BLOOD COMPONENT SUPPORT OF RH(D) NEGATIVE INDIVIDUALS

REASON FOR ISSUE: Review of section 4 along with changes in requirement to inform TMS in respect of authorisation process (in appendix A.).

1. INTRODUCTION
Transfusion of Rh(D) positive blood components to an Rh(D) negative patient can result in the formation of anti-D.

- The risk is greatest when Rh(D) positive red cell components are transfused.
- Formation of anti-D following transfusion of Rh(D) positive platelets is also recognised.
- Sensitisation following transfusion of Rh(D) positive frozen plasma components is unlikely, as the small amounts of red cell stroma present are less immunogenic than intact red cells [1].

Whenever possible steps should be taken to avoid transfusion of Rh(D) positive red cell or platelet components to Rh(D) negative recipients. Clinical situations will however emerge when this is necessary. This policy aims to provide guidance on this issue.

The recommendations contained within this policy are based on BCSH Guidelines on the use of fresh frozen plasma [1] and platelets [2].

2. SCOPE
This policy applies to all Blood Banks. It provides guidance on the transfusion of Rh(D) positive components to Rh(D) negative recipients and guidance on the use of Rh(D) immunoglobulin following transfusion of Rh(D) positive components to Rh(D) negative recipients.

3. RISK ASSESSMENT
Any clinical intervention aims to ensure that the likely clinical benefit of a procedure exceeds the risks associated with the intervention. The formation of anti-D following transfusion of Rh(D) positive blood components might result in a number of consequences:

- An absolute requirement for Rh(D) negative support for future transfusions
  Within New Zealand this should be manageable. Problems might however be encountered in other countries.

- Haemolytic transfusion reactions when Rh(D) positive red cell components are transfused
  Delayed haemolytic reactions might occur in individuals who have been sensitised but in whom anti-D is not easily detectable by current pretransfusion testing approaches. The risk is likely to be higher in patients previously transfused with Rh(D) positive components and women who have had pregnancies.

- Haemolytic disease of the newborn
  This risk applies to females of child bearing age and female children. Particular care should be undertaken to avoid transfusion of Rh(D) positive components to this group of patients.

Formation of anti-D will not occur when Rh(D) negative components are transfused. Timely administration of Rh(D) immunoglobulin following transfusion of Rh(D) positive components may also prevent primary immunisation to Rh(D).

4. TRANSFUSION OF RED CELL COMPONENTS
Rh(D) negative red cell components are generally freely available.

Transfusion of Rh(D) Positive red cells to an Rh(D) negative recipient should only be considered in emergency settings when a patient is requiring large numbers of red cells units and this might result in a shortage of Rh(D) negative components for other patients.
The following principles (also summarised in appendix A) therefore apply:

- Transfusion of Rh(D) positive red cells to females of less than 55 years (including female children) should only be considered in life threatening situations. This should only take place following discussion with a Transfusion Medicine Specialist or Haematologist.

- Transfusion of Rh(D) positive red cells to Rh(D) negative males who do not have pre-existing anti-D may be necessary in clinical emergencies involving significant blood loss. In the event that such circumstances arise then an early decision on a switch to Rh(D) positive red cell units may avoid unnecessary depletion of Rh(D) negative units. This can be managed through local protocols. Advice should be sought from a Transfusion Medicine Specialist or Haematologist in the event of doubt or uncertainty.

- Transfusion of Rh(D) positive red cells to Rh(D) negative males undergoing elective surgery should only be considered when supplies of Rh(D) negative red cell components are low. This can be managed through local protocols. Advice should be sought from a Transfusion Medicine Specialist or Haematologist in the event of doubt or uncertainty.

- Rh(D) immunoglobulin is unlikely to prevent formation of anti-D when a whole unit of red cells is transfused. In the event that inadvertent administration of Rh(D) positive red cells is given then advice should be sought urgently from a Transfusion Medicine Specialist or Haematologist.

5. TRANSFUSION OF PLATELET CONCENTRATES

Limited supplies of Rh(D) negative platelet concentrates are available. The major NZBS manufacturing sites and blood banks will endeavour to ensure that at least one adult therapeutic dose of group O Rh(D) negative platelets is available at all times.

Two types of platelet concentrate are currently available namely pooled buffy coat derived platelets (manufactured from a pool of four donations) and apheresis platelets. All platelet concentrates are leucodepleted pre-storage.

Red cell contamination levels with these products is less than with previous forms of platelet products. Red cell contamination does however still occur with leucodepleted concentrates and so the risk of sensitisation is reduced but not eliminated.

Recent analysis of NZBS PAS pooled and PAS apheresis platelets indicates red cell contamination levels of 0.078 and 0.012ml respectively. Evidence indicates that as little as 0.03ml of red cells can lead to alloimmunisation to Rh (D).

The policies described in section 5.1 and 5.2 that follow, apply to Rh(D) negative patients requiring platelet concentrates.

5.1 Patients with Conditions other than Haematological Malignancies

The clinical priorities for using Rh(D) negative platelets are:

- Rh(D) negative females of less than 55 years (including female children) who require platelet support for trauma or surgery i.e. where the requirement for support is short lived; and

- Rh(D) negative females of less than 55 years (including female children) requiring repeated platelet support for non-malignant conditions where future pregnancies are possible.

Whenever Rh(D) positive platelets are transfused to a Rh(D) negative recipient in the above categories then Rh(D) immunoglobulin must be offered. If the requirement for Rh(D) immunoglobulin is in doubt then it should be offered. Section 7 of this document provides advice on the administration and required dose.
In thrombocytopenic patients or those with severe coagulation disorders an Rh (D) immunoglobulin product suitable for intravenous administration is preferred. When not available a standard Rh (D) immunoglobulin product can be given by subcutaneous injection.

Other Rh(D) negative patients who require short term platelet support should be given Rh(D) negative platelets if available. Particular efforts should be made to provide Rh(D) negative platelets to young male children (on paediatric wards). If however Rh(D) positive platelets are transfused in this setting then Rh(D) immunoglobulin is not required.

5.2 Patients with Haematological Malignancies and Other Patients requiring Long Term Platelet Support.

The management of Rh(D) negative patients with haematological malignancies and similar diseases is particularly problematic. Repeated platelet support is likely to be required. The risk of sensitisation is however less because of the immunosuppressive effects of treatment and in some cases the underlying primary condition [3, 4]. The following approach will be adopted:

- Rh(D) negative children should whenever possible receive Rh(D) negative platelets. Rh(D) immunoglobulin should be considered when Rh(D) positive platelets are given to female children in this group. The final decision on the appropriateness of Rh(D) immunoglobulin lies with the consultant responsible for the care of the patient. In the event that Rh(D) immunoglobulin is required then section 7 (and similarly appendix B) of this document provides advice on the administration and required dose.

- Whenever possible female patients of child bearing age should receive Rh(D) negative platelets. Rh(D) immunoglobulin is not normally required when these patients receive Rh(D) positive platelets. The consultant responsible for care of the patient may make an exception to this for individual patients with good prognosis disease. In this setting the consultant will be responsible for ensuring that the hospital blood bank and ward staff are aware of the requirement to administer Rh(D) immunoglobulin. In the event that Rh(D) immunoglobulin is required then section 7 (and similarly appendix B) of this document provides advice on the administration and required dose.

- For other patients, Rh(D) positive platelets may be used unless there is a specific protocol (agreed by TMS / Haematologist) to the contrary.

- Other than where identified above, Rh(D) immunoglobulin treatment is not necessary when Rh(D) positive platelets are administered to this group of patients.

6. TRANSFUSION OF FRESH FROZEN PLASMA AND CRYOPRECIPITATE

Although frozen plasma components may contain small amounts of red cell stroma, sensitisation following transfusion of Rh(D) positive units is most unlikely, as stroma is less immunogenic than intact red cells.

Therefore FFP and cryoprecipitate of any Rh(D) type may be given regardless of the Rh(D) type of the recipient.

No Rh(D) immunoglobulin need be given if Rh(D) negative patients receive Rh(D) positive FFP or cryoprecipitate [1].

7. DOSAGE AND ADMINISTRATION OF ANTI-D IMMUNOGLOBULIN

Where a requirement for administration of Rh(D) immunoglobulin has been identified then the following approach must be adopted:

- Rh(D) immunoglobulin should be administered as soon as possible following transfusion and must be completed within 72 hours of commencement of the transfusion.

- The standard dose of 625 IU Rh(D) immunoglobulin will be more than adequate to cover a single transfusion episode. It is acceptable in most situations to use the smaller 250iu dose for
single platelet transfusions. In the event that repeated transfusion occurs then further standard doses of Rh (D) immunoglobulin should be administered every 4 weeks.

- In thrombocytopenic patients or those with severe coagulation disorders an Rh (D) immunoglobulin product suitable for intravenous administration is preferred. When this is not available an intramuscular Rh (D) immunoglobulin product can be given by subcutaneous injection.

8. REFERENCES
1. BCSH Guidelines on the use of fresh frozen plasma. BJH 2004, 126, 11-28
2. BCSH Guidelines on the use of platelet transfusions. BJH 2003, 122, 10-23
Appendix A: Criteria For Use Of Rh(D) Positive Blood Components For Rh(D) Negative Recipients

1. Red Cell Components
   - Use of Rh(D) positive red cell components for Rh(D) negative recipients should only occur in emergency settings requiring large numbers of red cell units which would result in shortage of Rh(D) negative components.
   - Rh(D) positive red cells should only be considered in recipients who do not have pre-existing (or a history) of anti-D.
   - Administration of Rh(D) immunoglobulin is usually not required when Rh(D) positive red cell components are transfused to a Rh(D) negative recipient in an emergency. If an Rh(D) positive transfusion is inadvertently administered in women of child bearing potential, specialist advice must be sought where a decision to administer of Rh (D) immunoglobulin will be made which will include appropriate dosage.

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Reason For Transfusion</th>
<th>Criteria</th>
<th>Authorisation / Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females &lt;55 years old (including female children)</td>
<td>Clinical emergency with significant blood loss</td>
<td>Life threatening emergency only, when insufficient Rh(D) Neg red cells available</td>
<td>TMS / Haematologist</td>
</tr>
<tr>
<td>Males</td>
<td>Clinical emergency with significant blood loss</td>
<td>Make early switch to Rh(D) Pos red cells to conserve Rh(D) Neg red cell stock</td>
<td>Registered Medical Laboratory Scientist</td>
</tr>
<tr>
<td></td>
<td>Elective surgery</td>
<td>Only if supplies of Rh(D) Neg red cells are low</td>
<td>Document on Technical Advice form for regular TMS review</td>
</tr>
</tbody>
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2. Platelet Concentrates
   (i) Patients with conditions other than haematological malignancies

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Reason For Transfusion</th>
<th>Criteria</th>
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</tr>
</thead>
</table>
| Females <55 years old (including female children) | Trauma or surgery needing short term support | - Clinical priority is to use Rh(D) Neg platelets  
- Use Rh(D) Pos platelets only if absolutely no Rh(D) Neg platelets available  
- Anti-D Ig should be given if Rh(D) Pos platelets used | TMS / Haematologist to use Rh(D) Pos platelets |
|                                        | On-going and future pregnancies possible         |                                                                          |                                                             |
| Young male children (On Paediatric wards) | Short term support                             | - Particular effort must be made to provide Rh(D) Neg platelets  
- Use Rh(D) Pos platelets only if insufficient Rh(D) Neg platelets available  
- Anti-D Ig is not required if Rh(D) Pos platelets given | Registered Medical Laboratory Scientist  
Document on Technical Advice form for regular TMS review |
### BLOOD COMPONENT SUPPORT OF Rh(D) NEGATIVE INDIVIDUALS

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<thead>
<tr>
<th>Patient Category</th>
<th>Reason For Transfusion</th>
<th>Criteria</th>
<th>Authorisation / Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Other patients</td>
<td>Short term support</td>
<td>• Decision based on likely availability of Rh(D) Neg platelets&lt;br&gt;• Use Rh(D) Pos platelets only if insufficient Rh(D) Neg platelets available&lt;br&gt;• Anti-D Ig is not required if Rh(D) Pos platelets given</td>
<td>• Registered Medical Laboratory Scientist&lt;br&gt;• Document on Technical Advice form for regular TMS review</td>
</tr>
</tbody>
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(ii) **Patients with haematological malignancies and other patients requiring long-term platelet support**

Patients should be given Rh(D) negative platelets if available. Although repeated platelet support is likely to be required, risk of sensitisation to anti-D is lessened due to immunosuppressive effects of treatment and in some cases the underlying condition.

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Reason For Transfusion</th>
<th>Criteria</th>
<th>Authorisation / Advice</th>
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</thead>
<tbody>
<tr>
<td>Female children</td>
<td>On-going support</td>
<td>• Clinical priority for use of Rh(D) Neg platelets; Only use Rh(D) Pos platelets if absolutely no Rh(D) Neg platelets available&lt;br&gt;• Anti-D Ig should be considered with decision made by Consultant responsible for care of patient</td>
<td>TMS / Haematologist to use Rh(D) Pos platelets</td>
</tr>
<tr>
<td>Male children</td>
<td>On-going support</td>
<td>• Use Rh(D) Pos platelets only if insufficient Rh(D) Neg platelets available&lt;br&gt;• Anti-D Ig is not required if Rh(D) Pos platelets given</td>
<td>• Registered Medical Laboratory Scientist&lt;br&gt;• Document on Technical Advice form for regular TMS review</td>
</tr>
<tr>
<td>Females of childbearing age (&lt;55 years old)</td>
<td>On-going support</td>
<td>• Rh(D) Neg platelets should be used whenever possible. Use of Rh(D) Pos platelets at TMS / Haematologist discretion based on likely availability of Rh(D) Neg platelets&lt;br&gt;• Anti-D Ig is not normally required - Consultant responsible for patient may make exception if good prognosis expected</td>
<td>TMS / Haematologist to use Rh(D) Pos platelets</td>
</tr>
<tr>
<td>Other patients</td>
<td>On-going support</td>
<td>• Rh(D) Pos platelets may be used unless Rh(D) Neg platelets specifically requested by TMS / Haematologist (within agreed local protocol)&lt;br&gt;• Anti-D Ig not normally required – Consultant responsible for patient may make exception if good prognosis expected</td>
<td>• Registered Medical Laboratory Scientist&lt;br&gt;• Document on Technical Advice form for regular TMS review&lt;br&gt;• TMS / Haematologist – if unable to meet protocol</td>
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</tbody>
</table>
3. **Fresh Frozen Plasma / Cryoprecipitate**

Although frozen plasma components may contain small amounts of red cell stroma, sensitisation following transfusion of Rh(D) positive units is most unlikely, as stroma is less immunogenic than intact red cells.

FFP and cryoprecipitate of any Rh(D) type may be given regardless of the recipient's Rh(D) status. *No anti-D immunoglobulin need be given* if Rh(D) negative recipients receive Rh(D) positive FFP or cryoprecipitate.

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**Appendix B: Dosage And Administration Of Rh(D) Immunoglobulin**

<table>
<thead>
<tr>
<th>When</th>
<th>Dosage</th>
<th>Route Of Administration</th>
<th>Frequency</th>
</tr>
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<tbody>
<tr>
<td>ASAP and within 72 hours of commencing</td>
<td>Standard Dose i.e. 100 IU/ml of Rh(D) Pos</td>
<td>Subcutaneous</td>
<td>• Single transfusion episode - standard dose*</td>
</tr>
<tr>
<td>transfusion</td>
<td>red cells transfused*</td>
<td></td>
<td>of Rh(D) Ig normally adequate</td>
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<td></td>
<td></td>
<td>Intravenous – thrombocytopenic patients or those with severe coagulation disorders**</td>
<td>• Repeated transfusions - Rh(D) Ig should</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td>be administered every 4 weeks</td>
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</tbody>
</table>

* CSL Rh(D) Immunoglobulin available as 625 IU single dose vial

** Use product registered for intravenous use