**On approval of the HLA-laboratory Regulation**

*Invalidated Unofficial translation*

Order of the Minister of Healthcare of the Republic of Kazakhstan dated April 8, 2019 KR MHC-21. Registered in the Ministry of Justice of the Republic of Kazakhstan dated April 9, 2019, № 18479

*Unofficial translation*

Footnote. Abolished by order of the acting. Of the Minister of Health of the Republic of Kazakhstan dated October 27, 2020 No. ҚР DSM-159/2020 (shall be enforced upon expiry of ten calendar days after the day of its first official publication).

In accordance with paragraph 13 of Article 169 of the Code of the Republic of Kazakhstan dated September 18, 2009 "On Public Health and Health Care System", I ORDER:

1. To approve the attached Regulation on the HLA-laboratory.

2. The department of medical assistance organization of the Ministry of Healthcare of the Republic of Kazakhstan in the manner established by the legislation of the Republic of Kazakhstan shall ensure:

1) state registration of this order in the Ministry of Justice of the Republic of Kazakhstan;

2) within ten calendar days from the date of state registration of this order, sending its copies in paper and electronic form in the Kazakh and Russian languages to the Republican state enterprise on the right of economic management "Republican Center for Legal Information" for official publication and inclusion to the Standard control bank of regulatory legal acts of the Republic of Kazakhstan;

3) placement of this order on the Internet resource of the Ministry of Healthcare of the Republic of Kazakhstan after its official publication;

4) within ten working days after state registration of this order, submission of information on implementation of measures provided for in subparagraphs 1), 2) and 3) of this paragraph to the Department of legal service of the Ministry of Healthcare of the Republic of Kazakhstan.

3. Control over execution of this order shall be assigned to the Vice-Minister of Healthcare of the Republic of Kazakhstan L. M. Aktayeva.

4. This order shall be enforced upon expiry of ten calendar days after its first official publication.

*Minister of Healthcare*
*of the Republic of Kazakhstan* *E.Birtanov*

Approved

by the order of the
Minister of Healthcare of the
Republic of Kazakhstan
dated April 8, 2019,
№ KR MHC-21

# Regulations on HLA-laboratory

## Chapter 1. General provisions

1. This Regulation shall regulate the activity of laboratories, carrying out immunological support for transplantation of tissues (parts of tissues) and (or) organs ( parts of organs), including hematopoietic stem cells in the Republic of Kazakhstan.

2. HLA-laboratories function as a structural division of organizations, carrying out activity in the field of blood donation, blood collection, its components and preparations.

3. HLA- laboratories include:

1) central laboratory for immunological typing of tissues (parts of tissues) and (or) organs (parts of organs) (hereinafter-the Central laboratory) which is created at the Scientific-production center of transfusiology, subordinated to the Ministry of Healthcare of the Republic of Kazakhstan;

2) local laboratory for immunological typing of tissues (parts of tissues) and (or) organs (parts of organs) (hereinafter-local laboratory) which is created at the Republican blood center, as well as in the blood centers of Aktobe, East Kazakhstan regions and the city of Shymkent.

4. The HLA- laboratories are governed by the Constitution of the Republic of Kazakhstan, Code of the Republic of Kazakhstan "On Public Health and Health Care 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 transplantation of tissues (parts of tissues) and (or) organs (parts of organs) in their work.

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- laboratory

6. The main tasks of HLA- laboratories shall be:

1) central laboratory:

organizational and methodological management of local laboratories;

providing consultative assistance to local laboratories on the issues of immunological typing of tissues (parts of tissues) and (or) organs (parts of organs);

carrying out scientific activity for the study of human leukocyte antigens;

carrying out educational activity on the issues of immunological examination of donors and recipients during transplantation of tissues (part of tissues) and (or) organs ( part of organs);

conducting immunological examination of donors and recipients during transplantation of tissues (part of tissues) and (or) organs (part of organs) of the supervised region;

conducting immunological control over the engraftment of transplanted organs and tissues.

2) local laboratory:

conducting an immunological study of patients and donors, being in health care organizations of the supervised region, including studies of people who are in the waiting List;

organization of collection of serums of recipients, needing transplantation of tissues (part of tissues) and (or) organs (part of organs);

conducting immunological control over the engraftment of transplanted organs and tissues.

Chapter 3. Functions of HLA- laboratories

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

1) conducting studies in patients and donors for kidney and pancreas transplantation from a living and/or cadaveric donor:

conducting all necessary studies to determine tissue compatibility during kidney and pancreatic transplantation in the direction of a hospital transplant doctor and (or) the Republican transplant coordinator of the Republican state enterprise on the right of economic management "Republican center for coordination of transplantation and high-tech medical services" of the Ministry of Healthcare of the Republic of Kazakhstan (hereinafter-RCCTHMS);

conducting primary determination of leukocyte antigens for a living donor and recipient by loci A, B, and Cw of class I using the serological method at a low-resolution level;

conducting confirmatory typing of leukocyte antigens of loci A, B, and DRB1 before transplantation of the recipient and selected donor using the molecular-genetic method at a low-resolution level by the method SSP and/or SSO from a new blood sample;

conducting of additional typing of the donor by loci HLA-C, DQB1, DQA, DPB, DPA at a low-resolution level using the molecular-genetic method SSP and (or) SSO,

if necessary at a high resolution level (SBT) for the diagnosis of donor-specific antibodies;

conducting typing by loci HLA - A, B, and DRB1 for a cadaveric donor using the molecular-genetic method SSP and (or) SO at a low-resolution level;

determination of presence of antibodies to the patients in preparation for transplantation, in the presence of antibodies, determination of their level and specificity with the patient's serum, selected no earlier than 48 hours before the operation;

conducting the presence of antibodies by IFA method (Elisa test) or fluorescent cytometry (SSO) and in complicated cases to assess the sensitization by leukocyte antibodies of two methods;

conducting mandatory "cross-match" compatibility test for all recipient and donor pairs;

conducting all studies on determination histocompatibility for the persons, who are not residents of the Republic of Kazakhstan and receiving transplant care on the territory of the Republic of Kazakhstan within the framework of the contract, concluded with transplant clinics;

2) conducting studies in patients and donors during transplantation of liver, heart, and other organ from a living and/or cadaveric donor:

conducting all necessary studies to determine tissue compatibility during transplantation of liver, heart, and other organ in the direction of the hospital's transplant doctor and (or) the Republican transplant coordinator of the RCCTHMS;

determination of the presence of antibodies to patients in preparation for transplantation, in the presence of antibodies, determination of their level and specificity with the patient's serum, selected no earlier than 48 hours before the operation;

determination of the presence of antibodies by IFA method (Elisa test) or fluorescence cytometry (SSO) and, in complicated cases, to assess the sensitization by leukocyte antibodies of two methods;

conducting HLA typing by loci A, B, and CW of class I and by locus DRB1 of class II of the HLA system and cross-match compatibility tests for recipients and their donors in the presence of leukocyte antibodies in the recipient;

conducting typing by loci HLA - A, B, and DRB1 for a cadaveric donor using the molecular genetic method SSP and (or) SSO at a low-resolution level;

3) setting up a test for compatibility of the donor and recipient "cross-match":

conducting a cross-match compatibility test during transplantation of organs on the direction of the hospital's transplant doctor and (or) the Republican transplant coordinator of the RCCTHMS;

conducting a cross-match compatibility test using a serological method based on a lymphocytotoxic test, if necessary to confirm the results, obtained by the serological method by conducting a compatibility test using a flow cytometry method;

setting up a primary cross-match compatibility test for making a decision on compatibility of the donor and recipient at the stage of selecting a donor from among living donors;

setting up an up-to-date cross-match compatibility test with serum selected within 48 hours prior to operation;

4) conducting studies in patients included in the waiting List:

determination of HLA-antigens and HLA-antibodies on the direction of the regional coordinator or specialized specialists;

determination of leukocyte antigens to the patients by loci HLA-A and B of class I and by locus DRB1 of class II using the molecular genetic method SSP and (or) SSO at a low-resolution level.

conducting confirmatory typing by the molecular-genetic method at a low-resolution level using SSP method and/or SSO from a new blood sample by loci A and B of class I and by locus DRB1 of class II when a related donor appears to a patient on the waiting List;

determination of the presence of HLA- antibodies when patients who need organ ( tissue) transplantation are included on the waiting List or are preparing for related transplantation,

determination of the presence of antibodies to the patients who are on the waiting List with a frequency of once every three months;

entering information about HLA-antigens and the presence of HLA-antibodies of the examined patient into the electronic database of the waiting List.

5) post-transplant monitoring of HLA-antibodies in patients who have undergone organ (tissue) transplantation:

conducting studies on determination HLA-antigens and HLA-antibodies on the direction of the regional and (or) republican coordinator, coordinator of the transplant center or a specialized specialist (nephrologist, hepatologist, cardiologist) of the healthcare department of the corresponding region;

determination of the presence of antibodies to the patients who have undergone organ (tissue) transplantation from a cadaveric or living donor, with frequency of once every three months by fluorescence cytometry method (SSO);

6) determination of the HLA-phenotype in patients and donors during transplantation of hematopoietic stem cells (bone marrow)):

conducting studies on determination of HLA-antigens on the direction of a hematologist of a medical organization;

conducting primary determination of HLA-antigens to the recipient and his/her potential donors by loci A, B, and C of class I and by loci DRB1, DQB1 of class II at a low-resolution level using the molecular-genetic method SSP and/or SSO when planning transplantation of hematopoietic stem cells (bone marrow);

determination of final histocompatibility at the specified loci to confirm the results of typing the recipient and the selected donor using the molecular-genetic method at a high-resolution level (SBT) from a new blood sample;

conducting all studies on determination histocompatibility for the persons who are not residents of the Republic of Kazakhstan and receiving transplant care on the territory of the Republic of Kazakhstan within the framework of a contract, concluded with transplant clinics.

7) determination of the HLA- phenotype in potential donors for forming a Register of donors of hematopoietic stem cells:

conducting typing for the persons, who have expressed a desire to be a hematopoietic stem cell donor by loci A, B, and C of class I and by loci DRB1, DQB1 of class II using the molecular-genetic method at a high resolution level (SBT);

conducting of a confirmatory typing of a donor who matches the genotype of a potential recipient using the molecular-genetic method at a high-resolution level (SBT) from a new blood sample;

entering the results of HLA-antigen studies of the donor into the electronic database of the Register.

8) determination of a donor chimerism in patients after transplantation of hematopoietic stem cells (bone marrow):

conducting determination of a donor chimerism for the patients who have undergone transplantation of hematopoietic stem cells (bone marrow) in the direction of a hematologist of a medical organization;

determination of a donor chimerism using a molecular-genetic method by performing a fragment analysis of STR-loci, using patient blood samples taken before and after transplantation, and a donor blood sample;

carrying out individual selection of platelets based on a donor HLA- antigens for sensitized patients and monitoring of post-transfusion reactions by immunological methods.

9) organizational and methodological management and scientific functions of the Central laboratory:

coordination of activities of local laboratories for collecting sera of recipients who need organ transplantation to determine pre-existing antibodies and preparing panels of sera for "cross-match" compatibility tests;

carrying out organizational and methodological management of local laboratories in terms of collection, screening, preparation of antileukocyte sera and immunological

blood typing to identify correlations with various diseases in population scientific studies;

monitoring and analysis of local laboratories activity;

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

planning and coordination of personnel training for the Republic's tissue typing laboratories, participation in training for the specialists of local laboratories;

conducting of scientific works on the study of prevalence of HLA-phenotypes in the Kazakhstani population, relationships of the studied HLA-phenotypes with various types of diseases, researches of the human genome;

study and transfer of new research methods to the practice of immunological typing laboratories of the Republic;

implementation of immunogenetic and genomic studies in the diagnosis of various pathological states into practice of medical organizations, assessment and prediction of treatment effectiveness, formation of risk groups among the population in order to organize preventive measures for prevention of a number of diseases, conducting population studies, participation in forensic medical examination;

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

10) organizational and consultative functions of a local laboratory:

participation in preparation of plans to improve the skills of employees of the healthcare organization on the issues of immunological tissue typing;

organization of explanatory work on the issues of clinical significance of immunological studies;

submission of reports on the work done to the Central laboratory.

Chapter 4. Organizational activity of HLA- laboratories

8. Local laboratory is headed by a person who completed a specialization at the Central laboratory of immunological tissue typing (parts of tissues) and (or) organs ( part of organs), appointed in the manner established by the legislation.

9. The results of determination of tissue compatibility by the HLA -laboratory are provided only to the representative of a medical healthcare organization (attending physician or a courier, in availability of the power of attorney), transmission of results to a potential donor or recipient is not allowed.

10. HLA-laboratories use secure Internet channels and additional file password protection when transmitting work results in electronic form.