



On approval of the Rules for determining the immunological compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of tissue) and Regulation on the HLA-laboratory activities

Unofficial translation

Order of the Acting Minister of Healthcare of the Republic of Kazakhstan dated October 27, 2020, No. ҚР ДСМ -159/2020. Registered with the Ministry of Justice of the Republic of Kazakhstan on October 29, 2020, No. 21528.

Unofficial translation

In accordance with paragraph 2 of Article 211 of the Code of the Republic of Kazakhstan dated July 7, 2020 "On public health and healthcare system" **I HEREBY ORDER:**

1. To approve:

1) the Rules for determining the immunological compatibility of tissues during transplantation of organs (parts of an organ) and (or) tissues (parts of tissue) in accordance with Annex 1 to this Order;

2) the Regulation on the HLA-laboratory activities in accordance with Annex 2 to this Order.

2. To invalidate the Order of the Minister of Healthcare of the Republic of Kazakhstan dated April 8, 2019, No. ҚР ДСМ -21 "On approval of the Regulations on the HLA laboratory" (registered in the State Register of Normative Legal Acts under No. 18479, published on April 16, 2019, the Reference Control Bank of normative legal acts of the Republic of Kazakhstan in electronic form).

3. The Department of Medical Aid Organization of the Ministry of Healthcare of the Republic of Kazakhstan, in accordance with the procedure established by the legislation of the Republic of Kazakhstan, shall ensure:

1) state registration of this Order with the Ministry of Justice of the Republic of Kazakhstan;

2) posting this Order on the Internet resource of the Ministry of Healthcare of the Republic of Kazakhstan;

3) within ten working days from the date of state registration of this Order in the Legal Department of the Ministry of Healthcare of the Republic of Kazakhstan the information on the implementation of the measures provided for in subparagraphs 1) and 2) of this paragraph.

4. Control over the execution of this order shall be entrusted to the Vice-Minister of Healthcare of the Republic of Kazakhstan, A.Giniyat

5. This order shall come into effect upon the expiration of ten calendar days after the day of its first official publication.

Annex 1
to the Order of the Acting
Minister of Healthcare of the
Republic of Kazakhstan
dated October 27, 2020
No. ҚР ДСМ-159/2020

The Rules for determining the immunological compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of tissue)

Chapter 1. General Provisions

1. These Rules for determining the immunological compatibility of tissues during transplantation of organs (parts of an organ) and (or) tissues (parts of tissue) (hereinafter referred to as the Rules) have been developed in accordance with paragraph 2 of Article 211 of the Code of the Republic of Kazakhstan dated July 7, 2020 "On public health and health care system" (hereinafter referred to as the Code) and shall determine the procedure for determining the immunological compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of tissue).

2. The following concepts shall be used in these Rules:

- 1) allele - different forms of the same gene located in the same regions (locus) of paired chromosomes;
- 2) antigens - glycoprotein molecules located on the surface of the cell membrane of leukocytes, which are responsible for recognizing foreign agents;
- 3) hematopoietic stem cells - hematopoietic cells of the human bone marrow that have pluripotency and are in the process of life in the bone marrow, peripheral blood and umbilical cord blood;
- 4) register of donors of hematopoietic stem cells (bone marrow) - a list of persons who agree to the donation of hematopoietic stem cells (bone marrow) and typed according to the HLA system;
- 5) genes - sections of chromosomes encoding the structure and function of antigens;
- 6) tissue compatibility - the similarity of the tissues of the donor and the potential recipient for specific antigens of the HLA system, which determines the compatibility of the donor and recipient during organ transplantation (part of an organ) and (or) tissues (part of tissue);
- 7) locus - a linear portion of the chromosome occupied by one gene;
- 8) sequencing of nucleic acids - determination of their primary amino acid or nucleotide sequence;
- 9) sensitization - the acquisition of a specific hypersensitivity by the body to foreign antigens;

10) solid organs - all dense organs of the body, such as kidneys, heart, lungs, liver, pancreas;

11) HLA-studies - a set of laboratory tests carried out to determine the immunological compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of a tissue);

12) HLA-system - a system of antigens located on human leukocytes and determining the tissue compatibility of donor and recipient during organ and tissue transplantation, as well as hematopoietic stem cells;

13) HLA-phenotype - individual immunological parameters of a person, genetically encoded;

14) fragment analysis - determination of the size of DNA fragments and (or) the intensity of fluorescence of labeled DNA fragments;

15) STR-locus - molecular markers in genetic and genomic studies, which are varying regions in nuclear DNA, consisting of repeating monomers;

16) profile specialist - a medical worker with a higher medical education who has a certificate in a certain specialty;

17) republican transplant coordinator - a doctor coordinating the work of regional transplant coordinators and efficient interdepartmental interaction of medical organizations on the issues of transplantation service in the Republic of Kazakhstan, who is a full-time employee of the Coordination Center;

18) regional transplant coordinator - a doctor ensuring interdepartmental interaction of medical organizations in the field of (or) organs (parts of organs) and tissue transplantation (tissue parts) in regional centers, cities of republican significance and the capital, who is a full-time employee of the Coordination Center

19) stationary transplant coordinator - a doctor who is a full-time employee of a donor hospital and is subordinate to the regional transplant coordinator for the coordination of the transplant service in the relevant region, city of republican significance, the capital;

20) register of potential recipients of organs (parts of organs) and (or) tissue (parts of tissue) (hereinafter referred to as the register) – the database of potential recipients of organs (parts of organs) and (or) tissue (parts of tissue);

21) medical information system - a medical information system ensuring the maintenance of the processes of healthcare entities in electronic format;

22) SSP method - typing by polymerase chain reaction using sequence-specific primers;

23) SBT method - typing by nucleic acid sequencing by determining the nucleotide sequence of deoxyribonucleic acid;

24) SSO method - typing by the polymerase chain reaction method using fluorescently labeled microspheres carrying sequence-specific oligonucleotide probes on the surface;

25) NGS method is the sequencing of the next (or) new generation to determine the nucleotide sequence of DNA and RNA to obtain a description of its primary structure;

26) EIA method - determination of leukocyte antibodies by enzyme immunoassay;

27) method of fluorescence cytometry - determination of leukocyte antibodies using fluorescently-labeled microspheres carrying leukocyte antigens on the surface.

Footnote. Clause 2 as amended by the Order of the Minister of Healthcare of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

Chapter 2. The procedure for determining the immunological compatibility of tissues during transplantation of organs (parts of an organ) and (or) tissues (parts of tissue)

3. Determination of the immunological compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of tissue) shall be carried out:

1) for potential recipients and their donors during transplantation of organs (part of an organ) and (or) tissues from an intravital and (or) posthumous donor;

2) for potential recipients, who do not have a living donor and are included in the register;

3) for recipients and donors for hematopoietic stem cell transplantation.

Footnote. Clause 3 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

4. Determination of the immunological compatibility of the recipient and the donor shall be carried out based on the following provided to the HLA-laboratory:

1) citizens of the Republic of Kazakhstan receiving transplant services on the territory of the Republic of Kazakhstan within the guaranteed volume of free medical care, referrals from the transplant center of the Republic of Kazakhstan, where the provision of transplant services is planned;

2) by persons who are not citizens of the Republic of Kazakhstan and receiving transplant services on the territory of the Republic of Kazakhstan within the framework of an agreement concluded with transplant centers, referrals from these transplant centers;

3) by persons who are not citizens of the Republic of Kazakhstan, acting as a potential intravital donor for a citizen of the Republic of Kazakhstan receiving transplant services on the territory of the Republic of Kazakhstan within the guaranteed volume of free medical care , referrals from the transplant center of the Republic of Kazakhstan, where it is planned to provide transplant services ;

4) by persons who are not citizens of the Republic of Kazakhstan and who do not receive services for the transplantation of solid organs in the territory of the Republic of Kazakhstan, within the framework of a paid contract with a laboratory, a referral drawn up on the official letterhead of the authorized body in the field of healthcare of the country of which the potential living donor is a citizen and (or) recipient;

5) by persons who are not citizens of the Republic of Kazakhstan and do not receive services for transplantation of hematopoietic stem cells in the territory of the Republic of

Kazakhstan, within the framework of a paid contract with a laboratory, a referral drawn up on the official letterhead of the authorized body in the field of healthcare of the country of which the patient is a citizen and (or) his potential living donor and/or foreign transplant center;

6) by persons who are citizens of the Republic of Kazakhstan planning to receive a paid service for the transplantation of a solid organ in a foreign clinic, within the framework of a paid contract with a laboratory, a referral drawn up on the official letterhead of the specified clinic or transplant center of the Republic of Kazakhstan, concluded with the recipient and (or) the donor;

7) persons who are citizens of the Republic of Kazakhstan planning to receive a paid service for transplantation of hematopoietic stem cells in a foreign clinic, within the framework of a paid contract with a laboratory based on a referral drawn up on the official letterhead of the said clinic or transplant center of the Republic of Kazakhstan;

8) by persons who are citizens of the Republic of Kazakhstan receiving services for transplantation of a solid organ or hematopoietic stem cells in a foreign clinic within the framework of the "Treatment Abroad" program, within the guaranteed volume of free medical care, referral of the authorized body in the field of healthcare care or the transplant center of the Republic of Kazakhstan.

5. The official letterhead of a medical organization shall indicate:

Surname, first name, patronymic (if any), date of birth, citizenship, nationality, blood type and Rh status, address of residence of the recipient and his potential intravital donor(s);

information about the diagnosis of the recipient;

blood transfusion, obstetric and transplant anamnesis of the recipient;

planned type of surgery;

information about the attending physician and his contacts for transmission of results.

6. After confirmation of the referral, blood samples are taken for HLA studies to determine the immunological compatibility of tissues during organ (part of an organ) and (or) tissue (part of tissue) transplantation.

7. Before blood sampling, the surname, first name, patronymic (if any), and date of birth of the recipient and (or) donor, blood group, and Rh status, date and time of collection are indicated on the test tube.

A blood sample shall be taken from a recipient and (or) donor from a vein into an appropriate vacuum tube in accordance with Annex 1 to these Rules. For HLA typing by the molecular genetic method, blood sampling shall not be performed from the fistula vein, as well as from recipients receiving heparin-containing drugs after the hemodialysis procedure.

After filling, the tubes with blood shall be gently mixed by inverting the tube 8-10 times.

Blood samples shall be accompanied by a referral with the obligatory filling of all columns according to the document proving the identity of the recipient and (or) donor and certified by the seal or stamp of the sending organization (doctor). If the recipient and (or) the donor has not reached the age of 18, the attached copy of the certificate of birth.

8. Blood samples shall be transported at temperatures from +2 ° C to +8 ° C in light-protected thermal containers (cooler bag) with heat-insulating properties and a tight-fitting lid. Samples shall be transported upright in test tube racks. Sample delivery time is 24 hours from the time of collection of a blood sample for serological tests and 72 hours for other types of tests.

9. In the presence of hemolysis, overheating, freezing, or after the expiration of the period from the moment of collection, the blood sample shall not be accepted for research.

10. The results of studies to determine histocompatibility carried out in foreign laboratories shall not be recognized as valid for deciding on the possibility of transplantation in the Republic of Kazakhstan.

The results of HLA studies shall be transferred to the healthcare organization (the attending physician or courier who has a power of attorney or an authorized person specified in the official letter) that sent the material for research. When transferring research results, secure Internet channels and additional file password protection shall be used in compliance with confidentiality standards.

It is not allowed to transfer the results to a potential donor or recipient, as well as to their relatives.

Paragraph 1. The procedure for determining immunological compatibility in recipients and donors during organ transplantation (part of an organ) from an intravital donor and (or) a posthumous donor

11. To determine the immunological compatibility in recipients and donors in kidney and pancreas transplantation from an intravital and (or) posthumous donor, the HLA-laboratory staff shall carry out an initial determination of histocompatibility at the A, B, and Cw class I locus and the DRB1 class II locus of the HLA system. To determine histocompatibility, typing of intravital donor and a recipient shall be carried out at the indicated locus.

Primary typing shall be carried out by the serological method at the low-resolution level of the A, B, and Cw class I locus. Confirmatory typing of the A, B, and DRB1 locus of the recipient and the selected donor shall be carried out by the molecular genetic method at a low-resolution level using SSP or SSO from a new blood sample.

A twice-determined typing result obtained using two different blood samples in immunological typing laboratories, determined in accordance with the legislation of the Republic of Kazakhstan, and shall be conclusive.

12. Recipients in need of organ (tissue) transplantation shall be checked for the presence of HLA antibodies in the direction of the inpatient transplant doctor and (or) the republican coordinator. When determining the presence of antibodies, their level and specificity shall be determined. Antibody levels shall be expressed as a percentage. Establishing the presence of HLA antibodies in the recipient's blood and determining their specificity shall be carried out to effectively select a donor.

If the recipient received transfusions of blood components, then antibody screening shall be carried out after 14 days from the moment of sensitization of the body (transfusion of blood components). Determination of the level (percentage) of sensitization shall be carried out with the recipient's serum sampled no earlier than 48 hours before the operation.

Determination of the presence of HLA antibodies shall be carried out by EIA (Elisa test) or fluorescence cytometry. In difficult cases, the assessment of sensitization by leukocyte antibodies shall be assessed in the combination of these methods.

In the presence of HLA antibodies in the recipient for the diagnosis of donor-specific antibodies, typing of intravital and (or) the posthumous donor shall be carried out at locus HLA-A, B, C, DRB1, DQB1, DQA, DPB, DPA. Typing shall be carried out by the molecular genetic method at the low-resolution SSP or SSO level.

13. For the final decision on the compatibility of the donor and the recipient in organ transplantation, a cross-match test shall be carried out for all pairs of recipients and the donor.

The "cross-match" test for compatibility shall be performed by the serological method based on the lymphocytotoxic test. A flow cytometric compatibility test shall be performed to confirm serological results.

The primary "cross-match" shall be carried out to determine compatible related donors at the stage of selection from among living donors, as well as with archived serum of recipients in transplantation from a posthumous donor.

Before the operation, an actual "cross-match" shall be placed with the serum sampled within 48 hours before the operation and is mandatory for selection among intravital and (or) posthumous donors.

To determine the predicted compatibility of the donor and recipient, the transplant doctor shall compare the results of typing of the donor and the recipient, taking into account the results of HLA antibodies and the test for cross-match compatibility.

Organ transplantation shall be carried out based on a negative result of the actual "cross-match".

Footnote. Clause 13 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

14. To determine the immunological compatibility in recipients and donors in liver transplantation from the intravital donor and in the liver, heart, and heart-lung organ complex transplantation from a posthumous donor, recipients are tested for the presence of HLA antibodies in the direction of a hospital transplant doctor and (or) republican coordinator.

If HLA antibodies are present, their level and specificity shall be determined according to the procedure and methods specified in paragraph 12 of these Rules.

In the absence of leukocyte antibodies, HLA typing of the recipient and the donor, as well as a cross-match test, is not necessary.

In the presence of leukocyte antibodies to recipients and their donors, HLA-typing and a cross-match test for compatibility shall be carried out in accordance with the order specified in paragraphs 11 and 13 of these Rules.

15. Recipients who have undergone transplantation of an organ (part of an organ) from a posthumous or intravital donor, upon referral of a specialized professional or a PHC specialist, shall be tested for the presence of HLA antibodies by fluorescence cytometry with the following frequency:

- on the 14th day after transplantation;
- one month after transplantation;
- in the first year, every 3 months after transplantation;
- in case of negative status, once a year;
- with a positive status, every 3 months.

To establish donor-specific antibodies, additional donor typing shall be carried out at loci HLA-A, B, C, DRB1, DQB1, DQA, DPB, DPA for the diagnosis of donor-specific antibodies upon referral of a hospital transplant doctor of the transplantation center, a specialized professional or a PHC specialist. Typing shall be carried out at a low-resolution level by the molecular genetic method SSP or SSO. If it is necessary to confirm the results obtained at the low-resolution level, high-level typing (SBT) shall be performed.

The presence of donor-specific antibodies shall be is an early marker of transplant rejection. In the presence of donor-specific antibodies in the results obtained, the level shall be corrected with immunosuppressive drugs.

Footnote. Clause 15 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

Paragraph 2. Procedure for determining immunological compatibility in potential recipients included in the register

Footnote. The title of Paragraph 2 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

16. To determine immunological compatibility in potential recipients included in the register, blood sampling for an HLA study shall be carried out based upon a referral from a specialized professional or a PHC specialist.

Blood sampling shall be carried out according to the schedule in the regional blood centers and/or polyclinics at the place of residence, except for recipients on dialysis. For dialysis recipients, blood is drawn at dialysis centers.

The provision of consumables for blood collection and delivery of blood samples to the HLA laboratories shall be carried out by the regional blood center.

Footnote. Clause 16 as amended by the Order of the Minister of Healthcare of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

17. For potential recipients included in the register, the HLA phenotype is determined. Recipients are typed at loci A and B of class I and locus DRB1 of class II. Typing shall be carried out by the molecular genetic method at a low-resolution level (SSP or SSO). When a living donor appears, the recipient who is in the register undergoes confirmation typing from a new blood sample.

For a posthumous donor, typing is performed at loci HLA-A, B, and DRB1 by a molecular genetic method and at low-resolution level (SSP or SSO) upon the referral of the republican transplant coordinator.

Information about the recipient's HLA phenotype shall be included in the medical information system.

Footnote. Clause 17 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

18. When included in the register or preparing for related transplantation, the potential recipients in need of organ (part of organ) transplantation shall be determined for the presence of leukocyte antibodies upon referral of a transplant doctor or a specialized professional (in his absence, a local therapist or general practitioner).

In the future, for persons included in the register, the presence of HLA antibodies shall be determined at a rate of once every three months. If antibodies are present, their level and specificity shall be determined. The level of HLA antibodies shall be expressed as a percentage. Determination of the presence of HLA antibodies shall be carried out by EIA (Elisa test) or fluorescence cytometry. In difficult cases, the assessment of sensitization by leukocyte antibodies is assessed in the combination of these methods.

Information on the level of sensitization expressed as a percentage shall be included in the medical information system.

Footnote. Clause 18 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

19. When a posthumous donor appears, a "cross-match" primary test for compatibility with a blood sample of potential recipients shall be carried out, sampled by the medical information system upon referral of the republican coordinator.

The actual "cross-match" test for compatibility shall be carried out upon the referral of the transplant doctor at the transplant center. Organ transplantation shall be carried out based on a negative result of the actual "cross-match".

Footnote. Clause 19 in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

Paragraph 3. Procedure for determining immunological compatibility in recipients and donors during hematopoietic stem cells (bone marrow) transplantation

20. To determine the immunological compatibility in recipients and donors during hematopoietic stem cells (bone marrow) transplantation, the staff of the HLA-laboratory shall carry out an initial determination of the histocompatibility of the recipient and his potential donors for locus A, B, and C of class I and locus DRB1, DQB1 of class II at the low-resolution level by the molecular genetic method (SSP or SSO) in the direction of a hematologist.

To determine the final histocompatibility at the indicated locus, confirmatory typing of the recipient and the selected donor shall be carried out by the molecular genetic method at a high level of resolution (SBT/NGS) from a new blood sample on the referral of a hematologist.

The determination of the predicted compatibility of the donor and the recipient shall be carried out by the hematologist by comparing the results of typing of the donor and the recipient.

21. For the diagnosis of donor-specific antibodies, the recipient is determined by the percentage of sensitization and (or) the specificity of HLA antibodies by fluorescence cytometry.

22. For recipients who do not have related donors, the National Register of Hematopoietic Stem Cell Donors (hereinafter referred to as the Register) shall be formed.

In persons who have expressed a desire to enter the Register, the HLA phenotype is determined by locus A, B and C of class I and locus DRB1, DQB1 of class II by a molecular genetic method at a high level of resolution (SBT/NGS) in the direction of specialists from the National Register.

If, as a result of a search in the Register, a donor is found that matches the genotype of a potential recipient, after obtaining the consent of the donor for a donation of hematopoietic stem cells, confirmatory typing with a high-resolution molecular genetic method (SBT/NGS) from a new blood sample is performed.

Information on the HLA phenotype of potential donors is included in the Register's electronic database.

Maintaining the Register of Hematopoietic Stem Cells Donors (bone marrow) shall be carried out in accordance with subparagraph 1) of Article 215 of the Code.

23. For recipients in need of stem cell transplantation, a cord blood bank is formed and, at the request of a hematologist, cord blood doses compatible with the HLA phenotype are selected.

HLA typing of umbilical cord blood shall be carried out at locus A, B, and DRB1 by the molecular genetic method at a low level of resolution (SSP/SSO) in the direction of the specialists of the cord blood bank.

Information about the HLA phenotype of the umbilical cord blood is transmitted to the specialists of the cord blood bank.

24. For recipients who underwent transplantation of hematopoietic stem cells, donor chimerism is determined in the direction of a hematologist to determine the degree of graft engraftment and predict the recurrence of the underlying disease.

Determination of donor chimerism shall be carried out by the molecular genetic method by carrying out fragment analysis of STR locus and (or) real-time PCR.

To determine donor chimerism in recipients after hematopoietic stem cell transplantation, the recipient's blood samples taken before and after the transplantation, and the donor's blood sample are used.

The result is expressed as a percentage of the presence of donor genes in the recipient's blood sample.

25. For recipients with immunological refractoriness and the presence of leukocyte antibodies, the employees of the HLA-laboratory carry out an individual selection of platelets.

At high percentages of sensitization of leukocyte antibodies in the recipient's blood, the recipient is typed at locus A, B and C of class I and locus DRB1, DQB1 of class II at a low-resolution level by the molecular genetic method (SSP or SSO) to search for a suitable blood donor by the HLA phenotype.

The base of HLA-typed blood donors is created for locus A, B and C of the I class of the HLA-system at a low-resolution level using the serological method.

Individual selection of blood components shall be carried out based on the "cross-match" lymphocytotoxic test with the recipient's serum and the donor's blood sample having the same antigens of the A, B and C locus of the I class of the HLA system. In the absence of a blood donor with the same HLA phenotype, an individual selection of platelets shall be carried out based on a lymphocytotoxic test "cross-match" without taking into account the donor's HLA phenotype.

For transfusion, platelets are given with a negative result of individual selection of blood components based on the lymphocytotoxic test "cross-match".

With a high sensitization of the recipient with leukocyte antibodies (above 50%), doses of platelets with the lowest level of cytotoxicity of the lymphocytotoxic test (2+ or 4+) are transfused.

In the absence of a donor with a negative and low level of cytotoxicity of the lymphocytotoxic test, platelet transfusion shall be carried out from donors with a large number of matches for antigens of locus A, B and C of class I of the HLA system.

compatibility of tissues during transplantation of organs (part of an organ) and (or) tissues (part of tissue)

List of studies for immunological compatibility of tissues during organ transplantation (part of an organ) and (or) tissues (part of a tissue)

Footnote. The list in the wording of the Order of the Minister of Health of the Republic of Kazakhstan dated 30.09.2021 No. KP ДСМ -101 (shall be enforced upon expiry of ten calendar days after the date of its first official publication).

Study name	Recipient and/or donor	Sample amount (ml)	Sample name, presence of filler	Study type
Immunological compatibility in recipients and donors during organ transplantation from an intravital and (or) posthumous donor				
Phenotyping of blood according to the HLA system by the serological method (class I antigens-Loci A, B, C) low resolution	Recipient	5-9	Blood, lithium anticoagulant-heparin	Serological
	Organ donor	5-9		Serological
Testing for compatibility "cross match"	Recipient	5-9	Blood, gel, and coagulation activator	Serological
	Organ donor	5-9	Blood, lithium anticoagulant-heparin	Serological
Blood genotyping by the HLA-system using the SSP method antigens class I and II, loci A, B, DRB1 medium resolution	Recipient	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
	Organ donor	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
Determination of the level of sensitization - the percentage of HLA antibodies in a serum sample by EIA (Elisa test)	Recipient	5-9	Blood, gel, and coagulation activator	EIA
Determination of the presence of HLA antibodies in a serum sample by flow fluorometry	Recipient	5-9	Blood, gel, and coagulation activator	Flow cytometry
Determination of the specificity of HLA antibodies of class I and II in a serum sample by flow fluorometry	Recipient	5-9	Blood, gel, and coagulation activator	Flow cytometry

Determination of the percentage of serum sensitization by HLA antibodies by flow cytometry	Recipient	5-9	Blood, gel, and coagulation activator	Flow cytometry
Blood genotyping for HLA-A, B, C, DRB1, DQB1/DQA1, DPB1/DPA1 genes by PCR-SSP method	Recipient and (or) donor	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
Individual selection of platelets for leukocyte antigens in recipients with platelet refractoriness				
Individual selection of blood components based on the "cross match" lymphocytotoxic test "ч"	Recipient	5-9	Blood, gel, and coagulation activator	Serological
	Donor of blood and its components	8-9	Blood, lithium anticoagulant-heparin	Serological
Determination of immunological compatibility in recipients and donors during hematopoietic stem cell transplantation from related donors				
Blood genotyping by the HLA system using the SSP method class I and II, loci A, B, C, DRB1, DQB1 medium resolution	Recipient	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
	HSC donor	5-9		Molecular genetic
Determination of genes of the major histocompatibility complex at loci A, B, C, DRB1, DRQB1 with division into haplotypes by the SBT (High resolution) method	Recipient	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
	HSC donor	5-9		Molecular genetic
Определение генов HLA - A, B, C, DRB1, DQA1/DQB1, DPB1/DPA1 на высоком разрешении методом NGS	HSC donor	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
Determination of immunological compatibility in potential donors of hematopoietic stem cells included in the National Register of donors of hematopoietic stem cells and umbilical cord blood banks				
Typing of HLA-A, B, C, DRB1, DQB1 genes without division into haplotypes (high resolution) by molecular genetic method	HSC donor для вступления в Регистр ГСК	8-9	Blood, anticoagulant K2EDTA	Molecular genetic

Determination of HLA genes - A, B, C, DRB1, DQA1 / DQB1, DPB1 / DPA1 at high resolution using the NGS method	HSC donor	8-9	Blood, anticoagulant K2EDTA	Molecular genetic
Blood genotyping by the HLA-system using the SSP method antigens class I and II, loci A, B, DRB1 medium resolution	Samples of umbilical cord blood	1-2	-	Molecular genetic
Conducting immunological compatibility in recipients included in the register				
Determination of antigens of loci HLA-A, B, DR by flow cytometry	Recipient and (or) donor	8-9	Blood, anticoagulant K2EDTA	Molecular genetic
Determination of the presence of HLA antibodies in a serum sample by flow fluorometry	Recipient	8-9	Blood, gel, and coagulation activator	Flow cytometry
Determination of the percentage of serum sensitization by HLA antibodies by flow cytometry	Recipient	8-9	Blood, gel, and coagulation activator	Flow cytometry
Determination of donor chimerism in recipients after transplantation of hematopoietic stem cells (bone marrow)				
Determination of chimerism in a patient after transplantation of hematopoietic stem cells by capillary sequencing	Recipient (blood sample before and after transplantation)	5-9	Blood, anticoagulant K2EDTA	Molecular genetic
	HSC donor	5-9	Blood, anticoagulant K2EDTA	Molecular genetic

Annex 2 to the order

The Regulation on the HLA-laboratory activities

Chapter 1. General Provisions

1. This Regulation on the HLA-laboratory activities has been developed in accordance with paragraph 2 of Article 211 of the Code of the Republic of Kazakhstan dated July 7, 2020 "On public health and healthcare system" (hereinafter referred to as the Code) and shall determine the regulation on the HLA-laboratory activities.

2. HLA - laboratories function as a structural subdivision of organizations carrying out activities in the field of donation, procurement of blood, its components, and preparations.

3. HLA – laboratories shall include:

1) central laboratory for immunological typing of tissues (parts of tissues) and (or) organs (parts of organs) (hereinafter referred to as the Central laboratory), which is created under the republican state medical organization carrying out scientific activities and activities in the field of donation, preparation of blood, its components and drugs;

2) local laboratory for immunological typing of tissues (parts of tissues) and (or) organs (parts of organs) (hereinafter referred to as a Local laboratory), which is created under state medical organizations operating in the field of donation, preparation of blood, its components and preparations in the areas and cities of republican significance.

4. In their work, HLA laboratories shall be guided by the Constitution of the Republic of Kazakhstan, the Code of the Republic of Kazakhstan "On public health and healthcare system", this Regulation, Orders of the Ministry of Healthcare of the Republic of Kazakhstan, regulating the issues of immunological examination of donors and recipients during tissue (part of tissue) transplantation and (or) organs (parts of organs).

5. HLA – laboratories shall carry out activities on the issues of immunological examination of donors and recipients during transplantation of tissues (parts of tissues) and (or) organs (parts of organs) around the clock.

Chapter 2. Tasks of HLA-laboratories

6. The main tasks of the HLA laboratory shall be:

1) central laboratory:

organizational and methodological management of local laboratories;

advice to local laboratories;

scientific activity on the study of human leukocyte antigens (hereinafter referred to as HLA);

educational activities on the issues of immunological examination of donors and recipients during transplantation of tissues (parts of tissues) and (or) organs (parts of organs);

provision of all types of immunological research of recipients and their donors for organizations carrying out organ transplantation (part of an organ) and (or) tissues (part of tissue);

conducting an immunological examination of recipients on the waiting list of the supervised region;

conducting expert laboratory studies on immunological examination of donors and recipients during tissue transplantation (parts of tissues) and (or) organs (parts of organs) for local laboratories in case of controversial and complex cases;

2) local laboratory:

provision of all types of immunological research of recipients and their donors for organizations carrying out organ transplantation (part of an organ) and (or) tissues (part of tissue);

conducting an immunological examination of recipients on the waiting list of the supervised region;

organization of the collection of sera from recipients in need of transplantation of tissues (parts of tissues) and (or) organs (parts of organs) (hereinafter referred to as recipients);

HLA studies for immunological control over the engraftment of transplanted organs and tissues.

Chapter 3. Functions of HLA-laboratories

7. In accordance with the assigned tasks, the HLA-laboratories shall carry out the following functions:

1) conducting HLA studies in recipients and donors in kidney and pancreas transplantation from an intravital and (or) posthumous donor;

2) carrying out HLA studies in recipients and donors during transplantation of other organs (liver, heart, and others) of an intravital and (or) posthumous donor;

3) carrying out HLA-typing of recipients and donors in the transplantation of hematopoietic stem cells (bone marrow) from related donors;

4) conducting HLA studies in recipients included in the waiting list of the supervised region;

5) HLA-typing of potential donors for the formation of the Register of hematopoietic stem cells and cord blood donors for the formation of the cord blood bank;

6) setting a test for compatibility "cross-match" between donor and recipient during organ transplantation;

7) determination of donor chimerism in recipients after transplantation of hematopoietic stem cells (bone marrow);

8) conducting post-transplant monitoring of HLA antibodies in recipients who underwent organ (tissue) transplantation;

9) implementation of individual selection of platelets for recipients based on the HLA phenotype, if necessary.

8. Organizational and methodological leadership and scientific functions of the Central Laboratory:

1) coordination of the activities of Local Laboratories for the collection of sera from recipients in need of organ transplantation for the determination of preexisting antibodies and a test for cross-match compatibility;

2) implementation of organizational and methodological management of Local Laboratories in terms of collection, screening, preparation of antileukocyte sera and immunological typing of blood to identify correlations with various diseases in population scientific research;

3) monitoring and analysis of the activities of Local laboratories;

4) formation of the main directions for improving the methods used in tissue typing;

5) planning and coordination of training for tissue typing laboratories of the republic, participation in training for specialists of Local Laboratories;

6) carrying out scientific work on the study of the prevalence of HLA-phenotypes in the Kazakh population, the relationship of the studied HLA-phenotypes with various types of diseases, studies of the human genome;

7) study and transfer of new research methods to the practice of immunological typing laboratories of the republic;

8) introduction of immunogenetic and genomic studies into the practice of medical organizations in the diagnosis of various pathological conditions, assessment and prediction of the effectiveness of treatment, the formation of risk groups among the population to organize preventive measures to prevent several diseases, conduct population studies;

9) development of a plan and program of international cooperation in the field of tissue typing, participation in international workshops, exchange of anti-HLA sera with foreign laboratories to improve test reagents, methods of tissue typing;

10) researching external assessment of quality and conducting interlaboratory comparative tests.

9. Organizational and advisory functions of the Local laboratory:

1) participation in the preparation of plans to improve the qualifications of employees of a healthcare organization on issues of immunological tissue typing;

2) organization of explanatory work on the clinical significance of immunological studies;

3) submission of reports on the work done to the Central Laboratory.

10. The structure and staffing standards of the Central Laboratory shall be determined in accordance with the legislation of the Republic of Kazakhstan.

11. The local laboratory shall be headed by a person who has undergone specialization in the Central laboratory for immunological typing of tissues (parts of tissues) and (or) organs (parts of organs), appointed to the position in the manner prescribed by law.