INTRODUCTION

A patient's level of immunologic risk for transplantation can be defined by:

- Sensitisation history.
- Detection and characterisation of HLA specific antibodies
- The titres of the various HLA-specific antibodies, as appropriate
- Repeat mismatches from previous transplants.
- Aggressiveness of immune response to previous transplant
- Numbers of pregnancies and date of most recent pregnancy
- Antibody trend – decreasing or increasing.
- Donor relationship – husband to wife or child to mother
- Likelihood of repeat transplant and avoidance of donors with high eplet mismatches or loads.

An assessment of the above factors provides the scientist information to define a list of HLA donor antigens that would be unacceptable for an individual recipient to be transplanted.

The HLA Antigens in the Unacceptable Antigens (UA) list will be used in the Transplant Waiting List (TWL) and Kidney Paired Donation (KPD) Matching algorithms to exclude the patient from an offer of an incompatible organ.

For patients being matched via the Match Profile Comparison algorithm, UA list will warn the Transplant Unit of the presence of an antigen defined as Unacceptable using specific criteria. The Transplant Unit may then make an informed decision about whether to proceed.

UNACCEPTABLE ANTIGENS IN ORGANMATCH TWL MATCHING ALGORITHMS

In the TWL matching algorithms, exclusions based on UA depend on the resolution of the HLA typing of the deceased donor and the level of definition of the UA.

In most cases, the deceased donor typing resolution will be one field. However, 2 fields will be required to define certain antigen groups; for example, B*15:01, B*15:02, DQB1*03:01, DQB1*03:02 are common examples.

OrganMatch logic:

- If the UA-TWL are assigned at 1 field only, and the donor HLA typing is defined at 1 field then a comparison of the loci and Allele occurs at 1 field.
- If the UA-TWL are assigned at 2 field only, and the donor HLA typing is defined at 2 field then a comparison of the loci and Allele occurs at 2 fields.
- If the UA-TWL are assigned at 2 field only, and the donor HLA typing is defined at 1 field then a comparison of the loci and Allele occurs at 1 field.
- If the UA-TWL are assigned at 1 field only, and the donor HLA typing is defined at 2 field then a comparison of the loci and Allele occurs at 1 field.

If the donor HLA typing and the UA returns a match, the recipient is blocked during the High Level Compatibility Check (HLCC) during the matching process.

Logic	Donor Antigen	Recipient UA	Excluded in HLCC
1	DQB1*03	DQB1*03	Yes
1	DQB1*03	DQB1*02	No
1	A*02	A*03	No
2	DQB1*03:01	DQB1*03:01	Yes
2	DQB1*03:01	DQB1*03:02	No
3	DQB1*03	DQB1*03:01 DQB1*03:02 DQB1*03:03 DQB1*03:xx	Yes Yes Yes Yes
3	DQB1*06	DQB1*06:04 DQB1*06:09	Yes Yes
4	DQB1*03:01	DQB1*03	Yes

In the situation where the donor typing needs to be defined at 2 fields, if there is more than one allele that defines the same antigen, they should both be added to the UA.

For example if the patient has a UA to B*15:11 they should be excluded from all donors that are typed as B75. B*15:02 should also be added to the UA for this patient to avoid them being offered a B75 donor which would be considered incompatible. See Appendix 2 for further examples.

Similarly if the previous donor typing is not the common allele and the patient has not developed antibodies to the common allele, the addition of the common allele to the UA should be considered.

For example if the previous donor mismatch is B*15:25 and the patient hasn't developed antibodies to B62, if the patient is to be excluded from B62 donors then B*15:01 should also be added as a UA.

USE OF ACCEPTABLE ANTIGENS IN ORGANMATCH

If the UA-TWL are assigned at 2 field only and the donor HLA typing is defined at 1 field then a comparison of the loci and allele occurs at 1 field (as per logic 3 above). However, there may be an allele from which the recipient should not be excluded; that is, the HLA allele is an acceptable mismatch.

For example: Recipient HLA typing: HLA A*01,*02; B*07,*08; DRB1*04; DQB1*03:01.

The recipient may have become immunised against DQB1*03:02 due to a previous donor mismatch, so DQB1*03:02 is defined as UA.

Compatible future donors will need to be matched for DQB1*03:01. DQB1*03:02 donors are incompatible

Using logic 3 above, this patient would be excluded from all donors typed as DQB1*03 due to UA listed as DQB1*03:02

In order for a recipient to be considered for matching and not excluded with the donor during the High Level compatibility check, DQB1*03:01 should be added as an acceptable antigen (AA).

This will result in the following matching outcomes:

Donor Antigen	Recipient Acceptable Antigen	Recipient UA	Exclusion (Yes/No)
DQB1*03	DQB1*03:01	DQB1*03:02	No
DQB1*03:01	DQB1*03:01	DQB1*03:02	No
DQB1*03:02	DQB1*03:01	DQB1*03:02	No – but flagged as potentially UA

COMMON SITUATIONS

See the following common situations requiring Acceptable Antigens (specific to One Lambda bead panel), and impact of Acceptable Antigens on donor availability:

Example 1: A*11:02 is UA, but A*11:01 antibodies not detected.

A*11:01 should be added as an Acceptable Antigen. As a result, the recipient will not be blocked from A*11 donors at the HLCC, but will instead generate a Match Event with Potential UA to A*11:02.

The A*11:01 allele is present in 98.9% of A*11 allele typed donors, A*11:02 is present in only 1.1%. The presence of the A*11:01 AA increases the chance of this patient finding an appropriate matched donor.

Example 2: A*24:03 is UA, but A*24:02 antibodies not detected.

The A*24:03 allele is present in only 2.14% of A*24 allele typed donors. Without the presence of an A*24:02 AA, this patient will be excluded from all A*24 donors, 98% of which are actually acceptable.

Example 3: DRB1*04:02 is UA, but DRB1*04:01 is self

DRB1*04:01 must be added as an AA. Without the appropriate AA, the HLCC will block this patient from being matched to all DRB1*04 donors, thus depriving them the opportunity of a DRB1 matched donor.

Acceptable Antigens should only be assigned with 2 fields.

DEFINING UNACCEPTABLE ANTIGENS IN ORGANMATCH

In OrganMatch, these HLA antigens will be defined as unacceptable antigens (UA) and can be categorised as follows:

- Antibody sourced
- Previous donor mismatches
- Other

ANTIBODY SOURCED

Unacceptable antigens may be defined by identification and characterisation of HLA-specific antibodies.

Serum samples are obtained from all patients on the transplant waiting lists and KPD programs and tested regularly for identification of anti-HLA specific antibodies to detect any changes in antibody levels or specificity.

Additional antibody screening should be performed following notification of a potentially sensitising event. In addition to transfusion, transplantation and pregnancy, such events may include trauma, infection, vaccination, or any condition that provokes an inflammatory response.

If a change in antibody titre and/or specificity is detected, the patient's listing of antibody defined, unacceptable antigens should be reviewed and updated in a timely manner in OrganMatch.

PREVIOUS DONOR MISMATCHES

For patients enrolled in the kidney TWL and KPD programs HLA mismatches for HLA A, B, DRB1 from previous grafts are commonly defined as unacceptable antigens in the Matching algorithms.

HLA mismatches with HLA C, DQA1, DQB1, DPA1, DPB1 may also be assigned as UA.

For kidney TWL patients with a functioning previous transplant (e.g. lung or liver), it may be appropriate to review whether previous mismatches are defined as unacceptable antigens. This review must be performed in the context of the sensitisation history of the patient, and in collaboration with the transplant unit and clinical unit as appropriate.

OTHER

UA may be defined and categorised as UA–Other in OrganMatch for a number of reasons, as follows:

PAEDIATRIC AND YOUNG ADULT RECIPIENTS

Many young patients will require multiple transplants during their lives and therefore strategies to prevent HLA sensitisation are important.

Some units attempt to avoid high eplet load mismatches. A strategy also used is to avoid paternal/maternal mismatched HLA antigens. These can be added to OrganMatch as Other-UA.

UNACCEPTABLE EPLET MISMATCH

Where an HLA Matchmaker eplet has been identified as unacceptable because of allo-immunisation, alleles belonging to this eplet that are not represented on the Luminex single antigen bead panel may be added using as Other-UA.

For example, DPB1*16:01 is part of the immunogenic DEAV epitope, however it is not included in the One Lambda SAG bead panel. DPB1*16:01 may be added as type Other-UA, with Reason as DEAV epitope. The epitope can be selected from the epitope column. A full list of antibody verified epitopes can be viewed from the epregistry.br website: https://www.eprigistry.com.br/.

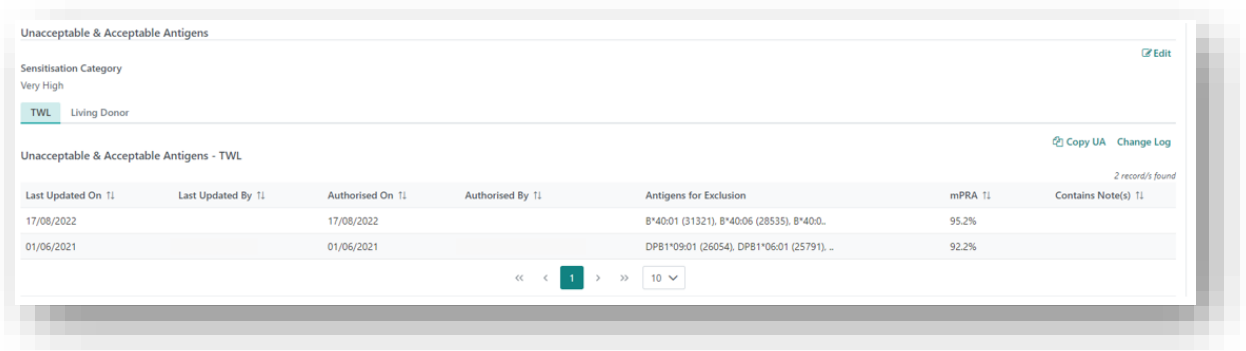
COMPATIBLE PAIRS PARTICIPATING IN KPD

Patients with a compatible live donor may participate in the KPD program to obtain improved HLA matching compared to their compatible donor. This can be achieved by entering the co-registered donor's HLA mismatches plus or minus the additional high eplet mismatched antigens as UAs in the LDD UA field, Match Profile.

TRACKING CHANGES OF UNACCEPTABLE ANTIGENS

Changes to a patients UA are traceable via the row Unacceptable and Antigen table, where the changes will be tracked and easily viewed. Information includes the following data:

- Last Updated On
- Last Updated By
- Authorised On
- Authorised By
- Antigens for Exclusion
- mPRA
- Contains Note(s)



The Change log will show the type of change made to the unacceptable antigens:

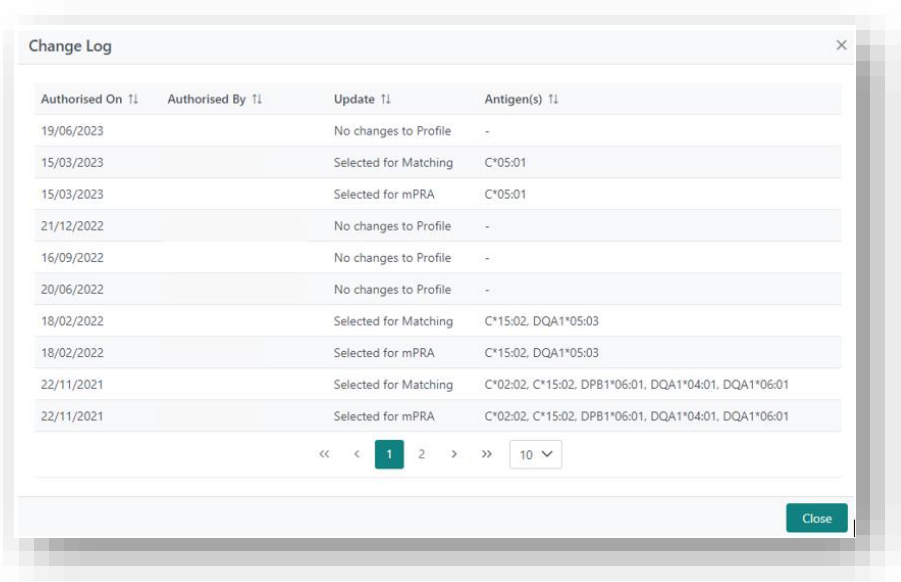
- Change in antigens selected for mPRA

- Changes in antigens selected for matching
- Changes in antigens used for exclusion

The Change log will also show the reasons for the change:

- Selected for matching
- Removed from matching
- Selected for mPRA
- Removed from mPRA
- No changes to Profile

Note: **No changes to Profile** will be displayed in the change log when there is no change in the antigens selected as unacceptable, even if there is an increase in MFI.



The Authorised UA can be copied which allows for the string of antigens to be available to paste where required. Click **Copy UA** to copy to the Authorised UA.

ADDING UNACCEPTABLE AND ACCEPTABLE ANTIGENS TO A RECIPIENT'S PROFILE

Patients with UA assigned will be excluded in the High Level Compatibility Check, and will not pass through to any matching algorithms in the TWL algorithms.

For further details see:

Principles of Kidney Matching Algorithms, OM-012
Principles of Kidney/Pancreas Matching Algorithms, OM-038
Principles of Lung Matching Algorithms, OM-041
Principles of Heart Matching Algorithms, OM-049.

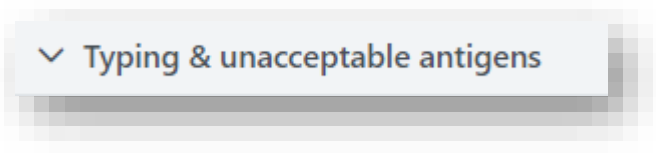
UA that are assigned in OrganMatch in:

- TWL and selected to use in matching will potentially exclude the patient from progressing through to the matching algorithms and are therefore ineligible to be offered an organ from any deceased organ donor with those antigens.
- LDD will also exclude the KPD patients from being eligible to be offered a kidney from a live donor on the KPD with those antigens.

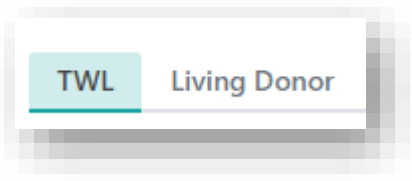
Ultimately, the decision of which HLA antigens are deemed 'unacceptable' is complicated. A myriad of donor, recipient, and institutional variables must be accounted for, such as immunosuppression, induction type, desensitisation strategies, prior donor rejection episodes, ischemia time, and number of mismatches.

ADDING UA AND AA

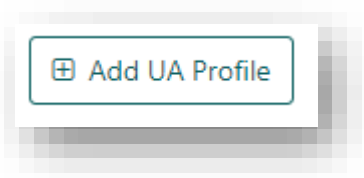
1. On the person's profile, click **Typing & unacceptable antigens**.



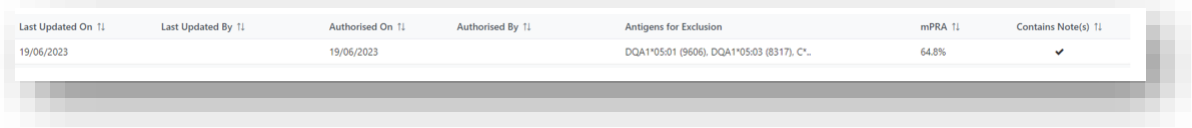
2. Click **TWL** or **Living Donor** depending on the UA to be added.



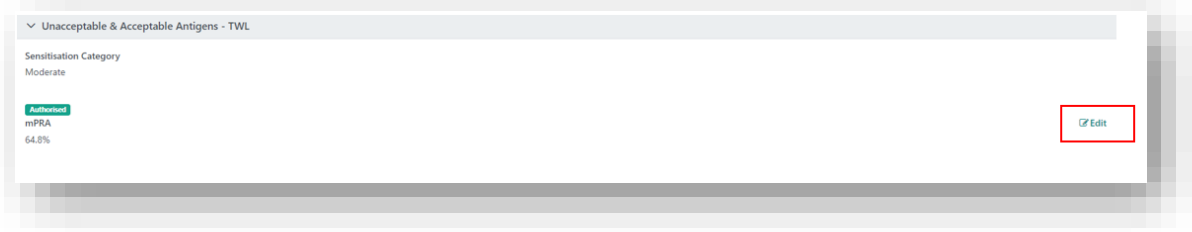
3. If there is no existing UA row, click **Add UA Profile**.



If there is an existing UA row, click on it to edit the UA.



4. A new page will open with the patients HLA typing, previous transplants and unacceptable and acceptable antigens. Click **Edit** in the **Unacceptable & Acceptable Antigens** section.

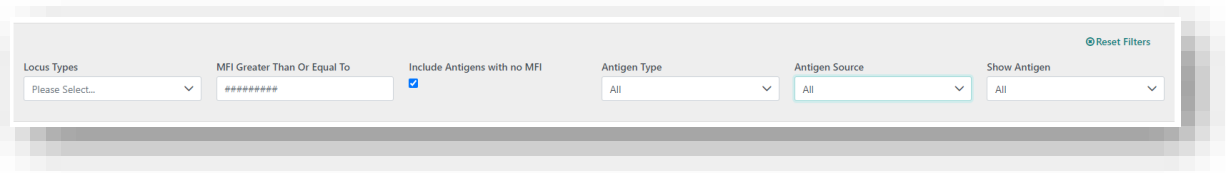


5. This **Unacceptable & Acceptable Antigens** section is populated with antigens from several areas, as relevant to the patient, such as:
   - Antibodies from the most recent antibody consolidation.
   - Previous donor HLA Typing – the donor's HLA typing from the match profile. Antigens that share the same first field as the recipient's typing will be highlighted in red.

   Note: If a previous donors typing is modified after the UA is authorised, a review of the UA is required, and the UA may need to be reauthorised.

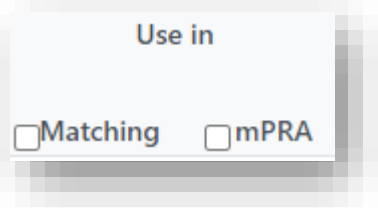
6. Enter the MFI and filter the UAs:
   - In the **MFI Greater Than or Equal to** field, enter an MFI cut-off to filter the Unacceptable Antigen list.
   - Select **Antibody Source** and then tick the **Matching** check box to select all the antigens on the screen to be included in the UA list. Antigens can also be selected individually by ticking the **Matching** checkbox on the specific row.
   - Use the filter for **Antigen Source** to ensure that only the intended antigens are included when using the overall **Matching** check box.
   - If different MFI cut-offs are required for different loci, use the Locus Types Filter to apply these criteria.
   - Any antigens that have the same first field as the patients typing will be highlighted red.

   Note: MFI is only starting point for assignment of UA. Each case needs to be reviewed.

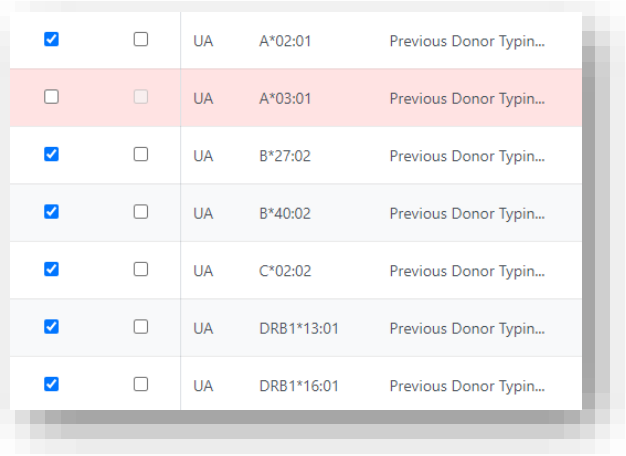


7. Tick the **mPRA** check box to select the unacceptable antigens to include in the mPRA calculation.

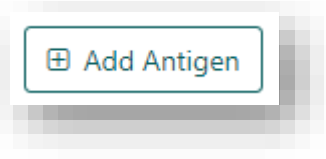
   Note: Use in **mPRA** check box can only be selected if the use in **Matching** check box has been selected.



8. Review the Previous Donor Mismatches details and tick the **Matching** check box to select antigens to be included in the UA list.

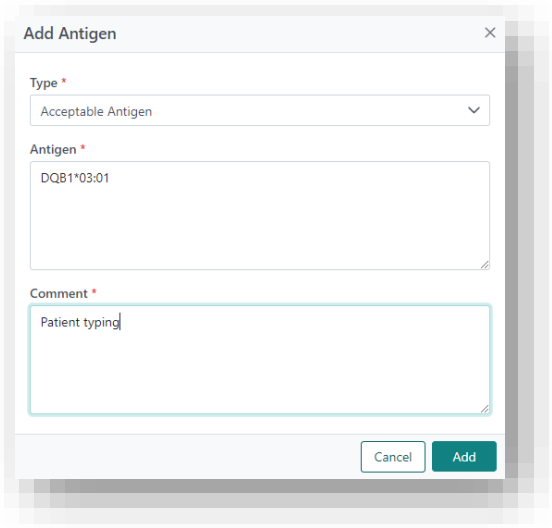


9. If required manually add other antigens by clicking **Add Antigen**.

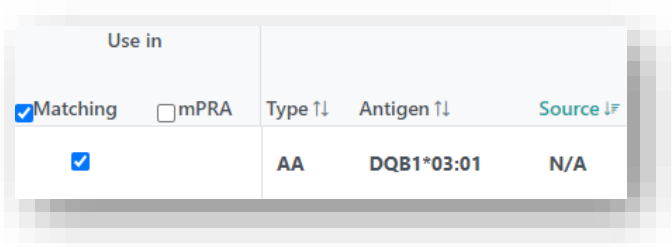


   Select the **Type** as **Acceptable Antigen** or **Unacceptable Antigen;** enter the **Antigen** and a **Comment** for the reason. Click **Add**.

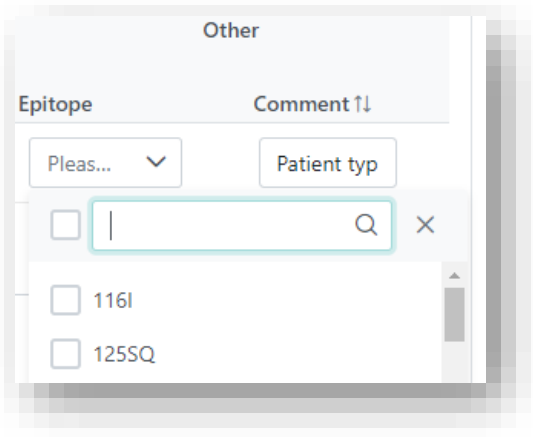
The UA can be 1 or 2 field but the AA should be entered as 2 field. If multiple antigens are to be added, separate the antigens with a comma.



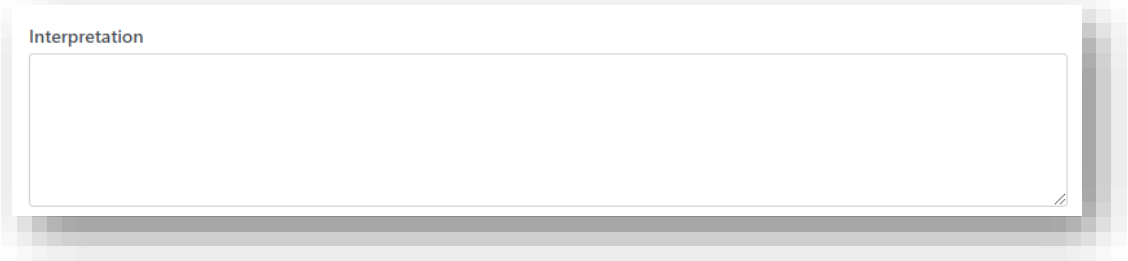
Note: The **Matching** check box is automatically ticked for each antigen added.



10. For any assigned antigen, an associated epitope may be selected from the **Epitope** dropdown.

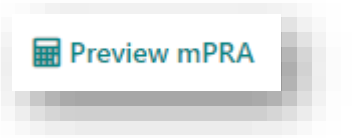


11. The **Interpretation** field may be used for communication to Transplantation Portal users. Contents of this field are visible in the Transplantation Portal.

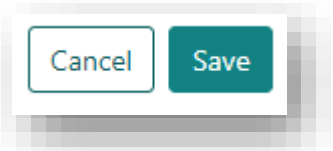


12. To calculate the mPRA prior to saving click **Preview mPRA**.

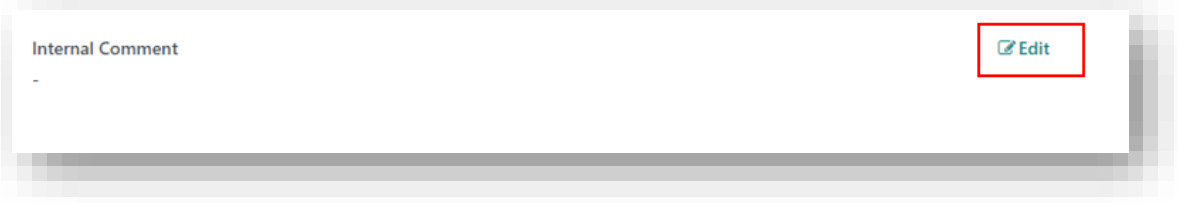
    If required further antigens can be ticked or unticked and the **Preview mPRA** button can be clicked again to update the mPRA prior to saving.



13. Once all applicable antigens have been selected, click **Save**.



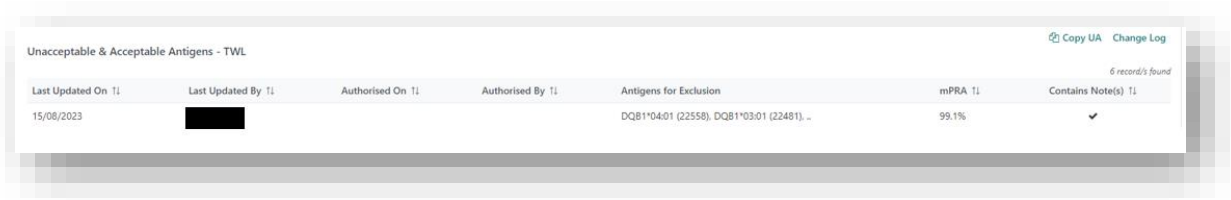
14. The **Internal Comment** field may be used for internal communication in the lab portal, contents of this field are not visible in the Transplantation Portal. To add comments to the **Internal Comment** field, click **Edit**, add the comment, and click **Save**.



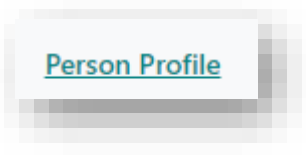
15. The notification ***Authorise Unacceptable & Acceptable Antigens*** is generated in the laboratory portal.

16. The Unacceptable and Acceptable antigen table will show the following information:
    - Last Updated On
    - Last Updated By
    - Antigens for Exclusion
    - mPRA
    - Contains Note(s)

    At this stage the Unacceptable and Acceptable antigens are NOT authorised. This is clearly indicated as the following columns are blank.
    - Authorised On
    - Authorised By



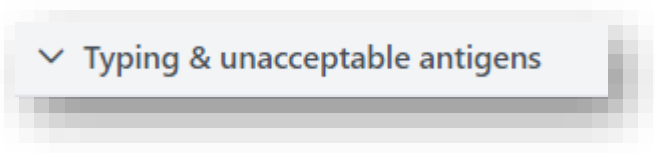
17. Click **Person Profile** to return to the patients record.



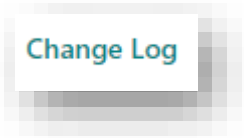
IMPORTANT! At this point, the new UA profile has not been promoted to match profile, and any matching that occurs in the interim period will access the previously authorised UA profile. It is important that the updated UA profile is authorised promptly, to prevent a patient being matched using outdated information.

AUTHORISING UA AND AA

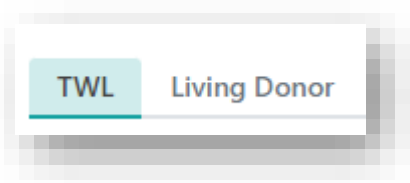
1. On the person's profile, click **Typing & unacceptable antigens**.



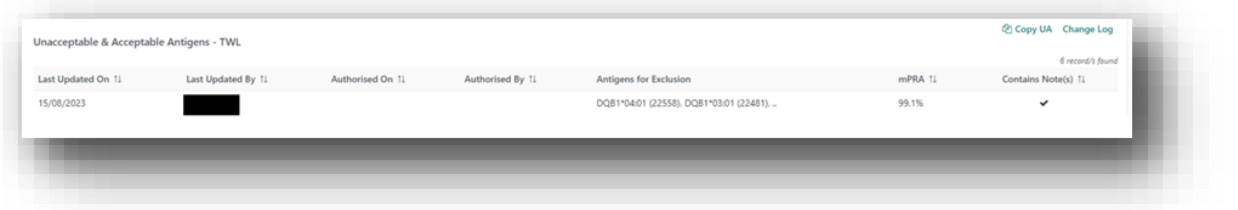
2. To view the changes in UA, click **Change Log**. Refer to **Tracking Changes of Unacceptable Antigens** for further information.



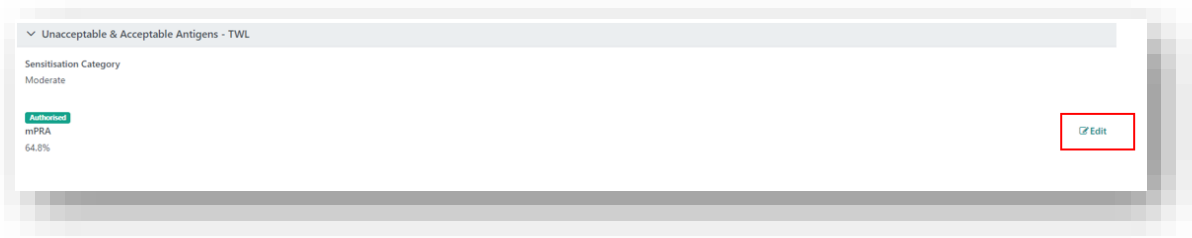
3. Click **TWL** or **Living Donor** depending on the UA to be authorised.



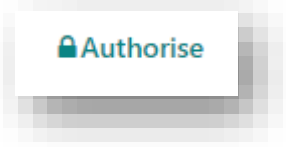
4. Click on the UA row to authorise.



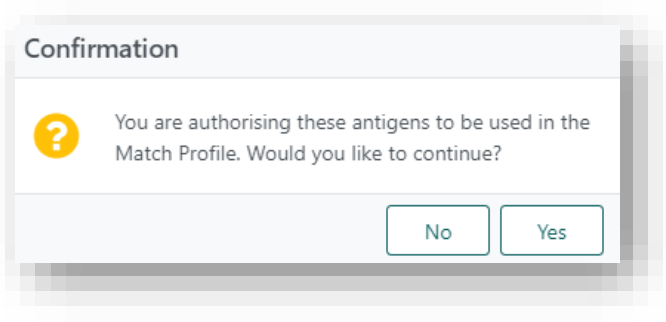
5. A new page will open with the patients HLA typing, previous transplants and unacceptable and acceptable antigens. Click **Edit** in the **Unacceptable & Acceptable Antigens** section.



6. Review the results and click **Authorise**.



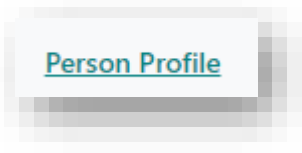
7. A confirmation box will pop up to warn the user that the authorised antigens will be used in the Match Profile. Click **Yes**.



8. The Unacceptable and Acceptable antigen table will show the following information:
   - Last Updated On
   - Last Updated By
   - Authorised On
   - Authorised By
   - Antigens for Exclusion
   - mPRA
   - Contains Note(s)

   All Authorised UA and AA will be visible to clinicians and transplant coordinators through OrganMatch Transplantation portal.

9. Click **Person Profile** to return to the patients record.



UPDATE OR EDIT PATIENT SENSITISATION CATEGORY

Patient sensitisation categorisation is based on the multiple factors, which includes an assessment of the HLA antibody results, history of sensitisation events and type of sensitisation. In OrganMatch, a single data field is used to categorise the patient. Once the patient has been reviewed, patient categorisation can be assigned.

A nationally consistent approach is required for all patients and this document should be used as a guideline in assigning this category.

The patient category was used in the implementation of virtual crossmatch to initially select the patients that required a physical crossmatch.

PATIENT CATEGORIES

There are 5 categories:

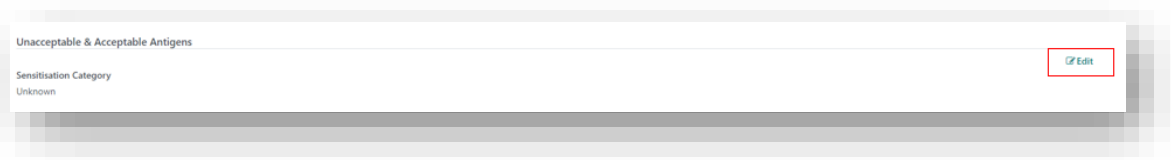
- Unsensitised
- Low
- Moderate
- High
- Very High

Patients all default to unknown prior to categorisation.
These categories are defined in Table 1 – Sensitisation Categorisation (see Appendix 1)

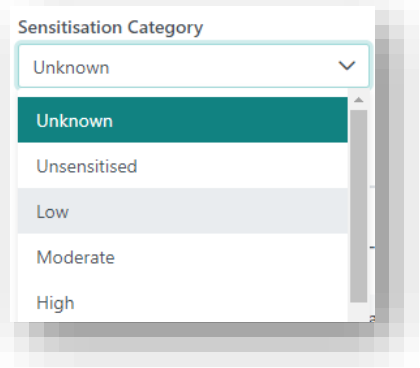
UPDATE PATIENT SENSTISATION CATEGORY

1. On the person's profile, click **Typing & unacceptable antigens**.

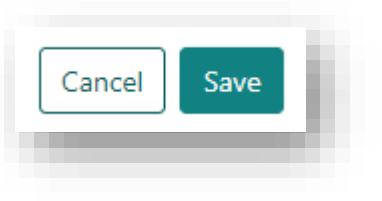
2. In **Unacceptable & Acceptable Antigens** click **Edit**.



3. In **Sensitisation Category** select the category from the dropdown.



4. Click **Save**.



APPENDIX 1: SENSITISATION CATEGORY

Sensitisation Category	HLA Antibodies Present	mPRA	UA Defined	Record of Sensitisation	Previous Transplant
Unsensitised	None Detected	Null	N/A	No	No
	Detected- no epitope defined	Null	N/A	No	No
Low	Detected - low level < 2000 (OLI) <1000 (Lifecodes)	Null	N/A	Yes/No	No
	Detected < 4000 (OLI), <2000 (Lifecodes) no epitope identified	Null	N/A	Yes/No	No
	None Detected	Null	Yes (pre tx mm)	Yes	Yes
Moderate	Detected - epitope identified	<80	Yes	Yes/No	No
High	Detected < 4000 (OLI), <2000 (Lifecodes) no epitope identified	Null	Yes (pre tx mm)	Yes	Yes
	Detected - epitope identified	<80	Yes	Yes	Yes
	Detected - epitope identified	80-95	Yes	Yes	Yes/No
Very High	Detected - epitope identified	95-100	Yes	Yes	Yes/No

APPENDIX 2: SUGGESTED UNACCEPTABLE ANTIGENS FOR INCLUSION

In using the below table the composition of the Single Antigen testing panel should be considered.

Antigen Group	Recipient UA
B45	B*45:01 and B*50:02
B61	B*40:02, B*40:03, B*40:04 and B*40:06
B62	B*15:01, B*15:04, B*15:06, B*15:07, B*15:20, B*15:24, B*15:25 and B*15:27
B63	B*15:16 and B*15:17
B71	B*15:10 and B*15:18
B75	B*15:02, B*15:11 and B*15:21
Cw10	C*03:02 and C*03:04
DP402	DPB1*04:02 and DPB1*105:01
DP13	DPB1*13:01 and DPB1*107:01
DQ7	DQB1*03:01 and DQB1*03:19
DR18	DRB1*03:02 and DRB1*03:03

DEFINITIONS

Term/abbreviation	Definition
AA	Acceptable Antigen. Antigens that may be considered for organ transplantation purposes.
HLCC	High Level Compatibility Check
KPD	Kidney Paired Donation
MFI	Mean Fluorescence Intensity
mPRA	Match calculated panel-reactive antibody. Provides an estimate of the percentage of deceased organ donors that will be incompatible for a recipient based on the antigens assigned as unacceptable for a recipient. This is based on a pool of donors from the Australian population and should represent the HLA antigen frequency in the population. If more than one HLA antigen is unacceptable, the mPRA is the total frequency of the HLA antigens.
LDD	Living Directed Donation
SAG	Single Antigen Luminex test
TWL	Transplant Waiting List
UA	Unacceptable (HLA) Antigen. Antigen that has been determined as high risk with any potential donor and should be avoided for transplantation purposes
UA List	The List of antigens that appear on the recipients Match Profile and will be used in the matching algorithms to exclude recipients with potential donors.

REFERENCED EXTERNAL DOCUMENTS

Document title	Source
Antibody verified epitopes	https://www.eprigistry.com.br/

REFERENCED INTERNAL DOCUMENTS

Document number	Source
OM-012	Principles of Kidney Matching Algorithms
OM-038	Principles of Kidney/Pancreas Matching Algorithms
OM-041	Principles of Lung Matching Algorithms
OM-049	Principles of Heart Matching Algorithms

CHANGE HISTORY

Version number	Effective date	Summary of change
-	-	For previous change histories contact the National OrganMatch Office.
8	26/07/2022	Update for OrganMatch sprint 34 – process change: • Section 1 updated to include Preview mPRA feature • Section 2 updated to include Copy UA feature
9	05/09/2023	• Update to new template • Addition of information in Unacceptable Antigens covering the scenarios of different alleles for the same antigen group • Update to Adding UA and AA section when a previous donor typing is modified. • Addition of Appendix 2
10	Refer to footer	• Annual document review, no changes.

ELECTRONIC SIGNATURE

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