1. Introduction

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

Virtual crossmatch (VXM) 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 to be implemented in February 2022.

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

Reduction in CDC Crossmatches – Phase 2b of VXM transition plan

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

2. Components of the Virtual Crossmatch

2.1. 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. The recipient's sensitisation category in OrganMatch is also defined by the laboratory. This will determine whether a virtual or CDC crossmatch will be performed at the time of a donor. If the recipient (Kidney or Kidney/Pancreas) is defined as unsensitised, only a virtual crossmatch assessment will be performed

when an organ is offered to the transplant units. If the recipient is defined as sensitised, a virtual crossmatch is performed in the first instance followed by a CDC crossmatch.

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 100 days and a dialysis start date for the kidney recipients on TWL. If these criteria are not met, the recipient will be deemed "not ready" and won't be matched against any donors.

2.2. 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 the laboratory will update the unacceptable antigens and select the recipient's sensitisation category (See Appendix 1). If the recipient was previously defined as unsensitised and has developed antibodies, they will be placed on hold until the next month trays are made. This ensures a CDC crossmatch is performed at the time of a donor rather than just a VXM, as they will still be on the virtual crossmatch tray until new trays are generated.

As the readiness criteria for matching includes a 100-day expiry for Single Antigen results, a notification will be sent to the Senior Lab User role 10 days prior to expiry. This alerts the laboratory about any recipients who require Single Antigen testing in the next 10 days to ensure they are ready for matching.

2.3. Trays – VXM vs. CDC

Solid Organ recipients active on the TWL are required to send a monthly sample to the laboratory for potential antibody assessment and crossmatch tray production. At the beginning of the month the laboratory generates and produces the crossmatch trays for the following month.

In OM a recipient set query (RSQ) is created to generate a group of patients that are suitable for inclusion on the trays. The sensitisation category is a selection criterion in the recipient set query to distinguish between the VXM tray and the CDC trays. Recipients categorised as unsensitised are included on a VXM tray and sensitised and patients not yet categorised are included on the CDC crossmatch trays.

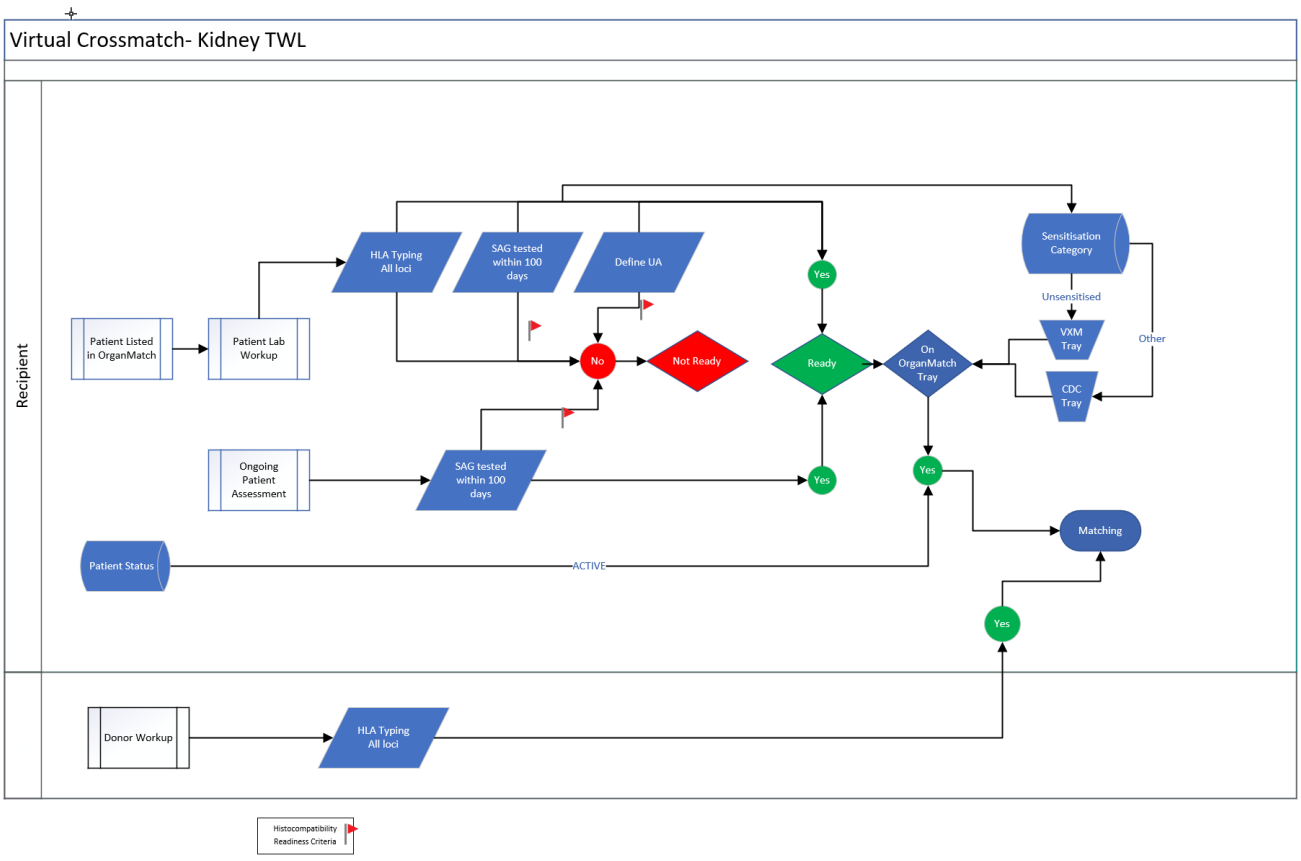
During tray production, serum is retrieved for sensitised recipients and plated onto a physical crossmatch tray. Unsensitised recipients that are allocated onto a VXM tray do not have serum retrieved as a physical tray is not plated. The VXM tray is used within OM to allow DSA assessment and matching of unsensitised recipients.

3. 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 initial organ offer list (OOL). The unsensitised recipients will only get a VXM so this is the final organ offer list (OOL) for this group. CDC crossmatching is performed for sensitised recipients, and when available the results are entered into OM and an updated OOL is generated.

The sensitisation category is displayed in the crossmatch assessment section of the OM – Match event histocompatibility assessment. When completing the match event laboratory staff can use this information to decide whether the recipient only requires a VXM or if a CDC crossmatch is to follow.

The following flow chart summarises the VXM process.



4. 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.

(https://www.donatelife.gov.au/sites/default/files/om-inf-013_om_how_to_guide_-_transplantation_portal_v8.pdf)

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.

The patient category will be used to create a virtual crossmatch tray.

There are 6 sensitisation categories:

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

The following table is used a guideline for assessing Sensitisation

Table 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 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	Yes (prev tx mm)	Yes or No	Yes or No
	None detected	Null	Yes (prev tx mm)	Yes	Yes
Moderate	Detected - epitope identified	<80	Yes	Yes or No	Yes or No
High	Detected - epitope identified	80-95	Yes	Yes	Yes or No
Very High	Detected - epitope identified	95-100	Yes	Yes	Yes or No

Definitions

Term / Abbreviation	Definition
CDC	Complement Dependent Cytotoxicity (assay)
FXM	Flow Cytometric Crossmatch
MFI	Mean Fluorescent Intensity
OM	OrganMatch (software)
OOL	Organ Offer List
RSQ	Recipient Set Query
TWL	Transplant Waiting List
VXM	Virtual Crossmatch

Change history

Version number	Effective date	Summary of change
1	Refer to footer	New process for Virtual Crossmatch.

Electronic signature

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