Australian and New Zealand Paired Kidney Exchange Program

Protocol 4: ANZKX Tissue Typing Laboratory Guidelines

Version 4
August 2019

donatelife

Australian + New Zealand Paired Kidney Exchange Program

ANZKX Tissue Typing Laboratory (TTL) Guidelines

This document outlines the Tissue Typing Laboratory requirements to enable implementation of the ANZKX Program.

Acronyms referenced in these Guidelines

CTTO = Coordinating Tissue Typing Officer

DSA = Donor-Specific Antibody

MFI = Mean Fluorescence Intensity

OLI = One lambda Inc. (antibody assay)

SAB = Single Antigen Bead

TTL = Tissue Typing Laboratory

TWL = Transplant Waiting List

Tepnel = Lifecodes Immucor Inc. (antibody assay)

Introduction

The ANZKX Program uses an algorithm to find matches among the pool of donor-recipient pairs to create 2 to 6 way exchanges, or non-directed donor chains of transplants.

First, matched pairs are found by comparing the ABO blood groups of each donor and each recipient, then by checking the Unacceptable Antigens of recipients and comparing these in turn with the HLA-typing of each ABO compatible donor.

Unacceptable Antigens include primarily HLA alleles to which a recipient has an antibody (with a default level of >2000 MFI for both class I and class II HLA alleles). They may also include mismatched antigens from previous transplants or pregnancies or those associated with a high eplet load as per each transplant unit's requirements.

These guidelines outline the requirements and processes necessary to achieve the goal of the ANZKX Program.

1 HLA typing requirements for donors and recipients

1.1Registration requirements for donors and recipients

It is important to submit the ***ANZKX Tissue Typing Registration Form*** as soon as the donor-recipient pair have been deemed suitable for the program, and noting in Section 4 of the form for which match run the pair is likely to be ready.

The Tissue Typing Laboratories will not usually accept new referrals within the 4 weeks prior to a match run (lock-down) to allow sufficient time to complete testing for that match run. Referrals can be made within the lockdown period if intended for subsequent match runs.

1.2 HLA typing requirements for donors

For donors all loci are required to be at 4-digit (2 field) level[#]. For entry onto the ANZKX register, donors must have an authorised HLA typing recorded into OrganMatch for each of the following mandatory HLA loci:

HLA-A*, HLA-B*, HLA-C*, HLA-DRB1*, HLA-DPB1*, HLA-DQA1*, HLA-DQB1* and HLA-DRB3/4/5*.

[#] HLA-DQA1 and –DRB3/4/5 typing are required to be at 2-digit level minimum, although typing at 4-digit level resolution is always encouraged where available. If HLA DPA1* is available that should also be entered.

1.2.1 Overseas Donors

Australian or New Zealand recipients are able to be co-registered with a donor who resides overseas if the following conditions are met:

- The donor is reviewed by the Australian or New Zealand unit prior to registration.
- HLA typing is performed in Australia or New Zealand to ANZKX specifications.
- Adequate blood is obtained at time of sampling to enable freezing of cells for later use e.g. crossmatch.
- TTL to verify that a sufficient number of cells are isolated from this sample to enable multiple crossmatches to be performed. If necessary recall donor for additional specimen (in case donor returns to home country prior to match run).
- The donor is able to accommodate any potential surgery timeline.

1.3 HLA typing requirements for recipients

For recipients (new and existing) all loci typing at 4-digit (2 field) level is required. For entry onto the ANZKX register, patients must have an authorised HLA typing recorded into OrganMatch for each of the mandatory HLA loci :

HLA-A*, HLA-B*, HLA-C*, HLA-DRB1*, HLA-DPB1*, HLA-DQA1*, HLA-DQB1* and HLA-DRB3/4/5*. If HLA DPA1* is available that should also be entered.

Full typing of recipients is required for the purposes of epitope matching and to exclude the possibility of self-reactive antibodies, particularly for DP locus.

1.4 Donors that express an HLA allele not included in one of the single antigen bead assays

Currently Organ Match is unable to exclude from matching recipients with donor-specific antibody (DSA) against a donor expressing a 4-digit HLA allele that is not covered by the Single Antigen Bead (SAB) assays. For this reason if a donor expresses a 4-digit HLA allele that is not covered by one of the SAB assays, special management procedures are required (e.g. C*07:01 is not currently included in the One Lambda Inc. (OLI) kit).

Prior to each match run the local Australian or New Zealand tissue typing scientist will be responsible for:

1.4.1 Supplying the CTTO with the HLA type of all the donor(s) they have entered into the ANZKX match run with any HLA alleles not covered by the SAB assay highlighted.

1.4.2 Entering the following comment into the OrganMatch donor record for each donor expressing an HLA allele that is not covered by the SAB assay.

"**Following alleles are not represented in the current OLI/Tepnel SAB lot: (e.g.) B*35:02, DRB1*08:03".**

1.5 HLA nomenclature

Whenever possible the 4-digit (2 field) molecular nomenclature (describing a specific allele of the antigen) will be used for HLA antigens and HLA-antibodies used in the OrganMatch database for the purpose of the ANZKX Program.

In exceptional circumstances information may only be available based on historical data obtained by serological typing. This could be the case if a patient had a previous transplant and HLA specificities for the previous donor are only available at the 2-digits (1 field) resolution to describe an antigen. In rare instances a patient may have a record of a historical HLA antibody demonstrated by serological methods, but the historical serum is no longer available to determine 4-digit specificity by Luminex SAB (see 5.1). In this instance the unacceptable antigen(s) based on the specificity of the serological antibody should be authorised in the APMM register (see 3.1).

As the 2 digit antigens will generally be identical to the first two digits of the four digit alleles, the few exceptions to this rule will need to be listed in the OrganMatch HLA antigen/allele relationships table exclusively using 2-digit molecular nomenclature. All the required antigen and allele code updates must be validated by the TTL.

Examples:	4-digit (2 field) molecular	2-digit (1 field) molecular	Serological
	A*11:01	A*11	A11
	C*03:04	C*03	Cw10
	DRB1*03:01	DRB1*03	DR17

2 HLA antibody screening of patients

For entry onto the ANZKX register, patients must have an authorised antibody record tested by one of the Luminex SAB test providers (OLI or Life Technologies) for both Class I and Class II HLA antibodies.

Patients newly registered on the Program and not previously antibody tested must have SAB testing performed and then confirmed within 3 months prior to the run. Confirmatory SAB testing must be performed using a sample collected at least one month later than the initial sample.

Individual antibody strengths expressed as mean fluorescence intensity (MFI) must be entered into the record (with reference to defined ranges listed in the code table) for all Luminex-detected Class I and Class II HLA antibodies.

Authorised antibodies to be used in defining unacceptable mismatches are assigned by each local Australian or New Zealand TTL in consultation with their clinicians. These should, in general, be the level which is likely to give a positive CDC crossmatch, ie >2000MFI for OLI and >1500MFI Tepnel. By using these cut offs we would expect that the CDC crossmatches will almost always be negative.

Antibody results at the **4-digit** level are required to be stored in OrganMatch along with MFI values for all excluded and non-excluded antibodies detected by SAB assay.

2.1 Testing frequency

For patients already registered in ANZKX and entered in previous match runs, testing should be repeated:

- Every 6 months if antibodies are detected or if they had a previous failed transplant;
- Every 12 months if they are non-sensitised, first transplant candidates and no antibodies are detected.

All patients must be tested by SAB assay after any sensitisation event AND if matched in a run (testing at the time of crossmatch).

2.2 HLA antibody strength

Published data indicates that in the presence of DSA, values of <2000MFI (by OLI kit) are unlikely to yield a positive **CDC-crossmatch**, whereas >8000MFI are extremely likely to have a positive CDC crossmatch. The cut-off for a positive **flow cross match** is somewhere around 1000 – 2000MFI and certainly a value below this is unlikely to have a positive flow cross match.

A review of the Asia Pacific Histocompatibility and Immunogenetics Association (APHIA) QC data has suggested that in general Tepnel has lower MFI and that a value of 1500MFI is the equivalent of a 2000MFI for OLI and using such cut -offs will result in very similar calculated panel reactive antibody (cPRA) amongst all TTL.

3 Additional considerations in the definition of unacceptable HLA antigens

3.1 Exclude previous Mismatches

Previous transplant data must where available be entered into the OrganMatch database.

Previously transplanted mismatched antigens will be considered as unacceptable in the organ matching process unless otherwise agreed between clinicians and the local TTL.

The HLA typing of a previous donor must be promoted to the HLA Typing Profile and authorised to enable the mismatched antigens to be visible in the unacceptable antigen table of the recipient.

From this table they can then be selected and authorised as unacceptable mismatches for matching.

Where possible this must be in a minimum of 1 field but ideally 2 field molecular typing format. If only serological historic previous transplant HLA Typing is available the unacceptable antigens will need to be entered into the Recipient Unacceptable Antigens Table using the “add antigen” button .

Type= unacceptable Antigen. Antigen = 1 or 2 field molecular results entered as a string separated by comma and space.

E.g. Historic typing = A2, 24; B62, B60, Cw10, Cw9 would be entered as a string

A*02, A*24, B*15:01, B*40:01, C*03:03, C*03:04

Reason: “previous transplant mismatch”

Clinicians, following discussion with the TTL, may deem it safe to remove a previously transplanted mismatched antigen from the authorised mismatches (because of current and historical absence of a specific antibody to the previous mismatch).

Clinicians, in consultation with their TTL, may decide to enter any other unwanted antigens into unacceptable antigens list.

Examples for this strategy are:

- incompatible spousal live donor pairs, where the donor is the husband/male partner and one or more specific antigens of the husband need to be excluded (for instance because of presence of DSA <2000MFI to husband antigens).

Exclusion of antigens where the predicted eplet load would be very high in case of a match, even if no antibodies to that antigen are detectable.

These additional unacceptable antigens will need to be entered into the Recipient Unacceptable Antigens Table using the “add antigen” button.

Type= unacceptable Antigen. Antigen = 1or 2 field molecular results entered as a string separated by comma and space.

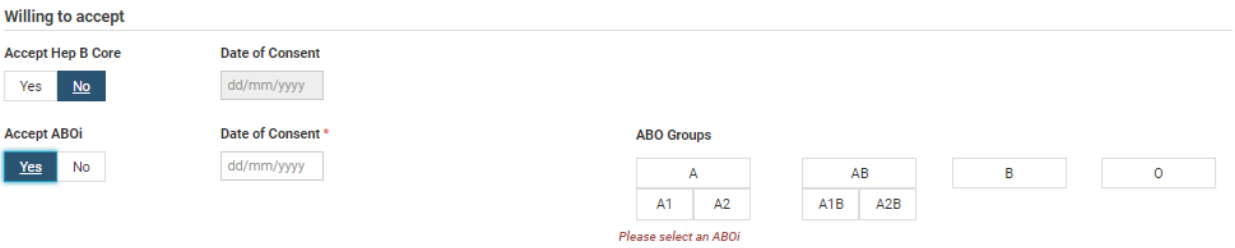
A*02:01, DRB4*01, DQB1*03:01

Reason: “high eplet load” or “spouse mismatches”.

4 Willing to accept ABO-incompatible transplant

An additional strategy to increase options for sensitised patients is to accept kidneys from ABO-incompatible, but HLA acceptable donors within the ANZKX pool. The acceptance of ABO-incompatible donors for some of the highly sensitised recipients in the ANZKX Program results in a “virtual” expansion of the donor pool

The TTL is required to enter acceptance of ABOi in the ‘Willing to accept’ tab of the KPD enrolment and also indicate which ABOi blood groups they are willing to accept and also enter a consent date. It is possible to select only A2 or both A1 and A2. OrganMatch requires the consent date to be entered.



The referring transplant unit is responsible to determine whether acceptance of an ABO-incompatible donor is a feasible option for their recipients.

5 Rules for inclusion of compatible pairs in the ANZKX Program

Participation of compatible pairs (CP) in ANZKX can be attractive to CP who have a high degree of HLA-mismatch, if the KPD allocation algorithm provides a better HLA match for the CP recipient.

Because the ANZKX program is not designed to help CP, it is important to define allocation metrics that enable the CP to receive a better-matched kidney, without disadvantage to incompatible pairs (ICP). The following pathway for inclusion of compatible pairs in ANZKX was approved by RTAC.

Compatible pairs can be included in ANZKX in order to gain a better HLA-matched donor, provided the HLA mismatch to the own donor has a high level of eplet mismatch (EpMM) (for example combined class I and II Eplet mismatch more than approximately 65).

- The majority of CP mismatched at HLA-A, B, DR will meet these criteria.
- The majority of these CP will able to find a match within the first 1-2 match runs.
- CP who do not meet the 65 EpMM threshold can also be considered, if they wish to avoid a specific mismatch that would impact a future chance of a repeat transplant.

Better immunological matching can be achieved by excluding unacceptable antigens (UA) in the CP recipient.

- The list of unacceptable antigens should translate into a virtual cPRA of approximately 70-80%:
- Assigning a virtual cPRA up to 80% will:
  - excessively not affect CP match probability;
  - not disadvantage ICP in favour of CP recipients;
  - not reduce match probability for highly sensitised ICP.

6 Method of matching by OrganMatch for ANZKX

The OrganMatch PKE program will match:

1. recipients Unacceptable antigens (UA) *against*
2. donors HLA antigens using 2 main principles:

— maximise the number of suitable donor-recipient pairs using match probability (to exclude unacceptable mismatches)

— maximise number of blood group ABO identical pairs (ABO identical > ABO compatible).

The Match Probability (MP) will be calculated as: MP = (a/b), where:

a = the number of acceptable donors in the run (i.e. donors having no HLA antigens to be excluded because of patient DSA or previously transplanted antigens)

b = total number of ABO compatible/acceptable donors in the run.

MP range is 0 to 1: 0 implies no compatible donors and

1 implies all ABO compatible donors are suitable matches.

Recipients HLA antigens are not used for the purpose of matching but are required when evaluating match offers.

6.1 Method of matching patient antibody against donor HLA

The default method of matching will be to match 4-digit patient UA to 4-digit donor HLA:

- A 4-digit patient UA specificity will result in exclusion of any donor with that precise allele authorised in the HLA typing. However donors with any authorised other allele of the antigen will not be excluded. This will enable a crossmatch to be performed.

Acceptable matches are identified by excluding donors with HLA alleles to which a particular recipient has donor-specific antibody (DSA) with a default reactivity of >2000 MFI for both class I and class II HLA alleles in the authorised serum.

Cut-offs for One Lambda Inc. (OLI) Luminex assay are as follows:

To be entered in OrganMatch by default as unauthorised, i.e. **do not exclude from matching**.

- Weak 500 – 2000

To be entered in OrganMatch by default as authorised, i.e. **will exclude from matching.**

- Moderate 2000 to 8000 or Strong >8000

Cut-offs for Lifecodes Immucor Inc. ('Tepnel') Luminex test are as follows:

To be entered in OrganMatch by default as unauthorised, i.e. **do not exclude from matching.**

- Weak 300 - 1500

To be entered in OrganMatch by default as authorised, i.e. **will exclude from matching.**

- Moderate 1500 to 4000 or Strong >4000

6.2 Selection of authorised serum to be used for the match run

Evidence suggests that the current serum may underestimate true sensitisation and post-transplant immunological risk. The default serum authorised for match run is the patient's 'peak serum', unless otherwise advised by the recipient's team.

It is acknowledged that the amount of one antibody may be high in one serum sample and another antibody may be higher in a different serum sample. In Organ Match an Antibody consolidation should be generated by selecting the sample results to include.

Ultimately, the selected panel of antibodies authorised for the match run is at the discretion of the patient physician in combination with the local Australian or New Zealand TTL.

6.3 Individualised assignment of unacceptable HLA antigens

In the ANZKX Program a high proportion of the incompatible pairs are enrolled as a result of HLA-incompatibility. Some highly-sensitised recipients with broad sensitisation have only a limited number of rare donor HLA genotypes that they can be matched with and this leads to the accumulations of patients with broad sensitization and high antibody strength against common antigens in the ANZKX pool. Alternative allocation strategies are required to assist these patients and one possible solution is the individualised assignment of unacceptable HLA antigens.

Therefore, there may be instances where a transplant team decides to deliberately allow some HLA antibody specificities with >2000MFI in a particular patient to increase the chance of them being matched. This means that donors with HLA alleles to which a particular recipient has donor-specific antibody (DSA) with a reactivity of >2000 MFI will not be excluded from matching with this recipient.

For these cases a recipient evaluation form outlining HLA antibody to be ignored (see appendix) should be made available to the CTTO and ANZKX Coordination Centre.

If DSA >2000 MFI are present in non-authorized sera the patient's physician will be notified after the potential match is identified, before a chain is offered for consideration to all centres involved.

The individualised assignment of unacceptable mismatches should consider the sensitisation status of the patient:

- Patients with a cPRA <75% are very likely to find a compatible donor in the ANZKX pool with no DSA to the matched donor.
- Patients with cPRA >75% (highly-sensitised) and in particular those with cPRA >95% are less likely to find a compatible donor in the ANZKX pool with no DSA to the matched donor.

It is suggested that individualised assignment of unacceptable mismatches should be reserved for highly-sensitised recipients.

The selection of the best available compatible donor with the longest projected graft lifespan should be considered for those likely to require retransplantation. Therefore, it is also possible to consider excluding 'acceptable' mismatches (where there would be no DSA to a specific donor HLA antigen) for patients with narrow sensitisation, in particular paediatric patients and young adults. In this instance one or more specific alleles can be listed Unacceptable antigens list as "others".

7 Further testing after a match run

7.1 CDC-crossmatching

CDC crossmatching is the cell-based immunological assay that will satisfy the requirements to safely proceed with live donor kidney transplantation in the majority of cases where no DSA or only weak DSA between recipient and matched donor are present. Based on the APHIA Consensus and the ANZKX experience with the first 100 matched pairs, DSA with MFI values of <2000 (by OneLambda) are unlikely to yield a positive CDC-crossmatch.

7.2 Flow cytometry crossmatching

Flow crossmatching is not performed routinely for ANZKX matched pairs, however flow cytometry crossmatching (FCXM) is available. It is suggested that FCXM be considered for all matched pairs with single or cumulative DSA > 2000MFI . The decision to perform FCXM rests solely with the patient's physician. If required, FCXM should be arranged with the appropriate laboratory to be performed at the same time as the CDC crossmatch. These results should be used to stratify immunological risk rather than as a decision making tool to exclude or accept matching.

Occasionally, non-specific positive CDC crossmatches in the absence of DSA can be observed. In these rare circumstances FCXM should be considered to determine whether it is acceptable to proceed to transplantation.

7.3 Allocation of a non-directed donor chain kidney (last in chain) to the transplant waitlist recipient

When a non-directed donor (NDAD, also known as altruistic donor) is referred to ANZKX and starts a chain of transplants, the last recipient in the chain will have a living donor who has not donated during the match cycle. This donor will donate to the deceased donor list (and close the chain) of either New Zealand or the relevant Australian state that entered the NDAD donor to ANZKX. Allocation of the last donor in the chain to the state-of-origin waitlist will follow the standard OrganMatch allocation rules for deceased donors in Australia, or NZKAS rules in New Zealand.

The timing of the allocation will be as close as possible to the scheduled date of surgery planned for the NDAD chain. However, the timing must take into consideration the need for crossmatching to be performed and reported to the recipient's team.

The unit performing the transplant of the waitlist recipient will also need sufficient time to assess/ review intended recipient medical suitability and for the laboratory to repeat a Luminex SAB test on a current serum, as there could be patients on the Transplant Waiting List (TWL) who have screening results up to 12 months previous as these are generally reviewed annually unless the labs have been notified of a sensitising event.

It is therefore suggested that allocation should take place no later than 3 weeks prior to the scheduled date for the Ahain surgeries. Possibly a shortlist of 3 possible recipients should be made in case a contraindication comes to light clinically or immunologically within that 3 weeks' time frame. The TWL enrolment of the recipient, once identified, must be put "on hold" pending transplant.

7.4 HLA antibody testing after matching and prior to transplantation

Following a successful match ideally transplantation should occur as quickly as possible and preferably prior to the subsequent match cycle. In the event of surgical delay (> 2 months since match run) HLA antibody testing should be performed within 4 weeks prior to scheduled surgical date. If the SAB profile has not altered significantly then a repeat CDC crossmatch is not required. If a repeat CDC crossmatch is required, based on altered SAB profile then it should be performed 7 days prior to scheduled surgical date.

8 Coordination of tissue typing work

The ANZKX Coordinating Tissue Typing Officer (CTTO) is responsible to track all the steps of the tissue typing process for enrolled pairs and provide updates to the ANZKX Coordination Centre, including:

- confirmation of completion of tissue typing of donors and recipients referred to ANZKX;
- post-run review of recipient's antibody record against matched donor to ensure no authorised DSA have been missed;
- coordination of crossmatch test dates;
- review of crossmatch results;
- generation of crossmatch reports (donor de-identified);
- distribution of reminders to local Australian and New Zealand TTL's for SAB retesting of matched patients, as required.

Following a match run the CTTO is responsible to ensure with the Australian and New Zealand TTL's that patients in matched pairs are place "On Hold" for their TWL enrolment. This will usually occur on the day an OrganMatch allocation has been executed and a combination report was generated. It will generally include all patients matched in the top ranked combination, unless any obvious mistake is evident upon first review of the combination reports.

Transplant candidates who have their TWL enrolment placed on hold will be reactivated in the OrganMatch waitlist on the advice of the CTTO in consultation with the ANZKX Coordination Centre when:

- A patient has an authorised, but unacceptable DSA identified following the post-run review of the patient antibody record that was missed in the computer allocation (e.g. donor HLA allele that is not covered by one of the SAB assays).
- The referring team refuses a match offered to one of their recipients (e.g. the team would accept ABOi donor, but no DSA or specific DSA, but only if ABOc donor).
- A patient has final positive cell-based crossmatch result to the matched donor (in this case the other patients in the same chain will be reactivated on the waitlist).
- A chain breaks down because of recipient or donor unsuitability reasons.

If the date of surgery for pairs in one chain following a match run is scheduled after the subsequent match run, these pairs will remain on hold.

If the date of surgery for pairs in one chain is unexpectedly delayed because of acute illness in one of the recipients and can't be rescheduled prior to the subsequent match run, the ANZKX Coordination Centre will advise the CTTO if patients in the chain will be reactivated on the waitlist and pairs entered in the next match run.

9 Protocol for non-directed altruistic donors (NDAD)

9.1. Overarching principles

- **Australian NDADs** must meet the usual donor criteria to be entered into ANZKX.
- NDADs can be either entered directly into the ANZKX program or some Australian/New Zealand Transplant Centre's might choose to first check whether they match a highly sensitised recipient on the transplant waiting list. The NDADs preference should be taken into account when deciding how to allocate their kidney.
- It was decided by RTAC that if the latter option is chosen then the NDAD should only be offered to a transplant waiting list recipient if matched at Level 1-3 match of the current National Matching Algorithm:
- HLA A+B+DR = 0 mismatches (level 1) or
- Class 1 PRA>80% and HLA A+B+DR ≤2 mismatches (level 2+3).
- If a match is not found in the National pool at level 1-3 then these donors will then be allocated through the ANZKX program.
- The last donor in chain will be allocated **nationally** to an Australian TWL recipient fulfilling Level 1-3 match, or a New Zealand equivalent as per the NKAS algorithm.
- **New Zealand NDADs** entered into ANZKX will be allocated to the ANZKX, with the last donor in the chain allocated in accordance with the NZKAS to a New Zealand recipient on the deceased donor waiting list.

9.2. Step-by-step pathway (Australian NDADs only)

9.2.1 NDAD-Assessment and tissue typing:

1 Any NDAD should be referred to a local Australian or New Zealand TTL for typing only once they are deemed suitable to donate (i.e. passed medical, surgical and psychological suitability investigations).

2 The ANZKX tissue typing referral form should be sent to the local Australian or New Zealand TTL.

3 Any suitable NDAD referred to the Australian or New Zealand TTL will be tested to the level required for ANZKX (i.e. including confirmatory typing and 4 digit all alleles), samples will need to be sent to the participating TTL 1 month prior to the next schedule ANZKX match run (lockdown period).

4 The participating Australian or New Zealand TTL will have the donor "ready" on OrganMatch as soon as required testing is complete and no later than one week prior to the scheduled match run date.

5 Matching of NDADs is performed at the time they are entered into ANZKX or at the time of a match run.

9.2.2 End-of chain donor allocation:

6 The end-of-chain donor will be allocated against the Australian/New Zealand TWL once the final outcome of the run is decided, according to the following rules:

a. Allocation to any recipient on the Australian TWL fulfilling level 1-3 match or New Zealand equivalent

if no suitable recipient:

b. Allocation to any recipient on the TWL of the Australian state or New Zealand equivalent

if still no suitable recipient:

c. Follow national Australian and/or New Zealand allocation override rules

if still no suitable recipient:

d. Repeat allocation closer to the date of surgery of NDAD chain as per rules a–c above.

7 The ANZKX coordinator will arrange a blood specimen* from the end-of-chain donor to be sent to their local Australian or New Zealand TTL for crossmatch against the TWL tray.

8 If the crossmatch against the end-of-chain donor is negative the matched recipient will also be temporarily off-listed.

***The TTL will freeze donor cells in the event there is no TWL recipient so they can be used for crossmatch several weeks later when that's sorted.**

Comment: *In the case that the kidney of the last donor in chain is directed to a recipient in an Australian state or New Zealand centre other than the NDAD origin state/centre, the standard payback rule will apply to compensate the state and/or centre of origin.*

10 Protocol for orphaned kidneys and recipients

10.1 Definitions

Orphaned kidney: refers to a kidney removed from an ANZKX donor that cannot be transplanted into the matched recipient.

Orphaned recipient: refers to an ANZKX recipient whose co-registered donor has donated, but who has been unable to receive a kidney from the matched donor.

The protocol for orphaned kidneys and orphaned recipients was developed by the National Paired Kidney Exchange Program Advisory Group and has been revised by ANZKX, RACOS and RTAC (in Australia). In NZ, the NRTLT is responsible for the oversight of the NZKAS, including dealing with orphaned kidneys and recipients.

In the rare event where an exchange cannot proceed due to unforeseen clinical or logistical circumstances, the following is recommended:

10.2 Orphaned kidney

On the day of transplant surgery a recipient may suffer an acute event immediately prior to going to theatre, during induction or during their operation such that the procedure needs to be abandoned. Because donor

surgery always occurs before recipient surgery, the donor has already had their kidney removed. This will result in an 'orphaned kidney'.

Donors are asked advance to consent to their kidney being allocated to someone suitable on the deceased donor transplant waiting list if this circumstance arises. It is for this unlikely, but possible, contingency that a specimen of donor's whole blood (40ml) is taken at anaesthetic induction and transported with the kidney.

10.2.1 Process for determination and allocation of an orphaned kidney

Recipient Centre: must immediately notify the ANZKX Coordination Centre if the recipient has become acutely ill and is unable to undergo or continue with transplant surgery.

Steps for allocation of an orphan kidney:

- Depending on the logistics, an allocation to a highly sensitized recipient on the deceased donor waiting list (Level 1-3 on the National Allocation formula) should be sought. A decision regarding whether further transport of the kidney is possible for such an allocation will be made by the ANZKX Coordination Centre although advice from RACOS can be requested if required.
- If this is not possible or there is no recipient matched at level 1-3 on the National Allocation formula then:
  - If the kidney is in transit, the kidney will be allocated to a recipient on the transplant waiting list in the state/country of destination.
  - If the kidney is still in the state/country of origin, it will be allocated to a transplant waiting list recipient within this state/country of origin.
  - In New Zealand the kidney would be allocated to the top ranked recipient in the country or transplant service as per NKAS algorithm.
- The ANZKX Coordination Centre will alert the CTTO to perform an urgent OrganMatch search/virtual crossmatch to identify a suitable recipient.
- The CTTO will generate an OrganMatch allocation list.
- Virtual crossmatch will be performed by the CTTO using the ANZKX matching criteria and the top 5 potential recipients.
- The CTTO will notify the ANZKX Coordination Centre about the identified potential match (state/country of origin or state/country of destination) and the transplanting centre under which the identified recipient is listed.
- The ANZKX Coordination Centre will contact the recipient's transplant centre to alert them of the probable allocation. The de-identified MMEx live donor report will be made available to the recipient's team.
- The CTTO will alert relevant TTL to prepare for an urgent cross-match test.
- The state TTL will perform CDC crossmatching against the top 5 recipients. This information may be provided to the physician retrospectively if necessary.
- The TTL performing the crossmatch will send a report to the recipient's centre, with copy to the ANZKX Coordination Centre and CTTO.
- The ANZKX Coordination Centre will ensure the waiting list recipient centre has been duly informed.
- The ANZKX Coordination Centre will report the critical incident to the OTA/ANZKX Oversight committee and monitor outcomes.
- The ANZKX Coordination Centre will facilitate communication of the resultant issues and outcomes between donor and recipient centres as required.

10.3 Orphaned recipient

The definition and approach to Orphaned recipients is outlined in ANZKX Protocol 1, section 5.2.

10.3.1 Priority listing of orphaned recipients

RTAC agreed that orphaned recipients should receive priority listing for a suitable kidney from the national deceased donor organ pool. This is because the recipient's co-registered donor has already donated his/her kidney and thus the recipient no longer has recourse to an ANZKX exchange.

The process of prioritisation for Australian patients is that the 'orphaned recipient' will receive OrganMatch priority listing (Level 4 interstate exchange) for a suitable kidney from the National deceased donor organ pool.

Orphaned recipients in Australia are assigned a base score of 57,500,000 before other modifiers are applied. This base score prioritises an orphaned recipient after a Rank 3 (58,000,000; 4/6 matched and cPRA >80) and ahead of a Rank 5 (57,000,000; 6/6 matched and cPRA <50).

In New Zealand the recipient would be allocated in Rank 1 as per the NKAS algorithm, available on the NRTLT website.

Pre-emptive recipients are not listed in OrganMatch, as activation on the deceased donor waitlist starts with the first day on dialysis. In these cases, exception will be made after notification and approval by RTAC that the pre-emptive recipient can be listed for priority allocation on the deceased donor waiting list.