

Title:

**SECTION 7.0 NZBMDR STANDARDS
PROCESS FOR DONOR IDENTIFICATION**

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FORMS

Preliminary Search Request	Form 110
Cancellation of Search	Form 115
Final Compatibility Test Results	Form 117
Donor Confirmatory Typing Test Results	Form 22CT

SECTION 7.0 NZBMDR STANDARDS PROCESS FOR DONOR IDENTIFICATION

THE FINAL DECISION ON DONOR SUITABILITY ALWAYS RESTS WITH THE TRANSPLANT CENTRE.

ALL DECISIONS SHOULD BE MADE BY THE TRANSPLANT CENTRE IN CONJUNCTION WITH THE TISSUE TYPING CENTRE.

DECISION POINTS

There are several decision points that are critical in conducting a successful search for a matched donor.

1 Family Search Request

This is the first step in the search for a stem cell donor and may be conducted independently of the NZBMDR. However the NZBMDR will organise Tissue Typing of family members both in New Zealand and overseas if requested.

An initial request is made to the Tissue Typing Centre from the physician or Transplant Centre for HLA typing of the patient, siblings and/or parents.

A report is issued by the Tissue Typing Centre with patient and/or immediate family tissue types. Where possible this should report the patient haplotypes.

2 Extended Family Search

The aim of an extended family search is to explore the possibility that relatives other than siblings may be suitable as stem cell donors for patients with haematological disorders, who do not have an HLA identical sibling. The decision to conduct an extended family search should be made following discussion between the Transplant Centre and the Tissue Typing Centre.

The rationale behind an extended family approach is that parents, grandparents, offspring and in some cases uncles and aunts can share one of the patient's haplotypes and there is a possibility that the other haplotype is introduced into the family via partners, hence the possibility that cousins or children may be HLA identical (or mismatched at only one antigen) with the patient.

The probability that this may occur is dependent on the frequency of the non-shared haplotype in the general population. In cases where the patient has two haplotypes of low frequency in the general population, the greatly reduced probability of finding an HLA matched donor in an extended family search makes this an approach with little hope of success **unless an A, B, C or DR mismatched donor is considered suitable**

2.1 One antigen mismatch related transplants

If one antigen-mismatched transplants from family members are considered, then patients who have 'incomplete' common haplotypes should also be considered for extended family searches. For example a patient who has a B, DR haplotype occurring with a relatively high

frequency in strong linkage disequilibrium, but with an A allele which does not usually occur on that haplotype e.g. A3 - B8 - DR3.

This approach assumes that an A, B or DR mismatch are all considered acceptable in a family context.

2.2 What is the basis of selection for an extended family search?

The basic selection strategy for an extended family search is to explore the side of the family from which the least common haplotype in the patient has been inherited in the hope that the common haplotype has been introduced.

An extended family search should be conducted on the basis of common haplotypes.

Haplotype frequency tables are available on the BMDW website and in the NMDP Search strategies folder.

With a Haplotype frequency of 60/10,000 the chances of finding a donor A, B, DR compatible to the patient in an 'average' size extended family is approximately 1%. A cut-off point of 60/10,000 was therefore chosen.

There is one major exception to the above proposal, that is ethnic groups where haplotype frequencies are not well documented and hence the above selection criteria cannot be invoked.

Typing of the extended family of patients without a common haplotype should be considered on a case by case basis and take into account :

- i) the probability of finding a suitable unrelated donor
- ii) the ethnic mix of the patient
- iii) the age of the patient and therefore the likelihood of mismatches on the non-shared haplotype being acceptable
- iv) the clinical urgency of the patient
- v) the availability of the extended family

2.3 Request for an extended family search - Process

If an extended family search is to be conducted by the NZBMDR the request should come from the treating physician in the Transplant Centre in conjunction with the Tissue Typing Centre. It is important that the laboratory performing the HLA typing is informed of the size of the family, the individuals involved and their relationships to the patient.

2.4 Order of testing family members

Valuable time and resources can be saved by careful evaluation of the order in which family members are tested. The suggested order is as follows: -

- i] [a] Grandparents (if available) on the side of the family from which the rare haplotype has been inherited;
[b] Partner of the patient, if there are children;
[c] Partner of siblings who share the rare haplotype (if they have children old enough to be donors).
- ii] If one of the grandparents has the *rare haplotype and the other has the common haplotype*, then all children (i.e. uncles and aunts of the patient) should then be

tested to determine if any are HLA identical with the patient, ie. have inherited both the rare and common haplotype.

- iii] If uncles and aunts are not matched, the partners of those with the rare haplotype **and** who have children should be tested to see if the common haplotype has been introduced.

If the common haplotype has been introduced into the family then the children (i.e. cousins) of that union should be tested to determine if any have inherited the rare and common haplotype together (i.e. identical with patient).

- iv] If one of the grandparents has the rare haplotype and the other does not have the common haplotype, then uncles and aunts cannot be identical with the patient. In this case the partners are tested as in paragraph iii].
- v] If the partner of the patient has the common haplotype and they have children, the children should be tested.
- vi] In cases where siblings of the patients have the rare haplotype, sisters or brothers-in-law should be tested to determine if the common haplotype has been introduced. In that case, the children of the union, i.e. nephews and nieces, should be tested.

Under usual circumstances the above individuals should be Class I typed initially. Class II typing can be performed at a latter stage if Class I compatibility is identified. However in the case of an urgent patient with relatives who live overseas, it is often necessary to perform Class I and II simultaneously.

NB. Legislation concerning donation of regenerative human tissue by a minor must be taken into consideration.

The decision to search simultaneously for an extended family member and search for an unrelated donor may be taken by the search team

3. Unrelated Donor Search Request

3.1 Bone Marrow Donors Worldwide (BMDW) preliminary search

The BMDW website contains a database of donors registered on volunteer bone marrow donor registries and cord blood banks throughout the world.

A search of this database is free, instant, and allows the search centre to see if potential unrelated donors may be available.

3.2 Formal Search

- i) The initial request for an unrelated search comes from the patient's physician.
- ii) Before a formal unrelated search is commenced the referring physician must consult with a Transplant Centre in order to register the patient on a transplant waiting list.
- ii) Preliminary Search Request Form 110 must be completed

3.3 Final Typing

To avoid instances where apparently successful searches are performed but where the patient typing is changed as a result of re-typing at a later stage, each patient must undergo confirmatory typing prior to extended typing being requested from unrelated donors. The patients must be typed on a minimum of two occasions, using two separate blood samples.

A report will be issued by the Tissue typing Laboratory stating that the typing has been confirmed

3.4 Search Progress

NZBMDR will forward Form 110 to Registries which identify potential donors or cord blood units (CBU) on the BMDW website.

In patients with `split' antigens e.g. Bw57, Bw58 it is advisable to search for both splits and the supertypic specificity, eg. search B17, Bw57, Bw58. This avoids the situation of failing to detect a compatible donor who is mistakenly assigned the wrong subtype or a donor where the subtype could not be assigned. If more than one phenotype is submitted this should be made clear to the ABMDR National Office through the NZBMDR.

Preliminary search results are issued within 48 hours

NZBMDR will communicate with the referring physician and/or the Transplant Centre reporting the availability and match degree of potential donors and/or CBU.

4.0 Search for Unrelated Adult Donor

4.1 Additional typing requests on donors

If time permits and there are no A,B,DR matched NZ donors identified, Class 1 matched NZ donors may be class 2 typed at the expense of the NZBMDR

If the search is urgent, additional typing, or a confirmatory Typing sample (CT) will be requested from registries with A,B,DR matched donors choosing those from NZ, then Australia and then other overseas registries

4.2 Donor Confirmatory Typing

Before a donor can be requested for donation to a NZ patient the NZ Tissue typing laboratory must confirm the tissue typing on a blood sample sent from the donor centre. If a NZ donor matches a patient from overseas a blood sample will be sent to their tissue typing laboratory for confirmatory typing

4.3 Donor Reservation and Feedback

Donors should be contacted no later than **eight weeks** after a confirmatory testing sample was drawn, to give them an update on the progress of the compatibility testing. A minimum of HLA A, B, C, DRB1* must be defined at high resolution

A donor from whom a CT sample is requested, is flagged for a total period of **ninety (90) days (three months)** while confirmatory testing (CT) takes place. It is expected that all confirmatory matching will have taken place within this time and the selection of a donor can

be made.

First release

One donor may be selected to hold for a further **six months if required**. All other donors are released back onto the registry after the ninety (90) day period. Donors may also continue to donate blood routinely after this ninety day period.

Second release

After nine months a first option procedure will be instituted and this is noted on the History File of the Donor Centre database.

The first option procedure means that the donor is released back into the pool and is available for searching by other patients. However, if the donor matches another patient the original or first patient is given first option to use that donor. The Transplant Centre should provide the registry with a clinical update and an estimate of the anticipated time to transplant.

The Scientific Expert Advisory Committee (SCEAC) will arbitrate any unresolved problems, particularly when medical urgency needs to be considered

4.4 Transport of Adult Haematopoietic Stem Cells

NZBMDR or the Transplant Centre will provide trained couriers to transport all stem cells from adult donors for NZ patients . See Chapter 14 Courier Guidelines

5.0 Search for Unrelated Cord Blood Units

5.1 Additional information and typing on selected Cord Blood Units

A unit report will be requested on selected CBUs which have sufficient Total Nucleated Cells and are matched at a level acceptable to the transplant centre. Cords may be selected which are 4/6, 5/6 or preferably 6/6 HLA matches. Low resolution typing at Class 1 and high resolution typing at DRB1* is required.

If the cord has not been high resolution typed at DRB1* this typing will be requested.

If several cords are available high resolution Class 1 typing including C typing may be considered.

5.2 Cord Blood Unit Confirmatory Typing

Each Cord Blood Bank has its own protocol which must be followed.

On request of a unit, confirmatory typing and quality assurance testing will be performed.

5.3 Transport of Cord Blood Units

NZBMDR or the transplant centre representative will travel to Australia to collect CBUs.

Units from other Cord Blood Banks will be transported by World Courier.

6.0 Continuing Searches when no donor has been identified

NZBMDR will be notified of any new potential donors from NZ, Australia or Thailand on a daily basis through the STAR system.

NMDP registry will notify NZBMDR of new potential donors in the USA through NMDP Webmail

The BMDW website is updated each month. A search for all current patients will be conducted monthly to identify new potential donors on all other registries .

7.0 Cancellation of Search

It is important that once a patient is on the search list, removal is an active process.

The decision to terminate a search may only be made by:

- i] The patient;
- ii] The referring physician, with the agreement of the patient;
- iii] The Transplant Centre, with the agreement of the referring physician and the patient.

To terminate a search, Form 115 should be completed or written communication sent to NZBMDR.