# 2005: Confirmation of HLA Typing

For transplants using an NMDP donor or cord blood unit, the donor’s HLA typing is reported on NMDP Form 22 (Confirmation of Donor HLA Typing) and the recipient’s HLA typing is reported on NMDP Form 117 (Final Recipient HLA Typing).

In all other situations, the Confirmation of HLA Typing form (Form 2005) is used to report HLA typing for both the donor and recipient on the Transplant Essential Data (TED) and comprehensive report form (CRF) tracks. This includes:

- Non-NMDP unrelated donor
- Non-NMDP unrelated cord blood unit
- Related cord blood unit
- HLA matched related donor
- HLA mismatched related donor
- Recipient of any of the donor types listed above
- Match siblings/syngeneic recipients and donors participating in the Related HCT Specimen Repository

A separate Form 2005 should be completed for each non-NMDP donor, recipient, or cord blood unit; however, only the recipient form is required for syngeneic transplants and HLA identical siblings. Both maternal and paternal typing should be submitted, if available, for all mismatched related donor transplants on the CRF track. Additionally, cord blood maternal typing should be submitted, if available, for all unrelated cord blood transplants on the CRF track. Maternal typing is requested in addition to, and not in place of, typing performed on the donor / CBU. Typing on the donor / CBU must be reported when meeting any of the descriptions above.

If the recipient is receiving a subsequent HCT from the same donor and HLA Typing Forms have already been completed for the first HCT, the center does not need to complete a second set of HLA Typing Forms for the subsequent infusion. However, if a recipient is receiving a subsequent HCT from a different donor fitting one of the descriptions above, the HLA Typing Form must be completed for the new donor.

The human immune system recognizes and defends against threats from outside the body. An important component of the immune system is the human leukocyte antigen (HLA) genes. These genes produce proteins, some of which are expressed on the surface of cells. These surface proteins allow cells to recognize self from non-self. Cells with matching proteins are recognized as self and passed over. However, when the proteins do not match between cells, one cell is identified as non-self, and an immune reaction is triggered to destroy it.

If the HLA of a donor and a recipient do not match closely, the immune response could result in the recipient’s body attacking the transplanted cells (resulting in graft failure), or the transplanted cells attacking the recipient’s body (graft-versus-host disease).

HLA genes are divided into three classes. The two classes that are important in matching donors and recipients are class I (HLA-A, B, C) and class II (includes HLA-DR, DQ). All HLA genes are encoded on an
area of chromosome six known as the Major Histocompatibility Complex (MHC).

Finding a good donor-recipient HLA match can be difficult because HLA is highly polymorphic, or variable. It can be completely unique to an individual. Since DNA is inherited from parents, the likelihood of a complete match is greater between full biological siblings than two unrelated individuals. Each individual has two copies of chromosome six (one from each parent). This means that each parent will be a haploidentical (half) match. A full sibling will have a 25% chance of being an identical HLA match, a 25% chance of being completely non-identical, and a 50% chance of being a haploidentical match.

Figure 1. Example of Single HLA-A Locus Inheritance

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<thead>
<tr>
<th>HLA-A Heredity</th>
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<tr>
<td>Biological Father</td>
<td>HLA-A*01</td>
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<tr>
<td>HLA-A*02</td>
<td>01, 02</td>
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<tr>
<td>HLA-A*24</td>
<td>01, 24</td>
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The nomenclature (naming system) of HLA is an ever-evolving field, with an international committee dedicated to maintaining standards for identifying the genes and their allele sequences. Allele names consist of 3 to 5 parts, depending on what is known about that individual allele.

Figure 2. HLA Nomenclature

[Diagram of HLA nomenclature]


The HLA prefix will precede the specific HLA locus (gene), which will be separated from allele-specific information by an asterisk. The first field will refer to a broad group of alleles (otherwise known as the “allele
family”); this designation will be separated from the next field by a colon. The second field will refer to the specific allele, which yields a specific HLA protein. Third and fourth fields may be specified, but are considered less important since they represent differences at a DNA level, rather than at a level of protein expression, due to a synonymous coding region (exon) or substitution in the non-coding region of the gene (intron). The name may be followed by a letter, which can alter the meaning of the preceding nomenclature. For example, the letter “N” signifies a null allele that does not test serologically.

DNA testing is done at low, intermediate, or high resolution.

Low-resolution testing is equivalent to serologic testing that identifies the allele group as represented by the first field of an HLA name (e.g., HLA-A*02).

Intermediate-resolution testing is molecular testing that may have remaining ambiguities. It reports allele groups that may contain 2 to 100 or more alleles. The nomenclature for these ambiguities is not internationally standardized; it is defined by the reporting lab or organization. NMDP reports frequently include letter sets that refer to possible genotypes within an allele group. Other laboratories may list all possible genotypes (e.g., DRB1*01:01 or 01:02, DRB1*01:01/01:02), where each specified allele is possible at a single locus.

High-resolution testing, or testing at the molecular level, provides further information about the gene itself, including what specific proteins will be expressed by the cells and even differences in sequence that do not impact protein expression. For cellular transplant, matching at the high resolution level is critically important.

Complete this form specifying the recipient or donor HLA at the level it was typed.

For a glossary of terms used in this section of the manual, see Appendix B.

Links to Sections of the Form:
Q1: Donor/Cord Blood Unit Identification
Q2-24: HLA Typing by DNA Technology
Q25-30: Antigens Defined by DNA Technology
Q31-47: Optional Antigen Reporting

Manual Updates:
Sections of the Forms Instruction Manual are frequently updated. The most recent updates to the manual can be found below. For additional information, select the manual section and review the updated text.

If you need to reference the historical Manual Change History for this form, please click here or reference the retired manual section on the Retired Forms Manuals webpage.

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<td><strong>2005:</strong></td>
<td>Modify</td>
<td>Version 4 of the 2005: Confirmation of HLA Typing section of the Forms</td>
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Last modified: Jan 27, 2020
Q1: Donor/Cord Blood Unit Identification

Question 1: Specify the person for whom this typing is being done

Indicate whether the reported HLA typing is the final recipient typing, or the final donor typing for this transplant.

The CIBMTR no longer collects optional typing on relatives that were not the donor for this transplant.

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Last modified: Dec 22, 2020
Q2-24: HLA Typing by DNA Technology

Complete this section for all typing done by DNA based methods. Examples of HLA typing by DNA technology may include: sequence-specific primer (SSP), sequence-specific oligonucleotide probe (SSOP), and sequence-based typing (SBT).

DNA technology can be used to type for a single allele, combinations of alleles (allele strings), or a “generic” allele designation similar to a serologic typing result. For this reason, the number of digits reported, as well as the number of alleles, will vary.

Laboratories may use “/”, “−” or a combination of numbers and letters on the typing report as a shorthand notation for the results. Transcribe the information onto the form as directly as possible. The letters, called allele codes, will be 1 or more characters in length and represent a combination of possible alleles at a locus. The same allele combination may be reported several different ways (e.g., DRB1*01:01 or 01:02, DRB1*01:01/01:02, DRB1*01:01/02, or DRB1*01:AB).

There will be two alleles reported for each locus, unless the individual is presumed homozygous (i.e., carries two copies of the same allele) at a locus. Transcribe the first allele designation in the first box, and the second allele designation in the second box. If the person is homozygous, leave the second box blank.

Question 2: Was documentation submitted to the CIBMTR (e.g., lab report)?

Indicate if a copy of the HLA typing report is attached. Use the “Add Attachment” feature to attach a copy of the HLA typing report in FormsNet3SM. Attaching a copy of the laboratory report assists in confirming the reporting of HLA typing and reduces the need for later data queries.

Class I

Questions 3-4: Locus A

Indicate whether the allele designations at HLA-A are “known” or “unknown.” If known, report the first A* allele and second A* allele designations in question 4; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 5. If question 3 is “unknown,” then question 25 (“A” antigens defined by serologic typing) is required.

Questions 5-6: Locus B

Indicate whether the allele designations at HLA-B are “known” or “unknown.” If known, report the first B* allele and second B* allele designations in question 6; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 7. If question 5 is “unknown,” then question 28 (“B” antigens defined by
serologic typing) is required.

Questions 7-8: Locus C

Indicate whether the allele designations at HLA-C are “known” or “unknown.” If known, report the first C* allele and second C* allele designations in question 8; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 9.

Class II

Questions 9-10: Locus DRB1

Indicate whether the allele designations at HLA-DRB1 are “known” or “unknown.” If known, report the first DRB1* allele and second DRB1* allele designations in question 10; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 11.

Class II (Optional)

Questions 11-12: Locus DRB3

Indicate whether the allele designations at HLA-DRB3 are “known” or “unknown.” If known, report the first DRB3* allele and second DRB3* allele designations in question 12; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 13.

Questions 13-14: Locus DRB4

Indicate whether the allele designations at HLA-DRB4 are “known” or “unknown.” If known, report the first DRB4* allele and second DRB4* allele designations in question 14; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 15.

Questions 15-16: Locus DRB5

Indicate whether the allele designations at HLA-DRB5 are “known” or “unknown.” If known, report the first DRB5* allele and second DRB5* allele designations in question 16; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 17.
**Questions 17-18: Locus DQB1**

Indicate whether the allele designations at HLA-DQB1 are “known” or “unknown.” If known, report the first DQB1* allele and second DQB1* allele designations in question 18; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 19.

**Questions 19-20: Locus DPB1**

Indicate whether the allele designations at HLA-DPB1 are “known” or “unknown.” If known, report the first DPB1* allele and second DPB1* allele designations in question 20; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 21.

**Questions 21-22: Locus DQA1**

Indicate whether the allele designations at HLA-DQA1 are “known” or “unknown.” If known, report the first DQA1* allele and second DQA1* allele designations in question 22; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 23.

**Questions 23-24: Locus DPA1**

Indicate whether the allele designations at HLA-DPA1 are “known” or “unknown.” If known, report the first DPA1* allele and second DPA1* allele designations in question 24; report a single allele, a string of alleles, or an allele code.

If “unknown,” continue with question 25.

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Last modified: Dec 22, 2020
Complete this section for all serologic typing. If serologic typing was not performed, leave this section blank. Report broad antigens only when your laboratory was not able to confirm typing for a known split antigen.

Each HLA locus has a serologically defined “X” antigen specificity: AX, BX, CX, DRX, DPX, and DQX. At this time, an “X” specificity is defined as "unknown but known to be different from the other antigen at that locus." This is different from a blank specificity, which is assumed to be the same as the other antigen at that locus." When comparisons between recipient and donor antigens involve an “X” or “blank” specificity, the “X” or “blank” is assumed to be homozygous for the antigen reported at the locus. In other words, the search algorithm treats typing containing “blank” or “X” antigens in the same manner as known homozygous typing.

Questions 25-27: Number of A antigens provided

Indicate if one or two HLA-A antigens were tested. If one antigen was tested, report the first antigen specificity in question 26 and continue with question 28.

If two antigens were tested, report the first antigen specificity in question 26 and the second antigen specificity in question 27. Continue with question 28.

Questions 28-30: Number of B antigens provided

Indicate if one or two HLA-B antigens were tested. If one antigen was tested, report the first antigen specificity in question 29 and continue with question 31.

If two antigens were tested, report the first antigen specificity in question 29 and the second antigen specificity in question 30. Continue with question 31.

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Last modified: Dec 22, 2020
Q31-47: Optional Antigen Reporting

Questions 31-33: Number of C antigens provided

Indicate if one or two HLA-C antigens were tested. If one antigen was tested, report the first antigen specificity in question 32 and continue with question 34.

If two antigens were tested, report the first antigen specificity in question 32 and the second antigen specificity in question 33. Continue with question 34.

Question 34: Specificity Bw4 present?

Bw4 refers to an epitope expressed by HLA-B alleles; epitopes are presented on the surface of the antigen and are recognized by the immune system. Bw4 and Bw6 are mutually exclusive and may confer reactivity with lymphocytes. Select “yes” if Bw4 specificity is present. Leave blank if specificity for Bw4 was not tested.

Question 35: Specificity Bw6 present?

Bw6 refers to an epitope expressed by HLA-B alleles; epitopes are presented on the surface of the antigen and are recognized by the immune system. Bw4 and Bw6 are mutually exclusive and may confer reactivity with lymphocytes. Select “yes” if Bw6 specificity is present. Leave blank if specificity for Bw6 was not tested.

Questions 36-38: Number of DR antigens provided

Indicate if one or two HLA-DR antigens were tested. If one antigen was tested, report the first antigen specificity in question 37 and continue with question 39.

If two antigens were tested, report the first antigen specificity in question 37 and the second antigen specificity in question 38. Continue with question 39.

Question 39: Specificity DR51 present?

HLA-DR51 is an HLA-DR variant that recognizes antigens from HLA-DRB5. Select “yes” if DR51 specificity is present. Leave blank if specificity for DR51 was not tested.

Question 40: Specificity DR52 present?

HLA-DR52 is an HLA-DR variant that recognizes antigens from HLA-DRB3. Select “yes” if DR52 specificity is present. Leave blank if specificity for DR52 was not tested.

Question 41: Specificity DR53 present?

HLA-DR53 is an HLA-DR variant that recognizes antigens from HLA-DRB4. Select “yes” if DR53 specificity is present. Leave blank if specificity for DR53 was not tested.
Questions 42-44: Number of DQ antigens provided

Indicate if one or two HLA-DQ antigens were tested. If one antigen was tested, report the first antigen specificity in question 43 and continue with question 45.

If two antigens were tested, report the first antigen specificity in question 43 and the second antigen specificity in question 44. Continue with question 45.

Questions 45-47: Number of DP antigens provided

Indicate if one or two HLA-DP antigens were tested. If one antigen was tested, report the first antigen specificity in question 46 and continue with the signature section.

If two antigens were tested, report the first antigen specificity in question 46 and the second antigen specificity in question 47. Continue with the signature section.

Signature

The FormsNet3SM application will automatically populate the signature data fields, including name and email address of person completing the form, and date upon submission of the form.

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