1. PURPOSE

The purpose of this document is to define how patients who are truly refractory to platelet transfusions should be managed. It is based on reviews of the literature and currently accepted practice.

2. BACKGROUND

When a patient does not have a satisfactory response to platelet transfusions it is important to find out why and in particular whether or not the failure is due to immunological or non-immunological (e.g. clinical) causes. For example, in recent years clinical factors such as sepsis, DIC, splenomegaly have largely surpassed alloimmunisation as the major cause of refractoriness.

Identifying patients with white cell (HLA) or platelet (HPA) antibodies is important since the use of HLA-matched (or HPA-matched) platelet components may result in improved transfusion responses. Similarly the identification of patients with other allo- and (rarely) autoantibodies is also important as it may be possible to find serologically (‘crossmatch’) compatible platelets in these situations.

However in deciding how to treat a refractory patient there may be a number of appropriate strategies for improving the response to platelet transfusions such as matching for HLA or HPA, identifying donors based on antibody specificity prediction (single antigen matching) and very rarely resorting to cross-match compatible platelets.

3. DEFINITIONS

- **Alloimmunisation** is defined as the development of HLA or HPA antibodies
- **HLA antibodies** are antibodies to HLA Class 1 antigens
- **HPA antibodies** are antibodies to Human Platelet Antigens
- **Refractoriness** is a failure to obtain a satisfactory response to transfusion of random donor platelets on two or more occasions. A poor platelet response is defined by a platelet increment of <10x10^9/L or (more accurately) a Corrected Count Increment (CCI) of <5000µL
- **Platelet increment** is the difference between pre- and post transfusion platelet counts. This may be a reasonable measure of refractoriness or used to calculate the CCI (see below). The post transfusion platelet count should be performed 10 to 60 minutes after the transfusion.
- **Corrected Count Increment** is determined using the following formula (where BSA represents the patient’s Body Surface Area):

  \[ CCI = \frac{\text{Platelet Increment} \times 10^9/L \times \text{BSA} \ (m^2)}{10^{11} \text{ platelets transfused}} \]

- **Body Surface Area** is determined using the following formula (also known as the ‘Mosteller’ formula):

  \[ \text{BSA} = \sqrt{\frac{\text{Height} \ (\text{cm}) \times \text{Weight} \ (\text{Kg})}{3600}} \]
4. KEY RESPONSIBILITIES

NZBS TMS (or MO)
Liaison with the patient’s physician. Initiates the request for ‘special platelets’ and coordinates the provision of suitable platelet components.

DHB Clinicians
Responsible for the patient and ensuring that the correct samples and tests are requested.

NZBS National Tissue Typing Laboratory
HLA and/or HPA typing of potential platelet recipients; testing for the presence of HLA and/or HPA antibodies; and the identification of suitable platelet donors.

NZBS Donor Services staff
Calling in and bleeding the appropriate platelet donors as identified by the National Tissue Typing Laboratory.

NZBS Manufacturing Services
Processing of the collected platelet donation.

NZBS Logistics And Customer Services
Ensuring that the appropriate platelet components are sent to the relevant location (e.g. hospital blood bank).

5. RELATED DOCUMENT(S)

- Request For Special Platelets (111M034)
- Special Platelet Requisition and Record Form (111F034)

6. POLICY

6.1 Request for Platelets
The first point of contact with NZBS will be a TMS (or MO). Samples may have been received by the Tissue Typing Laboratory without prior consultation. This will still necessitate communication between the TMS/NZBS MO and treating clinician.

6.1.1 Ascertain whether or not the patient is refractory i.e. has had a poor response to random donor platelets on two or more occasions (refer to figure 1: Algorithm To Determine If Patient Is Refractory To Platelets).

6.1.2 Determine the nature and urgency of the request in discussion with the patient’s physician.

6.1.3 Discuss with the treating physician as to what testing of the patient is required and what samples should be collected.

6.1.4 Initiate and coordinate investigation(s) to determine whether the refractoriness is due to immunological or non-immunological causes.

6.1.5 Liase with the National Tissue Typing Laboratory regarding provision of appropriate platelets. Refer to document Requests For Special Platelets (111M034).
6.2 Management Of Refractory Patients

6.2.1 Refer to figure 2: Algorithm For Management Of Patients Refractory To Platelets.

6.2.2 Depending on whether or not test results are available, the options shown below in (table 1) for managing the patient should be considered:

Table 1: Options For Managing Patients Refractory To Platelets

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>a. Patient’s HLA (‘tissue type’) not known and serum sample(s) not yet available</td>
<td>Consider transfusing ABO-compatible, single donor platelets (preferably ‘double-dose’)</td>
</tr>
<tr>
<td>b. Patient serum samples are available</td>
<td>Platelet antibody screen should be performed and serum sample retained for possible crossmatch or single antigen testing</td>
</tr>
<tr>
<td>c. Patient’s HLA type is known, and HLA-matched platelet donors are available</td>
<td>These should be considered particularly if HLA immunisation is suspected as the most likely cause of refractoriness</td>
</tr>
<tr>
<td>d. The patient has HLA and/or HPA antibodies</td>
<td>HLA-matched or single antigen matched compatible platelets should be selected for transfusion. Cross-matching rarely required.</td>
</tr>
<tr>
<td></td>
<td>Further antibody testing should be considered every 3 months or if refractoriness returns</td>
</tr>
<tr>
<td>e. The patient does not have HLA or HPA antibodies</td>
<td>The TMS (or MO) will advise the treating physician accordingly</td>
</tr>
<tr>
<td></td>
<td>Consideration should be given to non-immunological causes for which the TMS (or MO) will advise suitable management options.</td>
</tr>
</tbody>
</table>

6.3 Follow-up Post Transfusion

Following transfusion the TMS (or MO) will:

6.3.1 Ascertain the patient’s response to the platelet transfusion by requesting the treating physician to obtain a post transfusion platelet count (10-60 minutes post transfusion).

6.3.2 Inform the Tissue Typing laboratory of the patient’s response to assist in future selection of appropriate donors.

6.3.3 If the response to matched or cross-matched platelets is poor, TMS (or MO) will determine what further investigations are required in consultation with the treating physician.
Figure 1: Algorithm To Determine If Patient Is Refractory To Platelets

Consult NZBS TMS

Is the patient truly refractory?
i.e. Poor response to random donor platelets on two or more occasions.

Perform platelet count using EDTA sample collected 10 mins - 1 hour post infusion or calculate the 1 hour CCI

Has patient had an adequate response to platelet transfusion(s)?

Adequate response
>10x10^9/L increment post infusion or a CCI >5000/uL

Continue support with non-matched ABO-compatible platelets

Inadequate response
<10x10^9/L increment post infusion or a CCI <5000/uL

Patient Refractory
Figure 2: Algorithm For Management Of Patients Refractory To Platelets

1. **Patient Refractory**
   - Consult NZBS TMS

2. **Serum sample(s) available?**
   - Yes: Send sample(s) to the National Tissue Typing Laboratory
   - No: Perform an antibody screen

3. **Has patient been HLA Class I typed?**
   - No: Check availability of HLA-matched platelet donors
   - Yes: Continue with HLA-matched platelets

4. **Testing complete?**
   - No: Continue support with fresh ABO-compatible single donor platelets (preferably 'double-dose')
   - Yes: Make decision about further platelet support

5. **Are HLA/HPA antibodies present?**
   - Yes: Use HLA-matched apheresis, antigen matched or crossmatch compatible platelets
   - No: Treat cause (if possible)

6. **Is patient's response to HLA-compatible platelets adequate?**
   - Yes: Improve with HLA-matched platelets
   - No: Consider further aetiological testing. Discuss with NZBS TMS

   - Consult NZBS TMS

7. **Retest for HLA antibodies every 3 months or if refractoriness returns**

   - Improved Response: Continue HLA-compatible platelets
   - Two Poor Responses: Stop HLA compatible platelets

   - Consult NZBS TMS