Chapter 10

Histocompatibility Testing

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10.1 General

All Tissue Typing Centers (TTC) providing and/or handling histocompatibility data and participating in the frame of Eurotransplant (ET) <u>must</u> have a valid accreditation of the European Federation for Immunogenetics (EFI).

All TTC reporting data to ET <u>must</u> participate in all External Proficiency Testing (EPT) of ET organized by the Eurotransplant Reference Laboratory (ETRL) without any sample selection.

The Standards for Histocompatibility Testing of the EFI (EFI-Standards; http://www.efiweb.eu/) in their latest valid version apply for all described procedures unless stated otherwise in the Manual.

The Recommendations released by the Board of ET regarding histocompatibility testing, screening, and crossmatching **must** be followed.

In ET the official WHO HLA nomenclature is used, as indicated in the latest nomenclature report. For allocation and subsequent documentation purposes "matching determinants" are used for the report of HLA typing of patients and donors according to the listing of the ETRL (http://etrl.eurotransplant.nl/cms/index.php).

The TTC is responsible for the reliability, accuracy and consistency of all relevant histocompatibility data of their patients and donors reported to ET. They must follow the written and valid Standard Operation Procedures (SOP) released to meet the requirements for the ET-Manual and the EFI-standards.

The responsibilities of the ETRL are:

- 1. to organize and oversee all EPT exercises and release annual certificates.
- 2. to provide expertise and practical aid in the areas of histocompatibility testing to ET-associated TTC including a 24 h / 7 days a week on call service for immunological problems in organ allocation and allocation of organs via the Acceptable Mismatch (AM) Program.
- 3. to help affiliated TTC in defining acceptable mismatches for patients awaiting an organ and to control every application for patients entering the AM Program.
- 4. to visit TTC and help them in solving histocompatibility related problems and
- 5. to organize the annual ET Tissue Typers Meeting.

10.1.1 Registration of renal transplant patients

Relevant histocompatibility and immunological transplantation data of all potential organ recipients and donors are registered centrally in ET.

Every potential renal transplant recipient <u>should</u> be HLA typed on two different occasions using two different blood samples. Every patient <u>must</u> be typed for HLA-A, -B, -DR and <u>should</u> be typed for HLA-C and -DQ.

Every organ donor <u>must</u> be typed for HLA-A, -B, -DR and <u>should</u> be typed for HLA-C and -DQ. The information on HLA-C and DQ <u>should</u> be reported to ET if available.

If the phenotype of a potential recipient shows less than six HLA-A, -B, -DR antigens, a family typing or DNA typing <u>should</u> be done for the definition of possible homozygosity. Extended DNA typing can also be accepted for the definition of homozygosity.

Only trained personnel <u>should</u> submit the HLA typing results and the screening data ENIS, preferably via the TTC of the patient.

10.1.2 Material for histocompatibility testing

Prior to enter a renal transplant patient on the waiting list for organ transplantation HLA typing and a screening for HLA specific antibodies must be done. The applying medical doctor of the patient must contact the TTC affiliated to the transplant center and request information for the material.

In general, all material must be sent to the TTC, affiliated to the transplantation center, where a patient is registered. The samples must be labeled according to the EFI-Standards, (www.efiweb.eu). The samples must be accompanied by the needed administrative information, provided by the TTC, and should arrive in the TTC not later than 24 hrs post bleeding. Cooling of the samples or extreme heat should be avoided. An up-to-date listing of the TTC affiliated to ET is available at the central office of ET.

Typing for organ donors and crossmatching must follow the SOP's released by the TTC.

10.1.3 Typing for HLA class I (A, B, (C)) and class II specificities (DR, (DQ))

The TTC <u>must</u> follow the EFI-Standards. Within ET HLA-A and HLA-B, serological and molecular typing is accepted. For HLA-DR, HLA-C and HLA-DQ a molecular typing <u>must</u> be performed. HLA typing data translated to "matching determinants are reported directly to ET (addendum).

<u>Caution</u>: All immunologically relevant data (i.e. HLA typing and screening data) reported to ET <u>must</u> be controlled for clerical errors. Every mistake or inconsistency <u>must</u> be reported immediately for correction to ET.

10.2 Screening

Sera from potential organ recipients <u>should</u> be screened for HLA specific antibodies at regular time intervals: for kidney recipients a screening every three months <u>must</u> be performed unless otherwise specified.

A screening for HLA specific antibodies <u>should</u> be performed at 2 and 4 weeks after every immunizing event, e.g. blood transfusion, transplantation, pregnancy and graft removal. In all cases, the screening <u>must</u> be carried out tin time to prevent outdated screening leading to removal of the patient from the allocation list. The screening should follow the recommendations of the National Transplantation Society or the local Transplantation Center.

The TTC <u>should</u> control the waiting list with respect to histocompatibility related aspects. The screening is performed by the TTC affiliated to the transplant center where the patient is registered. The information <u>must</u> be recorded in the patient file and reported to ET.

The identification of autoantibodies or transplantation irrelevant antibodies <u>must</u> be done by the TTC. Such antibodies may lead to high panel reactive antibody values (%-PRA) and can often lead to false positive crossmatches. Therefore, the screening and the autocrossmatch using the patients own cells <u>must</u> be done with and without dithiothreitol (DTT). The TTC <u>must</u> report to ET if the patients have autoantibodies or not. The TTC <u>must</u> use screening methods for the definition of antibodies against MHC Class I and MHC Class II. At least once a year the screening <u>must</u> be done by complement dependent cytotoxicity. The TTC <u>must</u> report for every screening performed a %-PRA or virtual PRA value.

10.2.1 Screening for HLA specific antibodies

10.2.1.1 Definition of the %-PRA value

The %-PRA value represents the percentage of donors panel reacting positively with the patient serum. The definition of the %-PRA value **must** be done using a panel of HLA typed cells or by entering the specificities found as unacceptable antigens followed by a calculation of the virtual PRA value. Solid phase assays where a %-PRA value can be defined or calculated are also accepted. The %-PRA value **must** be calculated using the v-PRA program provided by the ETRL (http://etrl.eurotransplant.nl/cms/index.php). In case of complement dependent cytotoxicity (CDC +/- DTT) the panel **must** allow the definition of the %-PRA value and the definition of the HLA specificity and the specificities recognized by the patient serum:

- The number of HLA typed cell suspensions used should be 50.
- In case of a %-PRA value is >5%, an autocrossmatch <u>should</u> be done to exclude autoantibodies. The TTC **must** report this information to ET.
- The %-PRA value <u>must</u> be based on alloantibody reactivity only and consists of full numbers only.
- The serum of patients with autoantibodies only will not be included in the crossmatch serum exchange.

- The serum of patients with a mixture of auto- and alloantibodies with a %-PRA value <6% are not included in the crossmatch serum exchange.
- The serum of patients with alloantibodies, >5% PRA <u>must</u> be included in the crossmatch serum exchange, unless these are found only in solid phase assays.
- After every screening the recipient's TTC <u>must</u> update the antibody status of the patients on the waiting list and control if patients have an outdated screening. Furthermore, the TTC <u>must</u> define the autoantibody status of the patients, and <u>must</u> distribute the sera with a %-PRA value >5%, unless otherwise stated.

For other organs than kidneys, patients <u>must</u> be screened for HLA specific antibodies prior to enter the waiting list. In addition, further screenings are requested after every immunizing event.

10.2.1.2 Unacceptable HLA mismatches

Unacceptable mismatches are HLA antigens against which a patient has formed alloantibodies (current and / or historical). Following the policy of the center, mismatched HLA antigens of the previous organ donor or the HLA antigens of the partner of the patient, can be reported as unacceptable mismatches in ENIS. No offer will be made if an organ donor expresses these unacceptable HLA mismatches. Unacceptable HLA mismatches should be entered by the TTC after informing the relevant TC. These antigens are introduced in ENIS. HLA antigens, towards which the patient has formed alloantibodies defined in the current serum, must be reported as unacceptable mismatches. A direct link from defined specificities and unacceptable mismatches is not possible. The responsible TTC must confirm the unacceptable specificities separately.

10.2.2 Crossmatch

The crossmatch using the recipient serum and lymphocytes of the prospective donor is an integral step in the decision making process in transplantation. For kidney and combined kidney/pancreas transplantation a crossmatch **must** be done before transplantation using current sera as specified by the recipient TC and TTC unless otherwise decided by the National Transplantation Bodies. In addition, historical (peak) sera **should** be included. In case a crossmatch is not prospectively performed, the reasons, final decision, and outcome of the possible transplantation **must** be documented in the TTC, following the EFI standards.

For organs other than kidney a crossmatch <u>should</u> be done for patients who either have HLA specific alloantibodies, or had an alloimmunizing event such as pregnancy, blood transfusion, and previous transplantation in the past. Unless otherwise decided by the TC patients waiting for heart, lung, pancreas, and small bowel or a combination of those organs and being allosensitized, a crossmatch <u>must</u> be performed.

The TTC <u>must</u> use CDC for the crossmatch with or without DTT as requested by the ET allocation office or the local TC and can use additional techniques if the screening for HLA specific antibodies have been performed with the same methods and at the same degree of sensitivity.

10.2.2.1 The "allocation" crossmatch

The "allocation" crossmatch is done in the donor center and aims to avoid organ

dispatch to patients having preformed antibodies against the donor, not already included in the patient specific profile as unacceptable HLA mismatched antigens, where in addition to the class I also class II specificities can be entered. For this crossmatch procedure unseparated cells or T cells **must** be used as targets with addition or not of dithiothreitol according to the request of the allocation office. Any other target is not applicable. Crossmatches with B cells can be done only in case of local patients or patients from co-operating centers, where a formal request from the head of the transplantation center is available.

10.2.2.2 The "transplantation" or "decisive" crossmatch

The "transplantation" or "decisive" crossmatch is the one done in the Tissue Typing Center where the recipient is registered or the Center co-operating with the recipients Transplantation Center. Here, other than the above mentioned targets, unseparated cells and T cells, can be used, e.g. B cells or even endothelial cells. The evaluation of this decisive crossmatch prior transplantation follows the protocols established by the transplantation center.

10.2.2.3 Donor TTC

In the donor TTC, in Germany the regional TTC, crossmatches <u>must</u> be done for local patients irrespective of their immunization status and for sensitized (>5 % PRA) non-local patients selected by the ET allocation office.

For autoantibody positive patients a crossmatch with and without DTT <u>must</u> be performed and the results must be reported to the ET allocation office when indicated by the ET allocation office.

The TTC must apply policies allowing quick and reliable results avoiding any prolongation of the cold ischemia period.

10.2.2.4 Shipping of cell material for crossmatching

Anticoagulated (citrate or heparin) peripheral blood, a piece of spleen and / or lymph nodes in phosphate buffered saline or equivalent <u>must</u> be included in the respective container together with a sufficient number (if available) of isolated lymphocytes. Labeling of the vials and all information included <u>must</u> follow the EFI-Standards and must include the ET donor number.

10.2.2.5 Recipient TTC

The recipient TTC, in Germany the regional TTC, <u>must</u> perform the decisive crossmatch for transplantation of the selected patient and potential back-up of local/regional recipients selected by the ET allocation office.

For allosensitized patients a crossmatch with and without DTT <u>must</u> be performed when indicated by the ET allocation office and the results <u>must</u> be reported in this way to the ET allocation office. The recipients TC decides upon acceptance or denial of the offer.

Transplantation can only be performed in case of a negative crossmatch, unless otherwise decided by the local TC. The reasons **must** be reported to ET before transplantation.

The recipient TTC and TC are responsible for the histocompatibility of the transplant, including crossmatching.

10.2.2.6 Crossmatch serum exchange program

ET provides the TTC with a mailing list of all TTC performing crossmatches. An additional list of all potential recipients of the local TTC is included. Labels for each patient are printed locally. Dialysis centers collect sera of their potential kidney recipients four times a year and send them to their affiliated TTC.

The sera are screened for HLA specific antibodies and their %-PRA value.

For patients awaiting kidney transplantation only, sera with an allo-PRA value of >5% as depicted in the CDC are included in the crossmatch serum exchange program. Sera from patients with antibodies found in sold phase assay only, and patients with transplantation irrelevant antibodies only, are not included in the exchange program.

The TTC ships the serum samples together with a list indicating the patients, of whom serum is included, following the postal regulations. The receiving TTC <u>must</u> control if all sera have been included. In case sera are missing, the receiving TTC <u>must</u> inform the sending TTC.

10.2.3 Procedure

Use Beckman tubes type PAT22 or identical clones from other companies. The tubes <u>must</u> be labelled with the locally printed labels or with labels provided by ET if applicable.

The following procedure is recommended:

- Label the tubes.
- Fill the tubes with 50-250 microliter patient serum.
- Avoid any air bubble formation in the serum.
- Per patient a number of tubes corresponding to the latest list of TTC participating in the crossmatch serum exchange **must** be prepared and shipped.
- The ET-Nr. and name of the patient serum <u>should</u> be marked on the TTC list, which is sent to the TTC participating in the crossmatch serum exchange.
- For control reasons a copy of the list should remain locally.

In the receiving TTC the following steps are recommended:

- The accompanying list <u>must</u> be controlled. Any inconsistency <u>must</u> be reported to the sending TTC.
- New crossmatch sera <u>must</u> be put in the crossmatch serum storage system immediately after arrival, allowing a quick retrieval of the most current serum.
- For control purposes, the lists of the different TTC <u>must</u> be kept until the next exchange.

10.2.4 Sera from non-kidney recipients

Screening of sera from potential recipients of organs and tissues other than kidney is identical to the one described above. In case of immunized patients, sera <u>should</u> be sent to the TTC performing donor typing and crossmatching. Sera older than one calendar year <u>should</u> be discarded.

10.3 Acceptable Mismatch Program (AM)

The AM program is open for every highly sensitized kidney patient in ET. The AM program is conducted by the ETRL. Current or historical sensitization against HLA-A, -B, -C (Class I) and HLA-DR, -DQ (Class II) is regarded equally important. The TTC must control first whether their patients have anti Class I and/or II antibodies using solid phase assays. To be included, patients awaiting a kidney (re) transplant have to meet the following criteria:

Sera of at least two different bleedings <u>must</u> show *mainly cytotoxic* %-PRA value or a virtual PRA value of ≥85%, based on allosensitization and unacceptable HLA antigens. The panel <u>must</u> consist of ≥ 50 cell suspensions. Current or historical immunization is regarded equally important. Solid phase assays allowing the definition of virtual %-PRA values can also be used. Patients having antibodies found in solid phase assays only cannot be accepted in the AM Program, even if their virtual PRA value exceeds 85%.

This antibody reactivity <u>must</u> be due to allo-antibodies against HLA antigens. The reactivity of auto-antibodies should not contribute to this panel reactivity.

10.3.1 Definition of AM

AM can be found by analyzing the HLA typing of panel donors with negative reactions in the screenings. This is, however, only possible in cases where the %-PRA value of the serum is below 100%. Alternatively, selection and crossmatching of blood donors with a single mismatch to the patients HLA phenotype can be performed. Alternatively, the use of solid phase assays can be used. Subsequently, AM data of the patient are submitted using the relevant form (see http://etrl.eurotransplant.nl/cms/index.php) by e-mail to the ETRL (etrl@lumc.nl). Informative and relevant sera are sent to the ETRL, where the screening is repeated. After confirmation of the specificities the patient can be entered into the program on condition of the acceptance of the TC and the TTC.

10.3.2 Selection of potential organ donors

The HLA-A, -B and -DR typing of an organ donor is entered in ENIS. Potential recipients will be selected on the basis of their own HLA-A, -B and -DR antigens in combination with the AM. The AM are regarded, as patients own HLA antigens. Full compatibility between donor and patients including the AM is a prerequisite for allocation of kidneys via the AM program. For the first two years in the AM program patients **must** share one HLA-B and one HLA-DR or 2 HLA-DR with the organ donor. In case of a homozygous HLA-DR organ donor one HLA-DR sharing is acceptable. After two years on the AM waiting list no minimal criteria apply.

The ETRL immunologist on duty is informed about every potential offer. After acceptance the respective TC is informed, and if accepted, the kidney <u>must</u> immediately be dispatched. The crossmatch <u>must</u> be performed in the recipient TTC using both current and historical sera if available. In case of a negative crossmatch the transplantation can be performed.

Repeated HLA mismatches for broad and split HLA-A, -B, -DR antigens are regarded as a contraindication for transplantation, unless otherwise reported. In the same way antibodies against HLA-C and HLA-DQ are reported as unacceptable antigens but are taken into consideration only when the organ donor is typed for these specificities.

The order by which the kidneys will be offered in case of multiple recipients is according to the calculated chance to receive an organ as provided by the ETRL (Donor Frequency Calculator). Patients with the lowest chance get the highest priority.

10.4 ET proficiency testing

ET being an organ exchange organization **must** rely on the work of the affiliated TTC. One of the essential steps in maintaining the high standards of histocompatibility related matters within ET is the External Proficiency Testing Exercises. This is the only EPT where a center to center comparison is possible. Therefore, all ET affiliated laboratories entering data in ENIS must participate in all EPT without any sample selection and must fulfill the requirements of EFI. The ETRL has established these schemes in order to assess maintain and improve the quality of HLA typing, screening for HLA specific antibodies and crossmatching of TTC's affiliated to ET. The results form the basis for future decisions of bodies as the Tissue Typing Advisory Committee or the Kidney Advisory Committee of ET. The participants must use the local SOP for the EPT. The Standards released by the External Proficiency Testing Committee and approved by the Executive Committee of EFI form an essential basis for the Histocompatibility Quality Control and Assurance in ET. Modification of any of those Standards is done if deemed important. Every participant receives the results in an open way and with the center code given by ET. The participants receive the analysis of the results by e-mail and the results are finally published on the web. Every participant receives by January 31 of every calendar year a certificate of performance, where the fulfillment or not of the requirements is mentioned. In case of any inconsistency, changes in the certificate can be done until March 1, of the calendar year latest. A summary of the results is presented in the Annual Report of ET. The actual schemes include external proficiency testing exercises (EPT) for: HLA typing. crossmatching, and screening, and serum crossmatching.

10.4.1 EPT on HLA typing

This EPT, performed 4 times per year, consists of a shipment of peripheral blood from healthy blood donors for HLA typing. The TTC are divided into two groups for logistical reasons. The results **must** be reported back as matching determinants. All TTC submitting transplantation relevant HLA typing results to ET **must** participate without any selection of samples. The typing result of the organizer is regarded as the correct typing. In case a participant disapproves with the results, the secretary of the TTAC must be informed via e-mail. The point will then be discussed in the following TTAC meeting.

10.4.2 EPT on crossmatching

This EPT, performed 4 times per year must be done using the peripheral blood samples distributed for the serological part of the HLA typing quality control with sera from four potential organ recipients. All TTC performing crossmatches for organ donors and having access to the sera of ET patients **must** participate. The TTC **must** perform all crossmatches with and without DTT. The patient sera are selected because of specific as well as unspecific panel reactivity, meeting the daily work. The TTC are free to use unseparated lymphocytes, and/or separated T and/or B cells for the crossmatch following the local SOP's. The results are reported back to the TTC. TTC not having access to the sera of ET patients receive once per year eight sera for crossmatching. The TTC **must** perform the crossmatch with and without DTT. The

TTC are free to use unseparated lymphocytes, and/or separated T and/or B cells for the crossmatch as done for organ donors for their patients. The results are reported back to the organizer.

10.4.3 EPT on screening

This EPT, performed 2 times a year, consists of a shipment of 6 sera of patients or multiparous women with HLA specific antibodies. In the EPT on screening all TTC reporting screening data to ENIS <u>must</u> participate. The TTC <u>must</u> report the PRA value with and without DTT, the existence of MHC class I and/or MHC class II antibodies, and the specificity (-ies) if possible. Methods reported in the local SOP <u>must</u> be used. The use of additional methods is possible.

10.4.4 EPT on serum crossmatch

This EPT is designed for TTC having problems in receiving in due time the samples for the crossmatch EPT, because of postal or custom problems. The EPT is only for selected TTC and a short period of time. A set of defined sera is sent to the TTC where selected HLA typed suspensions <u>must</u> be used. The results <u>must</u> be reported immediately back to the ETRL. The standards of the External Proficiency Testing Committee of EFI apply.

10.5 Forms

All forms can be found and downloaded from the section Forms on the member site at www.eurotransplant.org.

10.6 Addendum

10.6.1.1 HLA-A

B = BROAD
S = SPLIT
P = PUBLIC
A = ALLELE

	ANTIGEN	SPLIT	BROAD		ANTIGEN	SPI IT	BROAD		ANTIGEN	SPI IT	BROAD
В	Δ1				A26		A10	s	A 33		A19
	A*0101		A1			A26				A33	A19
	A*0102		A 1			A26			A*3303		A 19
	A*01XX		Α1			A26	A10		A*33XX		A 19
	A2				A*2608	A26	A10		A74		A19
Д	A*0201		Α2	A		A26	A10		A*7401	A74	A 19
Α	A*0202		A2	s	A34		A10	А	A*74XX	A74	A19
Α	A*0203		Α2	Д	A*3401	A34	A10	В	A28		
Α	A*0205		Α2	Д	A*3402	A34	A10	s	A68		A28
Α	A*0206		A2	Α	A*34XX	A34	A10	Α	A*6801	A68	A28
Α	A*0207		Α2	S	A66		A10	А	A*6802	A68	A2 8
Α	A*0210		A2	Α	A*6601	A66	A10	Α	A*6803	A68	A28
A	A*0211		Α2	Д	A*6602	A66	A10	Α	A*68XX	A68	A28
Α	A*0217		A2	В	A11			s	A69		A28
Α	A*02XX		A2	Α	A*1101		A11	Α	A*6901	A69	A28
В	ДЗ			А	A*1102		A11	Α	A*69XX	A69	A28
Α	A*0301		А3	Α	A*11XX		A11	В	A36		
Α	A*0302		А3	В	A19			Α	A*3601		A36
Α	A*03XX		А3	S	A29		A19	Α	A*36XX		A36
В	A9			Α	A*2901	A29	A19	В	A43		
S	A23		Α9	А	A*2902	A29	A19	A	A*4301		A43
Α	A*2301	A23	A9	Α	A*29XX	A29	A19	Α	A*43XX		A43
Α	A*23XX	A23	А9	S	A30		A19	В	A80		
S	A24		A9	Α	A*3001	A30	A19	Α	A*8001		A80
Α	A*2402	A24	A 9	Α	A*3002	A30	A19	Α	A*80XX		A80
	A*2403	A24	Α9		A*3004	A30	A19				
	A*2407	A24	Α9			A30	A19				
	A*2408	A24	A9		A31		A19				
	A*24XX	A24	Α9	Α	A*3101	A31	A19				
	A10			Α	A*31XX	A31	A19				
	A25		A10	S	A32		A19				
	A*2501	A25	A10	Α	A*3201	A32	A19				
Α	A*25XX	A25	A10	Α	A*32XX	A32	A19				

10.6.1.2 HLA-B

B = BROAD
S = SPLIT
P = PUBLIC
A = ALLELE

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	ANTIGEN	SPLIT	BROAD	PUBLIC		ANTIGEN	SPLIT	BROAD	PUBLIC
В	B5			BW4	В	B13			BW4
s	B51		B5		A	B*1301		B13	
A	B*5101	B51	B5		A	B*1302		B13	
Α	B*5102	B51	B5		A	B*130XX		B13	
Α	B*5107	B51	B5		В	B14			BW6
Α	B*5108	B51	B5		A	B*14XX		B14	
Α	B*51XX	B51	B5		S	B64		B14	
S	B52		B5		A	B*1401	B64	B14	
Α	B*5201	B52	B5		S	B65		B14	
Α	B*52XX	B52	B5		A	B*1402	B65	B14	
В	B7			BW6	В	B15			
Α	B*0702		B7		A	B*15XX		B15	
Α	B*0703		B7		S	B62		B15	
Α	B*0704		В7		Α	B*1501	B62	B15	BW6
Α	B*0705		B7		A	B*1507	B62	B15	BW6
Α	B*0709		B7		A	B*1524	B62	B15	BW4
Α	B*07XX		B7		A	B*1525	B62	B15	BW6
В	B8			BW6	Α	B*1527	B62	B15	BW6
Α	B*0801		B8		Α	B*1530	B62	B15	BW6
Α	B*08XX		B8		S	B63		B15	BW4
В	B12				Α	B*1516	B63	B15	
S	B44		B12	BW4	Α	B*1517	B63	B15	
Α	B*4402	B44	B12		S	B75		B15	BW6
Α	B*4403	B44	B12		A	B*1502	B75	B15	
Α	B*4404	B44	B12		S	B76		B15	BW6
Α	B*4405	B44	B12		Α	B*1512	B76	B15	
Α	B*4410	B44	B12		S	B77		B15	BW4
Α	B*44XX	B44	B12		A	B*1513	B77	B15	
s	B45		B12	BW6	В	B70			BW6
Α	B*4501	B45	B12		S	B71		B70	
Α	B*45XX	B45	B12		A	B*1510	B71	B70	
Α	B*5002	B45	B12		Α	B*1518	B71	B70	
					S	B72		B70	
					Α	B*1503	B72	B70	
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	ANTIGEN	SPLIT	BROAD	PUBLIC		ANTIGEN	SPLIT	BROAD	PUBLIC
В	B16					B22			BW6
s	B38		B16	BW4	s	B54		B22	
A	B*3801	B38	B16		A	B*5401	B54	B22	
Α	B*3802	B38	B16		Α	B*54XX	B54	B22	
Α	B*38XX	B38	B16		s	B55		B22	
s	B39		B16	BW6		B*5501		B22	
	B*3901		B16			B*5502		B22	
Α	B*3902	B39	B16		Α	B*55XX		B22	
Α	B*3905	B39	B16		s	B56		B22	
Α	B*3906	B39	B16		А	B*5601	B56	B22	
	B*3910		B16			B*56XX		B22	
Α	B*39XX	B39	B16		В	B27			
В	B17			BW4	А	B*2702		B27	BW4
S	B57		B17		A	B*2703		B27	BW4
Α	B*5701	B57	B17		Α	B*2705		B27	BW4
Α	B*5702	B57	B17		Α	B*2706		B27	BW4
	B*5703		B17		А	B*2707		B27	BW4
Α	B*57XX	B57	B17		Α	B*2708		B27	BW6
s	B58		B17		Α	B*27XX		B27	BW4
Α	B*5801		B17		В	B35			BW6
A	B*5802	B58	B17		A	B*3501		B35	
Α	B*58XX	B58	B17		Α	B*3502		B35	
В	B18			BW6	Α	B*3503		B35	
Α	B*1801		B18		А	B*3505		B35	
A	B*18XX		B18		А	B*3508		B35	
В	B21				Α	B*3512		B35	
s	B49		B21	BW4	Α	B*3517		B35	
Α	B*4901	B49	B21		Α	B*3543		B35	
Α	B*49XX	B49	B21		Α	B*35XX		B35	
s	B50		B21	BW6	В	B37			BW4
	B*4005	B50	B21		Α	B*3701		B37	
Α	B*5001	B50	B21		A	B*37XX		B37	
Α	B*50XX	B50	B21						
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	ANTIGEN	SPLIT	BROAD	PUBLIC		ANTIGEN	SPLIT	BROAD	PUBLIC
В	B40			BW6	В	B67			BW6
Α	B*40XX		B40		Α	B*6701		B67	
s	B60		B40		Α	B*67XX		B67	
Α	B*4001	B60	B40		В	B73			BW6
S	B61		B40		Α	B*7301		B73	
Α	B*4002	B61	B40		Α	B*73XX		B73	
Α	B*4006	B61	B40		В	B78			BW6
В	B41			BW6	Α	B*7801		B78	
Α	B*4101		B41		Α	B*78XX		B78	
Α	B*4102		B41		В	B81			BW6
Α	B*41XX		B41		Α	B*8101		B81	
В	B42			BW6	Α	B*81XX		B81	
Α	B*4201		B42		В	B82			BW6
Α	B*42XX		B42		Α	B*8201		B82	
В	B46			BW6	Α	B*82XX		B82	
Α	B*4601		B46		В	B83			BW6
Α	B*46XX		B46		Α	B*8301		B83	
В	B47			BW4	Α	B*83XX		B83	
Α	B*4701		B47		Р	BW4			
Α	B*47XX		B47		Р	BW6			
В	B48			BW6					
Α	B*4801		B48						
Α	B*48XX		B48						
В	B53			BW4					
Α	B*5301		B53						
Α	B*53XX		B53						
В	B59			BW4					
Α	B*5901		B59						
Α	B*59XX		B59						

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B = BROAD	
S = SPLIT	
P = PUBLIC	
A = ALLELE	

10.6.1.3 HLA-CW

	ANTIGEN	SPLIT	BROAD	PUBLIC
В	CW1			
	CW*01XX		•	
				1
	CW*02XX			
	CW3			
	CW*03XX			
	CW10			
	CW*0302			
	CW*0304			
s	CW9		CW3	
	CW*0303			
	CW4			
Α	CW*04XX		CW4	
В	CW5			
	CW*05XX			
В	CW6			
Α	CW*06XX		CW6	
В	CW7			
Α	CW*07XX		CW7	
В	CW8			
Α	CW*08XX		CW8	
В	CW12			
Α	CW*12XX		CW12	
В	CW13			
Α	CW*13XX		CW13	
В	CW14			
	CW*14XX			
В	CW15			
Α	CW*15XX			
В	CW16			
Α	CW*16XX		CW16	
В	CW17			
Α	CW*17XX		CW17	
	CW18			
Α	CW*18XX	_	CW18	

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B = BROAD	
S = SPLIT	
P = PUBLIC	
A = ALLELE	

10.6.1.4 HLA-DR

	ANTIGEN	SPLIT	BROAD	PUBLIC		ANTIGEN	SPLIT	BROAD	PUBLIC
В	DR1				В	DR4			DR53
Α	DRB1*0101		DR1		Α	DRB1*0401		DR4	
Α	DRB1*0102		DR1		Α	DRB1*0402		DR4	
A	DRB1*0103		DR1		A	DRB1*0403		DR4	
Α	RB1*01XX		DR1		Α	DRB1*0404		DR4	
В	DR2			DR51	А	DRB1*0405		DR4	
S	DR15		DR2		Α	DRB1*0406		DR4	
A	DRB1*1501	DR15	DR2		A	DRB1*0407		DR4	
Α	DRB1*1502	DR15	DR2		Α	DRB1*0408		DR4	
Α	DRB1*1503	DR15	DR2		Α	DRB1*0409		DR4	
Α	RB1*15XX	DR15	DR2		Α	DRB1*0410		DR4	
S	DR16		DR2		Α	DRB1*0411		DR4	
Α	DRB1*1601	DR16	DR2		Α	DRB1*0412		DR4	
Α	DRB1*1602	DR16	DR2		Α	RB1*04XX		DR4	
A	RB1*16XX	DR16	DR2		В	DR5			DR52
В	DR3			DR52	s	DR11		DR5	
S	DR17		DR3		Α	DRB1*1101	DR11	DR5	
Α	DRB1*0301	DR17	DR3		Α	DRB1*1102	DR11	DR5	
A	DRB1*0304	DR17	DR3		A	DRB1*1103	DR11	DR5	
S	DR18		DR3		Α	DRB1*1104	DR11	DR5	
Α	DRB1*0302	DR18	DR3		Α	DRB1*1105	DR11	DR5	
Α	DRB1*0303	DR18	DR3		Α	RB1*11XX	DR11	DR5	
Α	RB1*03XX		DR3		s	DR12		DR5	
					Α	DRB1*1202	DR12	DR5	
					A	RB1*12XX	DR12	DR5	

B = BROAD
S = SPLIT
P = PUBLIC
A = ALLELE

ļ	ANTIGEN	SPLIT	BROAD	PUBLIC	COMMENT
В	DR6			DR52	
S	DR13		DR6		
Α	DRB1*1301	DR13	DR6		
Α	DRB1*1302	DR13	DR6		
Α	DRB1*1303	DR13	DR6		
Α	DRB1*1304	DR13	DR6		
Α	DRB1*1305	DR13	DR6		
Α	DRB1*1306	DR13	DR6		
Α	RB1*13XX	DR13	DR6		
S	DR14		DR6		
Α	DRB1*1401	DR14	DR6		
Α	DRB1*1402	DR14	DR6		
Α	DRB1*1403	DR14	DR6		
Α	DRB1*1404	DR14	DR6		
Α	DRB1*1405	DR14	DR6		
Α	DRB1*1406	DR14	DR6		
Α	DRB1*1407	DR14	DR6		
Α	DRB1*1408	DR14	DR6		
Α	DRB1*1409	DR14	DR6		
Α	DRB1*1410	DR14	DR6		
Α	RB1*14XX	DR14	DR6		
В	DR7			DR53	DR53 optinal
Α	DRB1*0701		DR7		DR53 optinal
Α	RB1*07XX		DR7		DR53 optinal

		ANTIGEN	SPLIT	BROAD	PUBLIC
	В	DR8			
	Α	DRB1*0801		DR8	
	Α	DRB1*0802		DR8	
	Α	DRB1*0803		DR8	
	Α	DRB1*0804		DR8	
	Α	DRB1*0805		DR8	
	Α	RB1*08XX		DR8	
	В	DR9			DR53
	Α	DRB1*0901		DR9	
	Α	RB1*09XX		DR9	
	В	DR10			
	Α	DRB1*1001		DR10	
	Α	RB1*10XX		DR10	
	Р	DR51			
	Α	DRB5*0101			DR51
		DRB5*0102			
	Α	DRB5*0201			
	Α	DRB5*0202		l .	
	Α	RB5*XX			DR51
		DR52			П. П.
	Α	DRB3*0101			DR52
	Α	DRB3*02			DR52
	A	DRB3*0301			DR52
	Α	RB3*XX			DR52
	Р	DR53			
	A	DRB4*01			DR53
	Α	RB4*XX			DR53
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	B = BROAD
	S = SPLIT
İ	P = PUBLIC
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10.6.1.5 HLA-DQ

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	ANTIGEN	SPLIT	BROAD	PUBLIC	
В	DQ1				
S	DQ5		DQ1		
Α	DQB1*0501		DQ1		
Α	DQB1*0502	DQ5	DQ1		
Α	DQB1*0503	DQ5	DQ1		
	DQB1*0504		DQ1		
	QB1*05XX		DQ1		
	DQ6				
1	DQB1*0601				
	DQB1*0602				
	DQB1*0603		DQ1		
	DQB1*0604		DQ1		
	DQB1*0605				
	DQB1*0606		D04		
	DQB1*0607		DQ1		
	DQB1*0608		DQ1		
	DQB1*0609		DQ1		
	OB1*06XX		DQ1		
	DQ2		<u> </u>		
1	DQB1*0201		DQ2		
	DQB1 0201		DG2		
	QB1*02XX		DQ2		
			DGZ		
	DQ3	•	DOO		
1	DQ7		DQ3		
	DQB1*0301		DO3		
Α	DQB1*0304		DQ3		
S			DQ3		
1	DQB1*0302				
i .	DQ9				
	DQB1*0303				
	QB1*03XX		DQ3		
1	DQ4				
	DQB1*0401				
	DQB1*0402				
Α	QB1*04XX		DQ4		