



HLA data entry in the EBMT Registry using ProMISe

The Nomenclature Committee of the World Health Organization (WHO) launched a new system of HLA nomenclature in April 2010. To learn more, visit the following website:

<http://hla.alleles.org>

where you will find relevant information and links.

EBMT Data Management was modified as follows:

- a. New labelled fields were added to the Registry database. Most of these fields are served by pull down menus to reduce typing errors and improve the quality of the data.
- b. The fields for donor HLA results are in the Donor table (Chapter: **Donor HLA : DNA results/Donor HLA : serology results**) and the fields for patient HLA results are in the HSCT assessment (Chapter: **Patient HLA : DNA results/Patient HLA : serology results**).
- c. Whenever possible existing data reported with the old nomenclature has been converted to the new nomenclature.

Understanding HLA data is not easy, we recommend that, if your National Registry provides HLA data entry you should forward the original HLA laboratory results to your collaborating National Registry.

For all the other centres that do data entry of the HLA themselves, the EBMT Registry has prepared these instructions on how to enter these data.

Table of contents

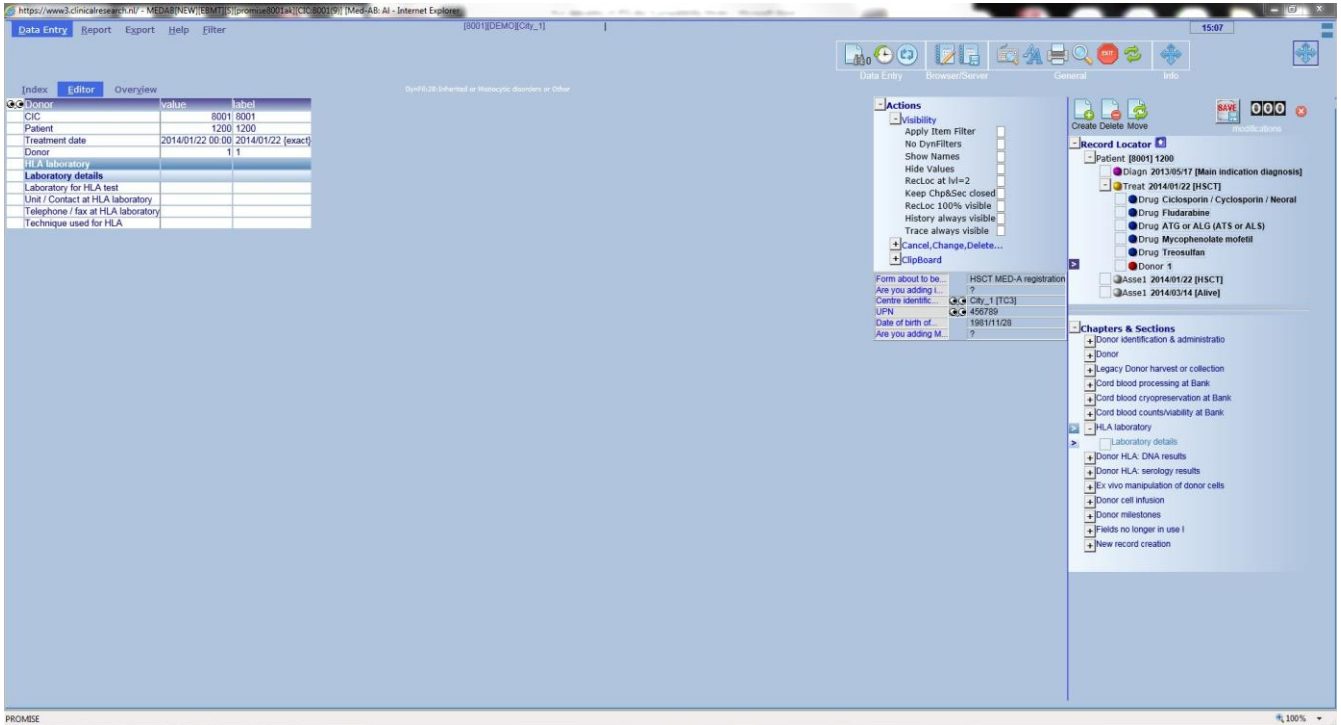
Instructions for data entry of HLA typing results :	2
1. Patient	4
<i>Reducing the size of the HLA DNA drop down menus.....</i>	<i>4</i>
2. Donor	6
3. Ambiguous results (Compressed Allele Lists - CALs).....	8
➤ MAC (multiple allele codes) - previously known as NMDP codes	9
4. Further recommendations.....	11
5. Useful links	13

Instructions for data entry of HLA typing results as part of data entry of a Med-A or Med-B form

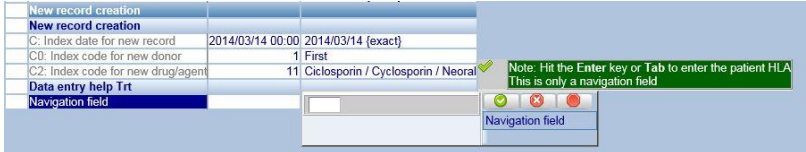
On the laboratory HLA typing results, identify the Donor and the Patient and the HLA results required by the EBMT registry: A, B, C, DRB1, DQB1, DPB1. Some other results, for instance DRB2 are not necessary for the EBMT.

Be careful with the order in which the results appear on the results typing form returned by the laboratory: they will not necessarily be in the same order as they appear in the Med-AB forms and in ProMISE.

If you are adding data retrospectively to an existing registration, please click on the **Donor** in the Record Locator (ensuring you have selected the correct HSCT if the patient had multiple HSCTs **AND** the correct Donor if multiple Donors were used for the same HSCT). Then go to **HLA Laboratory** in the Chapters below to enter the “Laboratory name” and “Technique used for HLA” if available:

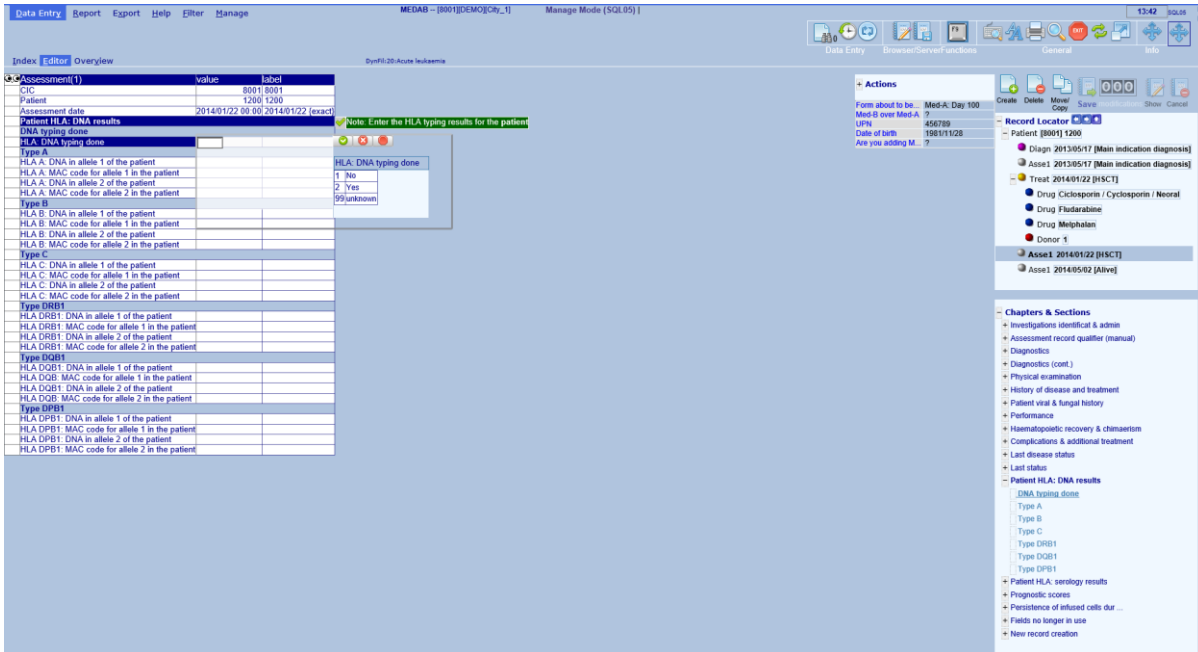


After entering “Technique used for HLA”, the next field, made necessary purely for proper navigation, will appear:



Press Return or Tab to proceed and the cursor will go to the first field of the Chapter **Patient HLA: DNA results**

Then the cursor will then move to the Patient record so you can enter the **Patient HLA: DNA results** (stored in the Assessment for the HSCT):



The fields to fill in the HLA typing results appear in the order shown below, first for the patient, and then for the donor(s):

Assessment(1)	value	label
CIC	8001	8001
Patient	1200	1200
Assessment date	2014/01/22 00:00	2014/01/22 {exact}
Patient HLA: DNA results		
DNA typing done		
HLA: DNA typing done		
Type A		
HLA A: DNA in allele 1 of the patient		
HLA A: MAC code for allele 1 in the patient		
HLA A: DNA in allele 2 of the patient		
HLA A: MAC code for allele 2 in the patient		
Type B		
HLA B: DNA in allele 1 of the patient		
HLA B: MAC code for allele 1 in the patient		
HLA B: DNA in allele 2 of the patient		
HLA B: MAC code for allele 2 in the patient		
Type C		
HLA C: DNA in allele 1 of the patient		
HLA C: MAC code for allele 1 in the patient		
HLA C: DNA in allele 2 of the patient		
HLA C: MAC code for allele 2 in the patient		
Type DRB1		
HLA DRB1: DNA in allele 1 of the patient		
HLA DRB1: MAC code for allele 1 in the patient		
HLA DRB1: DNA in allele 2 of the patient		
HLA DRB1: MAC code for allele 2 in the patient		
Type DQB1		
HLA DQB1: DNA in allele 1 of the patient		
HLA DQB1: MAC code for allele 1 in the patient		
HLA DQB1: DNA in allele 2 of the patient		
HLA DQB1: MAC code for allele 2 in the patient		
Type DPB1		
HLA DPB1: DNA in allele 1 of the patient		
HLA DPB1: MAC code for allele 1 in the patient		
HLA DPB1: DNA in allele 2 of the patient		
HLA DPB1: MAC code for allele 2 in the patient		

Assessment(1)	value	label
CIC	8001	8001
Patient	1200	1200
Assessment date	2014/01/22 00:00	2014/01/22 {exact}
Patient HLA: serology results		
HLA: serology typing done		
Serology HLA typing done		
Type A		
HLA A: serology in the patient 1		
HLA A: serology in the patient 2		
Type B		
HLA B: serology in the patient 1		
HLA B: serology in the patient 2		
Type C		
HLA C: serology in the patient 1		
HLA C: serology in the patient 2		
Type DRB1		
HLA DRB1: serology in the patient 1		
HLA DRB1: serology in the patient 2		
Type DQB1		
HLA DQB1: serology in the patient 1		
HLA DQB1: serology in the patient 2		
Type DPB1		
HLA DPB1: serology in the patient 1		
HLA DPB1: serology in the patient 2		

1. You will be asked to provide, for the patient, the DNA (molecular) results for each locus and allele respectively.

2. You will be asked to provide, still for the patient, the serologic results for each locus and allele respectively.

- ➔ once all the data for the patient have been completed,
- 3. You will be invited to fill in the DNA (molecular) HLA typing for the donor
- 4. You will be invited to fill in the serologic HLA typing for the donor

1. Patient

If DNA typing have been done for the patient, press 'Yes' and enter all relevant data in each locus and each allele.

> If the patient DNA typing has not been done, press 'No' to go to serologic results.

Patient HLA: DNA results	
DNA typing done	
HLA: DNA typing done	2 Yes
HLA A: DNA in allele 1 of the patient	
HLA A: MAC code for allele 1 in the patient	
HLA A: DNA in allele 2 of the patient	
HLA A: MAC code for allele 2 in the patient	
Type B	

HLA A: DNA in allele 1	
A*01	A*01
A*01:01	A*01:01

Please use the drop-down list:

HLA A: DNA in allele 1 of the patient	
A*01	A*01
A*01:01	A*01:01
A*01:01:01	A*01:01:01
A*01:01:01:01	A*01:01:01:01
A*01:01:01:02N	A*01:01:01:02N
A*01:01:01G	A*01:01:01G
A*01:01:02	A*01:01:02
A*01:01:03	A*01:01:03
A*01:01:04	A*01:01:04
A*01:01:05	A*01:01:05
A*01:01:06	A*01:01:06
A*01:01:07	A*01:01:07
A*01:01:08	A*01:01:08
A*01:01:09	A*01:01:09
A*01:01:10	A*01:01:10
A*01:01:11	A*01:01:11
A*01:01:12	A*01:01:12
A*01:01:13	A*01:01:13
A*01:01:14	A*01:01:14
A*01:01:15	A*01:01:15
A*01:01:16	A*01:01:16

There are 4 fields in which allelic information can be stored for each locus:

- > 2 for the 1st chromosome,
- > 2 for the 2nd chromosome.

One of the fields for each chromosome is a coded field such as you can see on this example.

The other field is used to store the MAC - multiple allele code which is used for ambiguous results. The use of MACs is explained later in the document

Reducing the size of the HLA DNA drop down menus

Some of the drop-down menus are very long. It is helpful to be able to shorten them and you can do this by typing part of the label. Note, however, that numbers cannot be used for this purpose unless they are preceded by a non numeric character. Therefore if you want to shorten the drop down menu you must always type first either the letters of the loci (A in the example above) or the * that precedes the numeric part or the : that lies between numeric parts.

Useful Tip: Always use that part of the result which is less common when looking for the correct entry. For example, if you have A*01:01:06, use :06 since the number of entries with 06 will be smaller than the number of entries with 01.

Shortcuts examples

Result	Start typing:
A*03:125	:125
A*30:01	*30
Not Evaluated (NE)	no
MAC (Multiple Allele Code)	ma
Only One Value Reported (OOVR)	on
To <i>redisplay</i> full list of labels	?

If Serologic typing has been performed for the patient, press 'yes' and continue with the Patient's HLA serology results.

- If the patient serology has not been studied, press 'no' and go to the next step.

Please use the drop-down list:

There are 2 fields in which serologic information can be stored for each locus:

- 1 for the 1st chromosome,
- 1 for the 2nd chromosome.

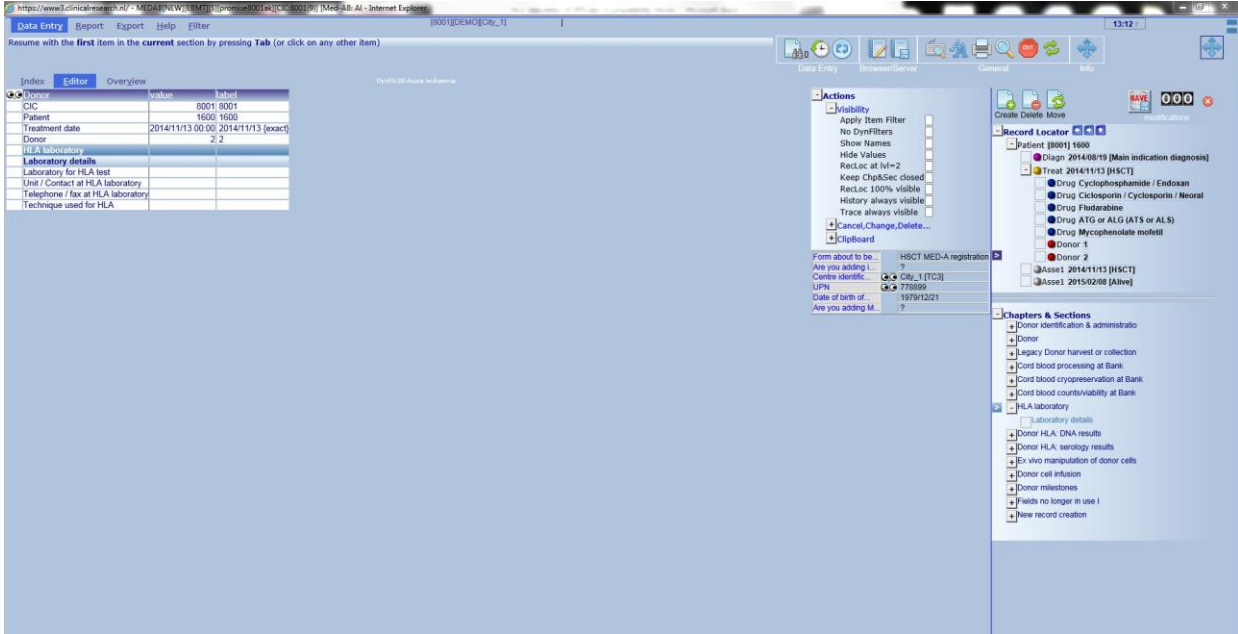
All fields for each chromosome are coded fields such as you can see below.

When this field appears again:

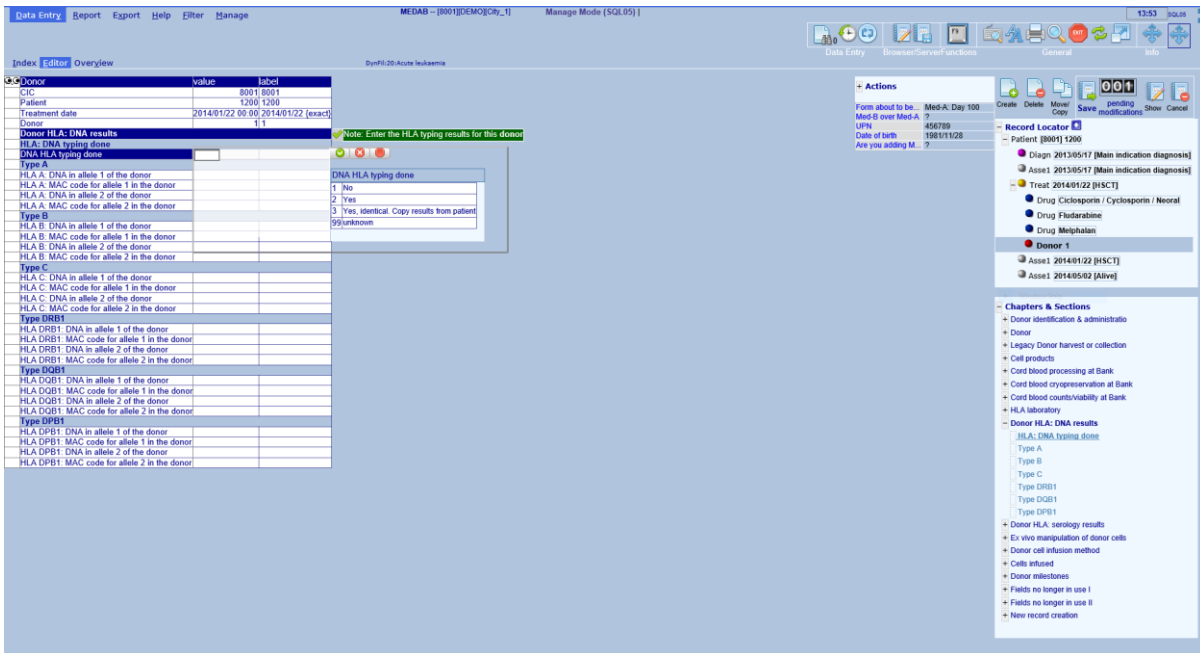
Press Return or Tab to proceed

2. Donor

(If you are adding data retrospectively to an existing registration, the fields for the Donor HLA results are in the Donor table. Please go to this record, ensuring you have selected the correct HSCT if the patient had multiple HSCTs AND the correct Donor if multiple Donors were used for the same HSCT).



The data entry for the donor is similar to that described for the patient with one more possibility; that of copying the patient data to the donor record when the HLA results are identical:



If DNA typing has been done for the donor and the results are different from that of the patient, press 'Yes' and enter all relevant data in each locus and each allele.

Donor HLA: DNA results	
HLA: DNA typing done	
DNA HLA typing done	2 Yes
Type A	
HLA A: DNA in allele 1 of the donor	
HLA A: MAC code for allele 1 in the donor	
HLA A: DNA in allele 2 of the donor	
HLA A: MAC code for allele 2 in the donor	A*01 A*01
Type B	A*01:01 A*01:01

- If the donor DNA typing has been done and the results are the same as that of the patient, press 'Yes, identical. Copy results from the patient'. The data from the patient HLA fields will be copied to the corresponding fields in the donor record.
- If the donor DNA typing has not been done, press 'No' to go to serologic results.
- The cursor will then take you to the serologic results.

If serologic typing has been performed for the donor, press 'yes' and proceed with the Donor's serology.

Index	Editor	Overview	value	label
Donor			8001	8001
Patient			1600	1600
Treatment date			2014/11/13 00:00	2014/11/13 {exact}
Donor			2	2
Donor HLA: serology results				
HLA: serology typing done				
Serology HLA typing done			2 Yes	
Type A				
HLA A: serology in the donor 1				
HLA A: serology in the donor 2				
Type B				
HLA B: serology in the donor 1				
HLA B: serology in the donor 2				
Type C				
HLA C: serology in the donor 1				
HLA C: serology in the donor 2				
Type DRB1				
HLA DRB1: serology in the donor 1				
HLA DRB1: serology in the donor 2				
Type DQB1				
HLA DQB1: serology in the donor 1				
HLA DQB1: serology in the donor 2				
Type DPB1				
HLA DPB1: serology in the donor 1				
HLA DPB1: serology in the donor 2				

- If the donor serologic typing has been done and the results are the same as that of the patient, press 'Yes, identical. Copy results from the patient'. The data from the patient HLA fields will be copied to the corresponding fields in the donor record.
- If the donor serology has not been studied, press 'no' and go to the next step.
- The cursor will then take you to the next step.

Follow instructions as for 1. Patient above.

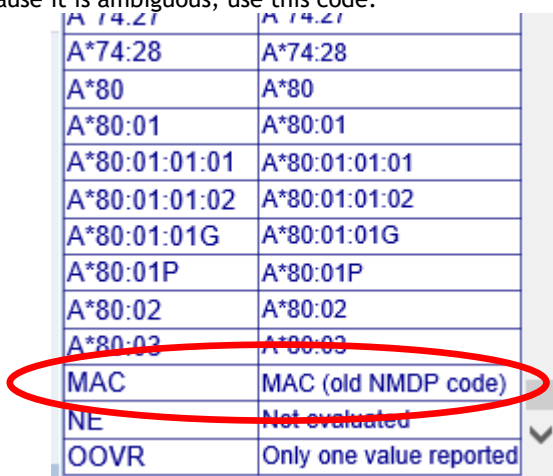
3. Ambiguous results (Compressed Allele Lists - CALs)

Some results are not completely precise: we know they can be something and we know they cannot be something else, but there are still options among which we cannot make a decision. For example, we could have a result that could be 01:04 or 01:06 but not anything else, or perhaps it can be 02:03 or 03:07. Ambiguities are represented with slashes separating all the possibilities. In these examples, the first one would be represented as 01:04/06 and the second as 02:03/03:07. These types of results are also known as CAL - Compressed Allele Lists.

The ambiguity of the results has to do with the type of antibodies used and it varies a lot.

To deal with this problem, the NMDP (National Marrow Donor Program®) has come up with a series of codes that are known as MACs (Multiple Allele Codes - Previously known as “NMDP codes”). Unfortunately, these codes cannot be added to the labels of the EBMT registry because there are too many (>80,000 different codes) and they represent entries that can have over 600 characters. If you encounter results that contain “/”, they should be dealt with using MACs.

At the end of all pull down menus for all DNA results, you will see the code **MAC**. If you cannot enter the result because it is ambiguous, use this code.



On selecting this code, the cursor will move to the next field where an entry reflecting the MAC code (*see further down in the document on how to find it*), can be entered for that particular case. The entry should be a maximum of 10 characters long for A, B & C and 14 characters long for DRB, DQB & DPB values:

Donor HLA: DNA results		
HLA: DNA typing done		
DNA HLA typing done		2 Yes
Type A		
HLA A: DNA in allele 1 of the donor	MAC	MAC (old NMDP code)
HLA A: MAC code for allele 1 in the donor	A*31:RBWU	A*31:RBWU
HLA A: DNA in allele 2 of the donor	A*32:08	A*32:08
HLA A: MAC code for allele 2 in the donor		
Type B		

So if the first field of each pair (*line 1*) contains **MAC**, the cursor will go to the next field for the MAC code to be entered (*line 2*).

But if the first field of each pair (*line 3*) contains an exact result (A*32:08 in the example above), the next field will be skipped and should remain empty (*line 4*).

➤ **MACs (Multiple Allele Codes) /previously known as NMDP codes/**

NOTE Do not use the MACs for a result which is precise but which does not appear in the pull down menus. See below for instructions on what to do in this case.

➤ **P & G codes**

Do not use the MAC Lookup tool (MAC Service UI) for results showing a P or G suffix. These are alleles that encode for identical peptide binding domains ('P') and alleles that share identical nucleotide sequences for the exons encoding the peptide binding domains ('G'). These notations are accepted by the NMDP but they are not included in the allele codes. The P and G groups have been added to the drop-down list of labels in ProMISe, so you can select them from here and enter them in the same way as you would an exact result.

In all other cases when the result is not precise, use the MAC Lookup tool (MAC Service UI) at:

<https://hml.nmdp.org/MacUI/>

Too look up an allele list to find MAC:

- Select IMGT HLA DB Release. Choose the version number of the IMGT allele database release that was used for the allele list generated. **If you don't know, use the highest release number.**
- Type whatever result (CAL - Compressed Allele list) you have, for example B*18:01/18:17N. You can enter between 1 - 50 different CALs or GL strings into the Encode Input box. Each CAL or GL string must be on its own line. The UI will assign a number to the CAL or GL string. This number will be used in the Encode Result box to link the request list and MAC together.
- Click the Look Up button. All MAC results for the CALs or GL strings entered will be displayed in the Encode Result box.

MAC Service UI Look up a compressed allele list (CAL) or GL String
Create multiple allele code (MAC)
new-allelecodes@nmdp.org
Version: 1.0.22 (38751)

Select IMGT HLA DB Release: 3.26.0

Encode/Look up Input: Enter a CAL or GL string to find a MAC for the list.
Look up does not assign a new MAC.
Encode assigns a new MAC if one has not been assigned.

1. B*18:01/18:17N

Look Up Encode

Examples
CAL: DRB1*13: 02/13:36/13:67/13:96/13:109
GL String: HLA-DRB5*01:01/HLA-DRB5*02:02/HLA-DRB5*02:04

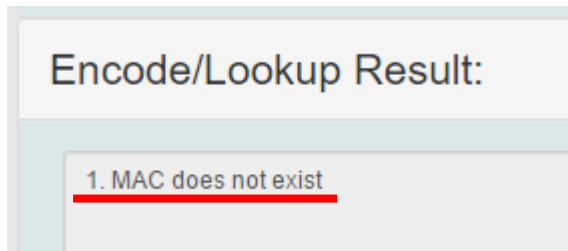
Encode/Lookup Result:
1. HLA-B*18:RRG

The result will be the letter identifying the [locus*] followed by a code of up to 7 characters, here B*18:RRG, which is universally accepted.

Type this entry exactly as shown in the corresponding MAC field in the EBMT database. You can also highlight the entry and copy/paste it into the corresponding field.

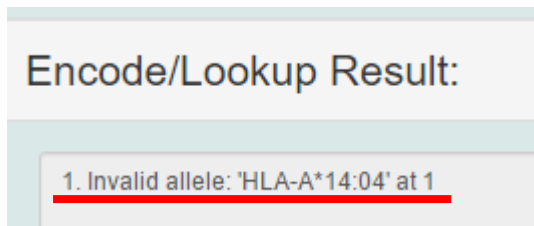
Note: lab results prior to 2010 will show the old nomenclature without : in between the digits (see example below).

If the MAC doesn't exist for the entered result (CAL or GL string) you will get the following message:



In that case you need to **encode** a new MAC with an allele list. After you entered your result(s) in the 'Input' window click the Encode button. It will generate new MAC(s) and return them in the Encode Result box.

If the entry is not valid you will get an error:



Please recheck your data.

More help and information on the MAC Lookup tool (MAC Service UI) can be found here:

<https://hml.nmdp.org/MacUI/static/instructions.html>

Another way to recheck your data is to do a search of all the known NMDP codes in existence. The webpages:

<https://bioinformatics.bethematchclinical.org/HLA/alpha.v3.html>

<https://bioinformatics.bethematchclinical.org/HLA/numeric.v3.html>

have all the MACs in alphabetical or numerical order with their corresponding allelic codes. You can use standard "find" shortcuts (Ctrl-F for English keyboards) to find the ambiguous code you are interested in. In the above example, you can search for "18:01/18:17N".

IMPORTANT NOTE - DONOR and PATIENT IDENTIFICATION

The Donor ID is an important part of the donor questions in the MED-AB forms and Donor Outcome forms and is used by the Donor Registries. PLEASE MAKE SURE TO FILL IT IN!

Another identification item that has been added in 2016 is 'Patient ID given by the Donor Registry or the Cord Blood Bank'. It is an Identification given by the Donor Registry or the Cord Blood Bank to the recipient. Although, this is currently an optional field, it is extremely important information, which helps in identifying the correct set of data. It is always the best practice to collect all possible unique identifications.

NOTE: The CIBMTR and NMDP have requested that the donor ID given by the registry, which we store in the field "Identification of donor given by donor registry" be entered as a number only, but retaining the leading zero if it exists.

Please do not enter dashes between numbers, nor add "NMDP" or other characters to the beginning of the donor id, and do not drop leading zeroes.

We provide some examples as illustration:

As it is now	As it should be	
0257-8376-2	025783762	No dashes between numbers
NMDP0323-4119-0	032341190	No additional characters, no dashes between numbers
81706343	081706343	Keep leading 0's
US033941345	033941345	No additional characters
0699-30685	069930685	No dashes between numbers

The reason for this is to facilitate the identification of the donor when EBMT forwards the data to the CIBMTR for those centres that have requested it and ensure data integrity.

Donor Identification: Cord Blood

In addition to the ID for Donor Registries, we have a specific ID field for Cord Blood banks. "Identification of the CBU given by the cord blood bank". Note that this field is be used exclusively for the identification of cord blood units. Please only fill for Cord Blood. The navigation in Promise should skip this field for other sources of cells (BM, PB). If you notice any problems please contact the EBMT Registry Helpdesk.

PLEASE REFER TO OUR MED-AB FORMS MANUAL UNDER THE SECTION "**DONOR AND STEM CELL SOURCE**" FOR FURTHER INFORMATION ON DONOR REGISTRIES, HLA MATCH TYPE, ETC.

4. Further recommendations

- 1) If results have not been provided by the laboratory for a certain locus (both alleles), please use the code **NE (Not evaluated)**:

DRB1*16:32	DRB1*16:32
DRB1*16:33	DRB1*16:33
DRB1*16:34	DRB1*16:34
DRB1*16:35	DRB1*16:35
DRB1*16:36	DRB1*16:36
DRB1*16:37	DRB1*16:37
DRB1*16:38	DRB1*16:38
DRB1*16:39	DRB1*16:39
DRB1*16:40	DRB1*16:40
DRB1*16:41N	DRB1*16:41N
DRB1*16:42	DRB1*16:42
DRB1*16:43	DRB1*16:43
DRB1*16:44	DRB1*16:44
MAC	MAC (old NMDP code)
NE	Not evaluated
OOVR	Only one value reported

- 2) Where only one result is reported for a certain loci (possible homozygous), you should enter the reported result in the 1st chromosome.
For the 2nd chromosome, use code **OOVR** (only one value reported):

C*18:01P	C*18:01P
C*18:02	C*18:02
C*18:03	C*18:03
C*18:04	C*18:04
C*18:05	C*18:05
C*18:06	C*18:06
C*18:07N	C*18:07N
C*18:08	C*18:08
C*18:09	C*18:09
C*18:10	C*18:10
MAC	MAC (old NMDP code)
NE	Not evaluated
OOVR	Only one value reported

- 3) If the result is precise but the code cannot be found in the pull down menu, this may have two different explanations: New HLA codes are being discovered continuously and they may not have been added to the labelsets as yet; alternatively, the results may contain typing errors and they would need to be corrected at source. Therefore, you should check for its existence. To do this, access the website pages:

<http://hla.alleles.org/alleles/class1.html> for loci A, B and C
<http://hla.alleles.org/alleles/class2.html> for loci DRB1, DQB1 and DPB1

- If you cannot find the code, contact the centre or laboratory from where the data originates and seek an explanation or correction.
 - If you find the code, contact the Registry helpdesk at registryhelpdesk@ebmt.org requesting that the code be added to the drop down menu.
- 4) Never derive serologic results from allelic results. If serology typing has not been done, this should be explicitly stated by answering “No” to the question **Serology HLA typing** done, and all the serology results fields will be left empty.
- 5) Sometimes, we can have DNA/molecular results (identified by a *) with 2 digits only. For instance, Cw*08 is a partial code of the set C*08:02:01, C*08:02:02, etc. because sometimes the whole matching is not done. In that case, enter this result as C*08 in the DNA fields.
- 6) In DNA results if a code with 4 or more digits cannot be found, it is acceptable to enter the first 2 digits while awaiting further clarification. For example, if you did not find B*07:113, then B*07 could be entered in the meantime.

- 7) If you have more than one type of result, which one should be entered?
- Generic and allelic (generic A*26:KDSK / allelic A*26:01, generic B*18:PZEN / allelic B*18:01, generic C*07:RGFU / allelic C*07:01) : we recommend entering the allelic, as it provides us with information about both the antigen and the allele.
 - An exact result (03:01) and an MAC (A*03:AXTK): please enter the exact result (03:01) as this is the specific allele rather than a range of allele options.
 - Between “A*02:XX1” and “A*02:KTUC”, please choose the MAC option, as it provides us with a range of options, as opposed to the first one, which gives us only the antigen and not the allele.
 - Between 2 MACs, please type both of them in the [MAC lookup tool](#) and choose the shortest of the 2 options, as this will give you the narrowest range of allele options.

Only enter data when you are sure they are correct.
For any problem, please contact the EBMT / National Registry.

5. Useful links

Full list of alleles:

<http://hla.alleles.org/alleles/class1.html>

<http://hla.alleles.org/alleles/class2.html>

MAC Lookup tool (MAC Service UI):

<https://hml.nmdp.org/MacUI/>

*Ambiguous codes: MAC (previously known as NMDP codes) Allele Code List
in Alphabetical Order:*

<https://bioinformatics.bethematchclinical.org/HLA/alpha.v3.html>

in Numerical Order:

<https://bioinformatics.bethematchclinical.org/HLA/numeric.v3.html>

G and P codes:

http://hla.alleles.org/alleles/g_groups.html

http://hla.alleles.org/alleles/p_groups.html