1 METHOD OF MATCHING BY NOMS FOR PKD

The NOMS PKD algorithm will match:
1) recipients’ HLA antibody* against (recipients’ HLA antigens are not used for the purpose of matching)
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: $MP = \frac{a}{b}$, where:

- $a$ = the number of acceptable donors in the run (i.e. donors having no HLA antigens to be excluded because of patient antibodies or previously transplanted antigens)
- $b$ = total number of ABO compatible donors in the run.

MP range is 0 to 1: 0 implies no compatible donors and 1 implies all ABO compatible donors are suitable match

1.1 Method of matching patient antibody against donor HLA

The 2-digit and 4-digit patient antibody/4-digit donor HLA will be matched with different business rules as follows:

A 2-digit patient antibody specificity will result in exclusion of any donor with the same antigen or 4-digit allele of that antigen authorised in the HLA typing.

A 4-digit patient antibody 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.

2 HLA TYPING REQUIREMENTS FOR PATIENTS AND DONORS

2.1 HLA typing requirements for donors

For donors all loci are required to be at 4-digit level. For entry onto the PKD register, donors must have an authorised HLA typing recorded into the NOMS for each of the following mandatory HLA loci:
   - HLA-A*, HLA-B*, HLA-Cw*, HLA-DRB1*, HLA-DPB1* and HLA-DQB1*.
Typing for the following loci may also be included:
   - HLA-DQA1*, HLA-DRB3*, HLA-DRB4* and HLA-DRB5*

2.2 HLA typing requirements for recipients

For recipients (new and existing) all loci are required to be at 2-digit level, although typing at 4-digit level is encouraged for all new recipients. For entry onto the PKD register, patients must have an authorised HLA typing recorded entered into the NOMS for each of the mandatory HLA loci (cf cadaveric list):
   - HLA-A*, HLA-B*, HLA-DRB1* and HLA-DQB1*. 
2.3 HLA typing issues
The HLA specificities will be expressed initially as either 2 digits to describe an antigen group or 4-digits to describe a specific allele of the antigen.

(Example HLA DRB1*0101 is an allele of the broad antigen HLA DRB1 *01)

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 NOMS HLA antigen/allele relationships table. All the required antigen and allele code updates must be validated by the Tissue Typing laboratories.

3. HLA ANTIBODY SCREENING OF PATIENTS

For entry onto the PKD register, patients must have an authorised antibody record tested by one of the Luminex test methods for both Class I and Class II HLA antibodies. There should be a means of recording individual antibody strengths (MFI) for future analysis both manually and automatically (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 would be assigned by each State TTL in consultation with their clinicians. These would in general be the level which is likely to give a positive CDC or flow cross match, ie >2000 for One Lambda >1500 Tepnel, though TTL could modify the threshold in individual cases. By using these cut offs we would expect that the CDC cross matches will almost always be negative and thus prevent a donor chain from "falling over".

Antibody results at the 4-digit level will be required to be stored in the NOMS along with MFI values and result ranges for all authorised and unauthorised antibodies.

3.1. HLA antibody strength

Consensus from the recent ASEATTA 2009 meeting is that MFI values of <8000 are unlikely to have a positive CDC crossmatch, whilst the cut-off for a positive flow cross match is somewhere around 1000 - 2000 and certainly a value below this is unlikely to have a positive flow cross match. All agreed levels from 1000 to 2000 are weak and most would not exclude from transplantation. Such antibodies are likely to be biologically relevant and should be interpreted in relation to other information (e.g. mismatched antigen in a previous donor or an antigen present in the patient’s offspring etc) and some physicians might monitor more carefully or modify the pre or post transplant immunosuppression.

A review of the ASEATTA QC data has suggested that in general Tepnel has lower MFI and that a value of 1500 is the equivalent of a 2000 MFI for One Lambda and using such cut-offs will result in very similar calculated PRA amongst all TTL.

Cut-offs for One Lambda Incorporated (OLI) Luminex test are as follows:
To be entered in NOMS by default as unauthorised, i.e. do not exclude from matching
Weak 500 – 2000
To be entered in NOMS by default as authorised, i.e. will exclude from matching
Moderate 2000 to 8000
Strong >8000

Cut-offs for Tepnel Life Sciences Luminex test are as follows:
To be entered in NOMS by default as unauthorised, i.e. do not exclude from matching
Weak 300 - 1500
To be entered in NOMS by default as authorised, i.e. will exclude from matching
Moderate 1500 to 4000
Strong >4000
4. PREVIOUS TRANSPLANTS

Previous transplant data should be entered into the NOMS database with the HLA typing authorised by the State Tissue Typing Laboratory HLA co-ordinator.

The following describes how the entry of previous transplant mismatches will work:

a. It will be the responsibility of State Tissue Typing Labs to enter previous transplant mismatches in the Authorised Previous MisMatch (APMM) register.

b. The default will be to enter all previous mismatches.

c. Clinicians following discussion with their immunologist may deem safe to remove a previous mismatched antigen from the authorised panel (because of absence of a specific antibody to the previous mismatch).

d. In this case the ignored antigen will be entered in the Ignored Previous MisMatch (IPMM) register for auditing purposes.

4.1. Exclude Previous MisMatches

Previous foreign transplanted antigens will by default be considered in the organ matching process unless otherwise agreed between clinicians and local tissue typing laboratory. Previous foreign antigens will result in exclusion of a potential donor bearing any of the previous mismatches listed in the “Authorised Previous Mismatch Register” (APMM).

4.2. Ignore Previous MisMatches

For audit purposes, any previous foreign transplanted antigens that are deliberately not considered for exclusion in the matching process will be entered in the IPMM Register. An IPMM register antigen allele will result in a recipient not being excluded for a donor bearing the IPMM-listed HLA antigen allele.

N.B. this differs from the current NOMS organ matching logic where all previously transplanted foreign antigens are excluded in matching.

4.3. Molecular equivalents of previous serological HLA types

The APMM register of authorised HLA antigens will be the molecular equivalent of the donor’s serological HLA types which were authorised at the time of the previous transplant. The Tissue Typing Laboratories will agree on a common list of unacceptable antigens to be entered as molecular equivalents for this purpose, where the existing previous donors’ authorised antigens are available only as serological types. The organ matching for a patient will exclude any donor bearing any of these alleles.