

INTRODUCTION

The Australian Organ donation and Transplantation system previously used complement-dependent cytotoxicity (CDC) crossmatches and Donor Specific Antibody (DSA) assessment to determine compatibility between an organ donor and potential transplant recipients.

The Virtual crossmatch (VXM) project was completed in February 2023 and uses detailed information about the HLA antibody profile of recipients combined with accurate HLA typing of the donor to assess whether potentially damaging antibodies are present. The VXM and DSA assessment are analogous.

Internationally many transplant programs have moved to conducting VXM only which provides comprehensive detail regarding the compatibility of the donor organ and recipient without the need for a physical crossmatch in most circumstances.

ENDORSEMENT OF VXM IMPLEMENTATION IN AUSTRALIA

The National Tissue Typing Committee (NTTC), Transplantation Society of Australia and New Zealand (TSANZ) and its subcommittee, The Virtual Crossmatch committee, OrganMatch Strategic Governance Committee (OMSGC) have endorsed the following changes which were implemented in February 2022 (Phase 2b), July 2022 (Phase 2c), October 2022 (Phase 3) and the final phase in February 2023.

It is an essential requirement for all potential recipients awaiting a solid organ transplant in Australia to be listed in OrganMatch (OM) to enable the VXM.

Refer to Appendix 1 – for detailed information of the VXM Transition plan

COMPONENTS OF THE VIRTUAL CROSSMATCH

PATIENT WORKUP

All patients being worked up for a solid organ transplant require histocompatibility testing to be eligible for activation onto the deceased donor transplant waiting list (TWL). High resolution HLA typing at all loci is performed as well as Luminex - Single Antigen Bead testing to identify the patient's HLA antibody profile. The Tissue Typing laboratory scientists will review any antibodies detected in the Single Antigen Bead assay with the recipient's sensitisation history, including previous transplants. The unacceptable HLA antigens are assigned by the laboratory which will be used to exclude recipients from an offer of an incompatible donor in the matching algorithms.

Once all testing is complete the recipient will be activated onto the TWL. The readiness criteria in OrganMatch (OM) also needs to be met for a recipient to be available for matching with a deceased donor. This readiness criteria includes:

- 1 field HLA typing at all loci,

- an authorised unacceptable antigen profile,
- ABO result confirmed in OrganMatch,
- Single Antigen Class I and II results tested within 120 days
- Specific organ clinical parameters
 - Kidney- dialysis start date for the kidney recipients on TWL.
 - Heart- Height and weight
 - Lung- Height, weight and acceptable donor height range
 - Kidney/Pancreas- waiting time calculated from the date eGFR became <15.

If these criteria are not met, the recipient will be deemed “not ready” and won’t be matched against any donors.

ONGOING PATIENT ASSESSMENT

An essential component for the implementation of VXM is increased frequency of HLA Single Antigen testing. Testing is performed four times a year for patients on the TWL. When reviewing the Single Antigen results, it is recommended, the laboratory will update the unacceptable antigens and select the recipient’s sensitisation category (See Appendix 1).

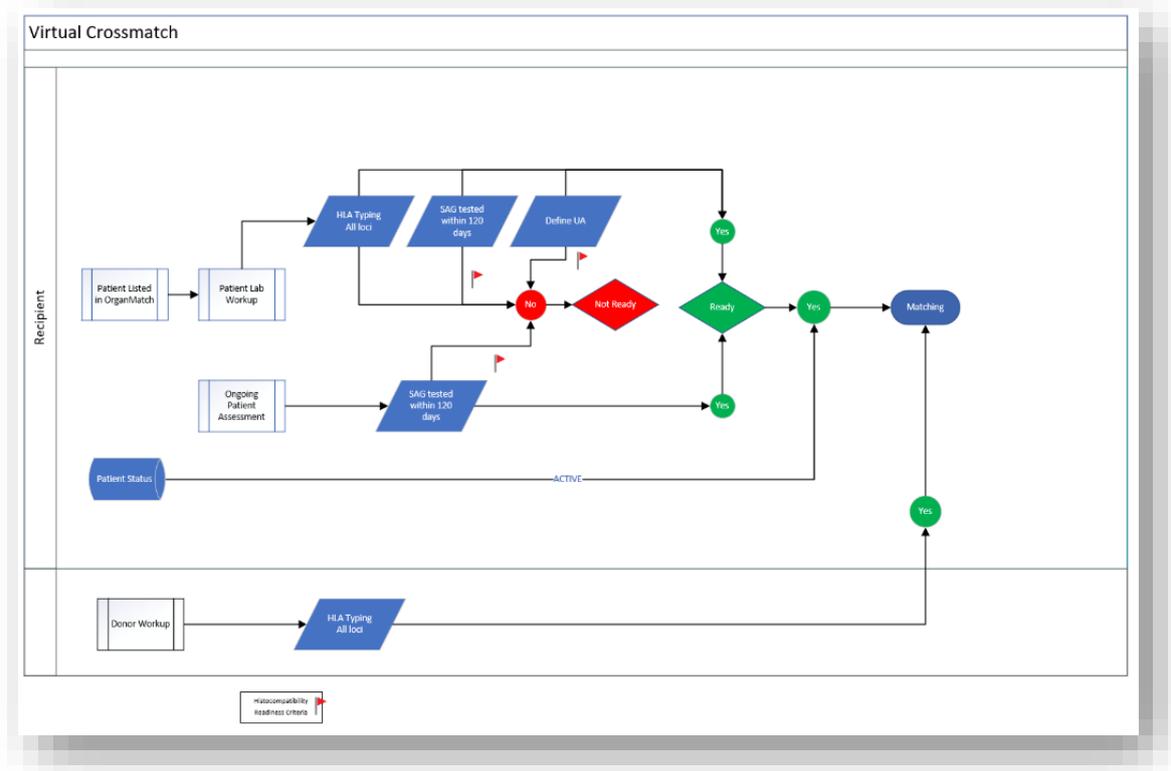
As the readiness criteria for matching includes a 120-day expiry for Single Antigen results, a notification will be sent to the Senior Lab User and Advanced Lab User role 20 days prior to expiry. This alerts the laboratory about any recipients who require Single Antigen testing in 20 days to ensure they are ready for matching.

MATCHING

When a potential deceased donor is identified, samples are sent to the laboratory for compatibility testing against potential recipients on the TWL. The donor demographics and medical information are entered into OM. HLA typing of the donor is performed and the ABO and HLA typing results are also entered into OM which allows the donor to be ready for matching. Once matching has occurred, laboratory staff perform a VXM for all recipients and issue an organ offer list (OOL).

The following flow chart summarises the VXM process.

ORGANMATCH THE VIRTUAL CROSSMATCH



POST-TRANSPLANT

Clinical and Transplant units have been requested to collect a pre-operative serum sample at the time of transplantation to be sent to the state Tissue Typing lab. This sample will be stored and tested if required.

Clinical and Transplant units should report any episodes of Antibody Mediated Rejection (ABMR) occurring within two weeks of transplantation to the state Tissue Typing laboratory. Reporting can either be via OrganMatch directly, using OrganMatch Transplantation portal, or via the Tissue Typing laboratory. Early ABMR should be added as a medical event in OrganMatch.

[Person Details – Transplantation Portal, OM-083](#)

APPENDIX 1: SENSITISATION CATEGORISATION

Patient sensitisation categorisation is based on multiple factors, which includes an assessment of HLA antibody results, history of sensitisation events, and type of sensitisation (e.g. previous transplant or pregnancy). In OrganMatch, a single data field is used to categorise sensitisation.

There are 6 sensitisation categories:

- Unsensitised
- Low
- Moderate
- High
- Very High
- Unknown

The following table is used a guideline for assessing Sensitisation:

Sensitisation Category	HLA Antibodies Present	mpra	UA defined	Record of sensitisation	Previous Transplant
Unsensitised	None detected	Null	N/A	No	No
	Detected - no epitope identified (Note these results are thought to be artefactual and not to constitute a risk to transplantation)	Null	N/A	No	No
Low	Detected - low level < 2000 (OLI) <1000 MFI (Lifecodes)	Null	N/A	Yes or No	No
	Detected < 4000 MFI (OLI), <1500 MFI (Lifecodes) no epitope identified	Null	N/A	Yes or No	No
	None detected	Null	Yes (prev tx mm)	Yes	Yes
Moderate	Detected - epitope identified	<80	Yes	Yes or No	No
High	Detected < 4000 MFI (OLI), <1500 MFI (Lifecodes) no epitope identified	Null	Yes (prev tx mm)	Yes	Yes
	Detected - epitope identified	<80	Yes	Yes	Yes
	Detected - epitope identified	80-95	Yes	Yes	Yes or No
Very High	Detected - epitope identified	95-100	Yes	Yes	Yes or No

APPENDIX 2 : VIRTUAL CROSSMATCH TRANSITION

REDUCTION IN CDC CROSSMATCHES – PHASE 2B OF VXM TRANSITION PLAN

- For kidney and kidney/pancreas recipients- CDC crossmatching was limited to sensitised recipients only.
- Unsensitised kidney and kidney/pancreas recipients only received a VXM at the time of organ offer.
- A separate VXM tray was created within OrganMatch (OM) to manage unsensitised recipients.
- The readiness criteria for kidney matching includes a 100-day expiry of Single Antigen results. A notification was sent to the Senior Lab User role 10 days prior to expiry.
- All heart, lung and liver transplant recipients continued to have a CDC crossmatch. Retrospective flow crossmatches (FXM) could be performed if required.

REDUCTION IN CDC CROSSMATCHES- PHASE 2C OF VXM TRANSITION PLAN

- For kidney and kidney/pancreas recipients the CDC crossmatching was limited to recipients with mPRA>80%.
- All other kidney and kidney/pancreas recipients received a VXM at the time of organ offer.
- Unsensitised heart and lung recipients received a VXM at the time of organ offer and sensitised recipients continued to have a CDC crossmatch.

REDUCTION IN CDC CROSSMATCHES- PHASE 3 OF VXM TRANSITION PLAN

- CDC crossmatching ceased for all kidney, kidney/pancreas, pancreas and pancreas islets recipients.
- Kidney, kidney/pancreas, pancreas and pancreas islets recipients received a VXM at the time of organ offer.
- CDC crossmatching ceased for unsensitised lung and heart recipients. These recipients received a VXM at the time of organ offer. The CDC crossmatch was limited to sensitised recipients with DSA present.

REDUCTION IN CDC CROSSMATCHES- FINAL PHASE OF VXM TRANSITION PLAN

- CDC crossmatching ceased for all lung and heart recipients.
- All recipients received a VXM at the time of organ offer.
- The readiness criteria for kidney, kidney/pancreas, heart and lung matching includes a 100-day expiry of Single Antigen results. A notification is sent to the Senior Lab User role 20 days prior to expiry.

Note: In December 2023 the readiness criteria was updated to a 120-day expiry of Single Antigen results.

DEFINITIONS

Term/abbreviation	Definition
ABMR	Antibody Mediated Rejection
CDC	Complement Dependent Cytotoxicity (assay)
eGFR	Estimated Glomerular Filtration Rate. A key indicator of kidney function.
FXM	Flow Cytometric Crossmatch
MFI	Mean Fluorescent 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.
NTTC	National Tissue Typing Committee
OM	OrganMatch (software)
OMSGC	OrganMatch Strategic Governance Committee
OOL	Organ Offer List
SAG	Single Antigen Luminex result
TSANZ	Transplantation Society of Australia and New Zealand
TWL	Transplant Waiting List
VXM	Virtual Crossmatch

REFERENCED INTERNAL DOCUMENTS

Document number	Source
OM-085	Person Details- Transplantation Portal

CHANGE HISTORY

Version number	Effective date	Summary of change
-	-	For previous change histories contact the National OrganMatch Office.
6	21/03/2023	Flow chart for VXM process updated to remove need to Kidney recipients to be on a tray. Content updated to past tense now that the VXM project has been fully implemented. Change over to the new template.
7	04/12/2023	SAG expiry readiness updated to 120 days in the below sections: <ul style="list-style-type: none"> • Final Phase VXM Transition. • Patient Workup • Ongoing Patient Assessment • VXM Flowchart VXM transition plan moved to appendix Additional entries added to the abbreviations table.
8	Refer to footer	<ul style="list-style-type: none"> • Annual document review • Updated reference for medical events and added referenced internal documents table.

ELECTRONIC SIGNATURE

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