-up of normal body oils which reduces skin shedding. Also, use skin lotions.
- Wear clean, unstarched, low-shedding garments.
- Where appropriate, shave daily and be clean shaven or wear appropriate hair covering.
- Avoid touching, rubbing, and scratching exposed areas of the body.
- Exercise extra care to rid the hands of normal residue from home duties such as starching, baking, plastering, wallpapering, painting, concrete work, carpentering or other particulate generating activity.
- Request duty outside the or away from the clean room area when you have a cold or other viral or bacterial infection.
thank you