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# Transitioning to a national virtual crossmatch protocol for solid organ transplant offers in Australia

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## Background

In Australia, the complement dependent cytotoxicity (CDC) crossmatch has been a key component of donor and recipient histocompatibility assessment since the start of most solid organ transplant programs. A CDC crossmatch is performed by isolating donor cells and exposing them to recipient serum with the addition of exogenous complement. A positive CDC crossmatch classically occurs in the setting of a strong donor-specific antibody (DSA), indicating that the potential recipient would be at increased risk of hyperacute rejection if the transplant was to proceed.

However, internationally, most transplant programs have moved away from performing routine CDC crossmatches in favour of a virtual crossmatch (VXM). VXM uses the complete human leucocyte antigen (HLA) type of the donor and the current HLA antibody profile of the recipient to assess transplant compatibility, without a physical crossmatch. The predictive value of VXM has been substantially enhanced in recent years by advances in HLA typing which now permits typing of all relevant HLA loci in a suitable timeframe for deceased donor transplantation.

VXM significantly reduces the workload for donor compatibility assessment and provides a faster turnaround time to generate compatible recipient lists, allowing transplant units to identify suitable recipients in a shorter timeframe than is experienced with CDC crossmatching. Internationally, this has reduced cold ischaemic times and enhanced the opportunity to share organs for highly sensitised recipients. This global shift to VXM has reduced demand for the consumables required for CDC crossmatches and, as such, many companies are no longer producing the consumables necessary to perform the assay. Through the enhanced functionality of OrganMatch to conduct VXMs and the reduction in availability of CDC consumables, it is an ideal time for Australia to implement a national VXM protocol to align with international best practice.

## The transition to the VXM project

The transition to the VXM project is a collaboration between the Transplantation Society of Australia and New Zealand (TSANZ), the Australian Red Cross Lifeblood (Lifeblood) and tissue typing laboratories across Australia, with support from the Australian government's Organ and Tissue Authority (OTA). The project will implement a national histocompatibility protocol for deceased donor solid organ transplantation with the aim of providing transplant clinicians with a timely and detailed assessment of histocompatibility for potential recipients on the waiting list.

In order for this transition to occur there will be a change to practice for transplant units and patients. Figure 1 outlines how VXM will be incorporated in clinical care and practice. Figure 2 shows how the transition to VXM is taking a three-phased approach which will involve CDC and VXM being conducted concurrently for a period during the transition. This will allow clinicians to become familiar with VXM and still have the CDC crossmatch result if required.

VXM assessments are highly effective at excluding the presence of high DSA with the assignment of unacceptable antigens (UA) and antigens for exclusion (AE). However, in highly sensitised recipients, there are times when it is desirable to proceed with transplantation despite the presence of a weak or moderate DSA. In some instances, a physical crossmatch to help stratify the immunological risk of proceeding with transplant may still be necessary. Australian tissue typing laboratories are in the process of transitioning to flow cytometry crossmatch (FXM) instead of a CDC crossmatch. FXM is much more sensitive than

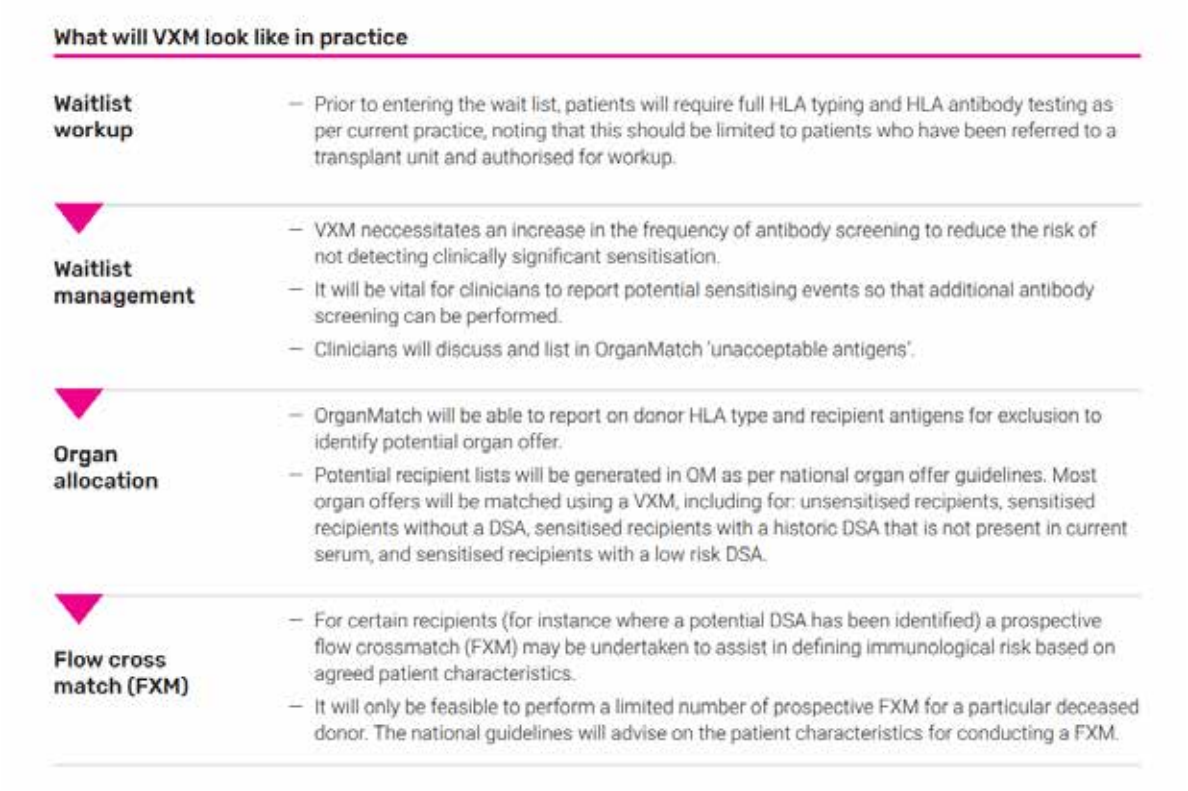


*Figure 1. How VXM will be incorporated in clinical care and practice*

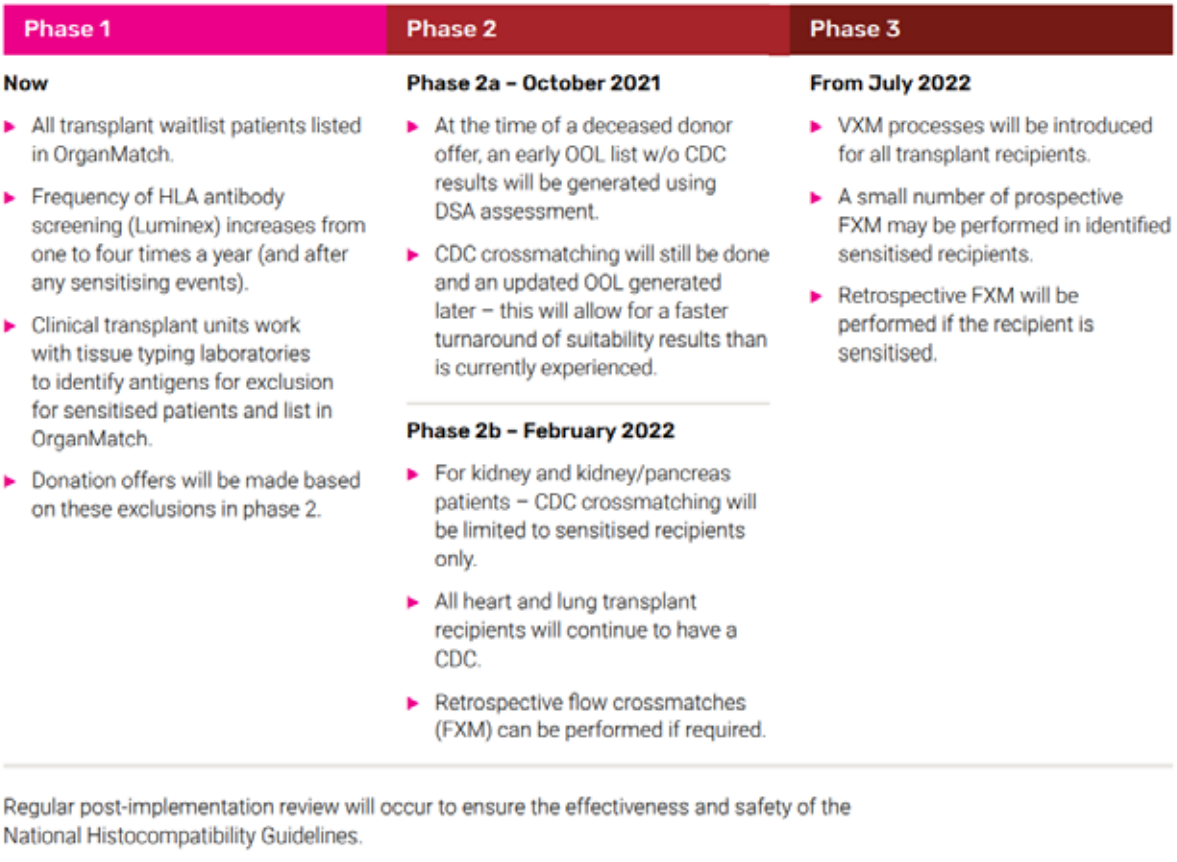


*Figure 2. How the transition to VXM is taking a three-phased approach*

CDC and can detect antibodies at the same level of sensitivity as the Luminex single antigen bead test. In the majority of instances, a FXM will occur retrospectively following transplant clinician consultation with tissue typing laboratories, although in selected cases it may be possible to perform a prospective FXM to guide organ offers.

## OrganMatch's role in the VXM project

In the transplantation portal, clinical and transplant units can view all the components that contribute to the VXM assessment which include the HLA antibody results, UA and AE assignment and patient sensitisation category. At the time of organ offer, the match event assessment which includes the DSA assessment is also viewable through the transplantation portal of OrganMatch.

## The next phase in the VXM project

Following commencement of the organ offer list (OOL) on 18 October 2021 the project will move to Phase 2b in February 2022. This phase will cease CDC crossmatching for non-sensitised kidney and kidney/pancreas transplant waitlist patients, meaning donation offers for these patients will be based on the VXM. All other transplant offers will continue to be made using the VXM initially, followed by the CDC when available. In Phase 3, from July 2022, CDC crossmatches will no longer be conducted, and all organ transplant offers will be made based on a VXM with a FXM conducted if required. Monitoring of outcomes will occur as part of Phases 2b–3 and as part of a post-implementation review. Further information on monitoring mechanisms will be available in early 2022.

Communication and education are a key part of the implementation strategy for the VXM project. The OrganMatch website and TSANZ website have further information on the project and educational resources. The Lifeblood transfusion website has a short course on virtual crossmatching that is available to those who register to the site.

## Summary

- All transplant waitlist patients should be enrolled in OrganMatch.
- Transplant waitlist patients should be having HLA antibody screening four times a year.
- Transplant units should work with tissue typing laboratories to identify UA and AE and document these in OrganMatch prior to organ offers.
- Phase 2b will be implemented in February 2022. This will cease CDC crossmatching for non-sensitised kidney and kidney/pancreas transplant recipients.
- It remains essential to identify potential sensitising events such as blood transfusion or kidney transplant nephrectomy and report these to the tissue typing laboratories so additional HLA antibody testing can be performed 4–6 weeks later.
- Regular post-implementation review will occur to monitor the effectiveness and safety of the national VXM protocol.

## Conflict of interest

The authors declare no conflicts of interest.

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