

# Provision of HLA Matched Platelets

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# Patient Categories for HLA Matched Platelets

- Refractory patients
  - Patients with platelet disorders e.g. Glanzmann's / Bernard Soulier's
  - HLA-selected platelets are directed donations for a named patient
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# Platelet refractoriness

## Definition

Increase in patient's platelet count of  $<10 \times 10^9/l$  at between 1 and 24 hours after the transfusion of an adult dose of ABO compatible platelets on two separate occasions



# Platelet Refractoriness

## Immune

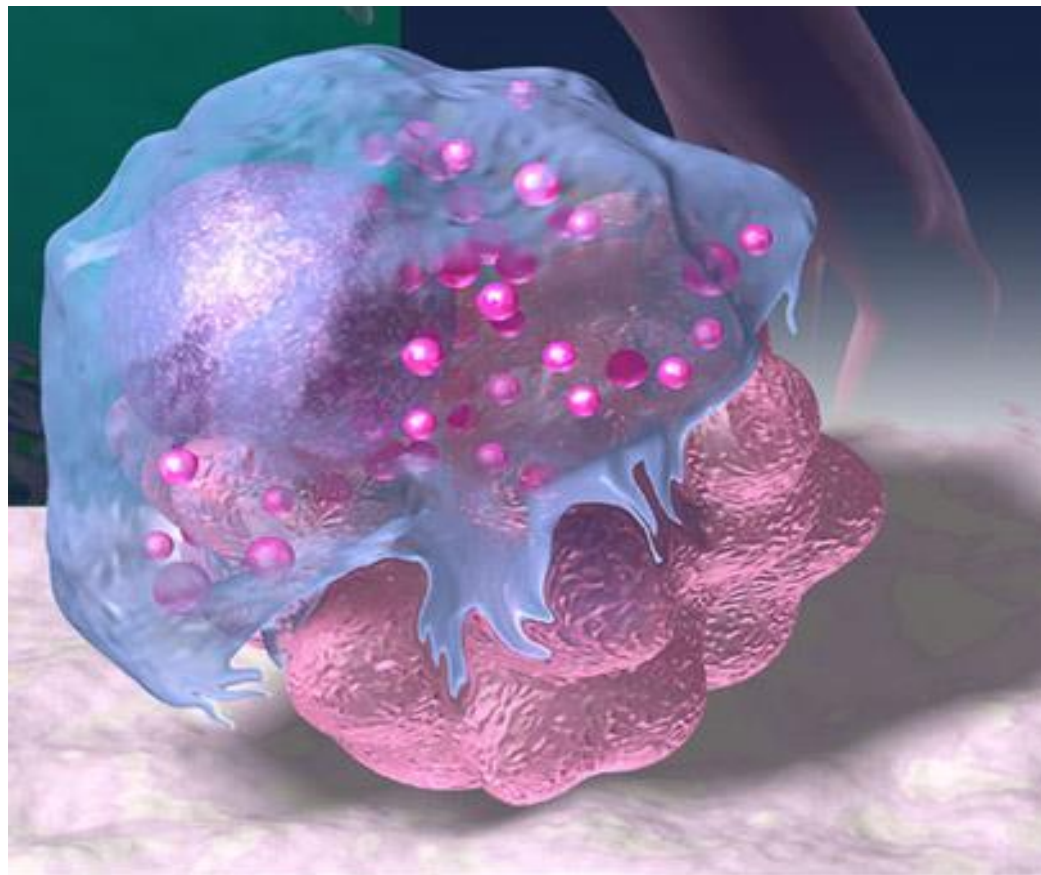
- Platelet alloantibodies
  - **anti HLA (>95%)**
  - anti HPA (<5% HPA + HLA, HPA only <1%)
- Other antibodies
  - Autoantibodies
  - Drug-dependent antibodies
  - ABO antibodies
- Immune complexes

## Non Immune (80%)


- Splenomegaly
- DIC
- Bleeding
- Consumption (eg ECMO)
- Infection and its treatment  
e.g. amphotericin B

## **Immune mediated platelet refractoriness**

**Splenic macrophages remove antibody coated platelets from circulation via Fc receptors**



# Platelet Refractoriness

- **Laboratory tests:** HLA type and HLA antibody test
  - **Diagnosis:** detection of HLA class I antibodies is required to confirm diagnosis of immunological refractoriness
  - **Management:** HLA matched platelets are provided, the degree of match grade assigned as:
    - A grade:** - matched at HLA A and B
    - B grade:** - selected donation, mismatched at 1-4 HLA A or B antigens
  - Monitor platelet increment following transfusions
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# Luminex Antibody Identification Technology



Blood and Transplant

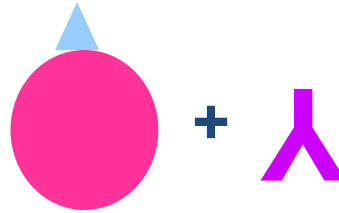
100 different colour coded polystyrene beads in a single well



Each bead population coated with selected class I or class II antigens or pool of antigens for screening purposes

## Procedure

1. Microbeads coated with HLA antigen incubated with patient serum

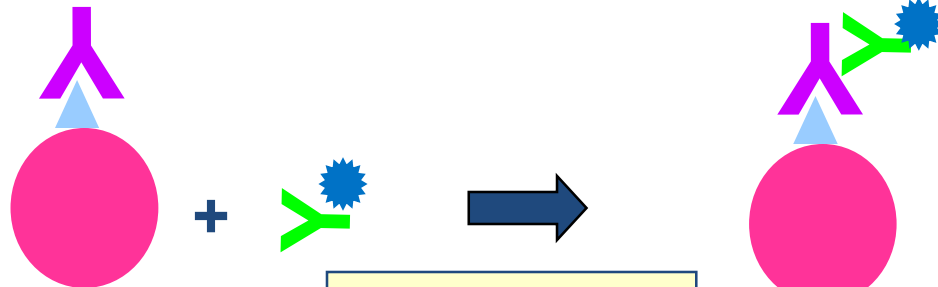


2. Wash beads



5. Run beads on LabScan 100™  
- assign assay reactivity and antibody specificities

3. Incubate with PE conjugated anti-human IgG



4. Wash beads

# Platelet selection

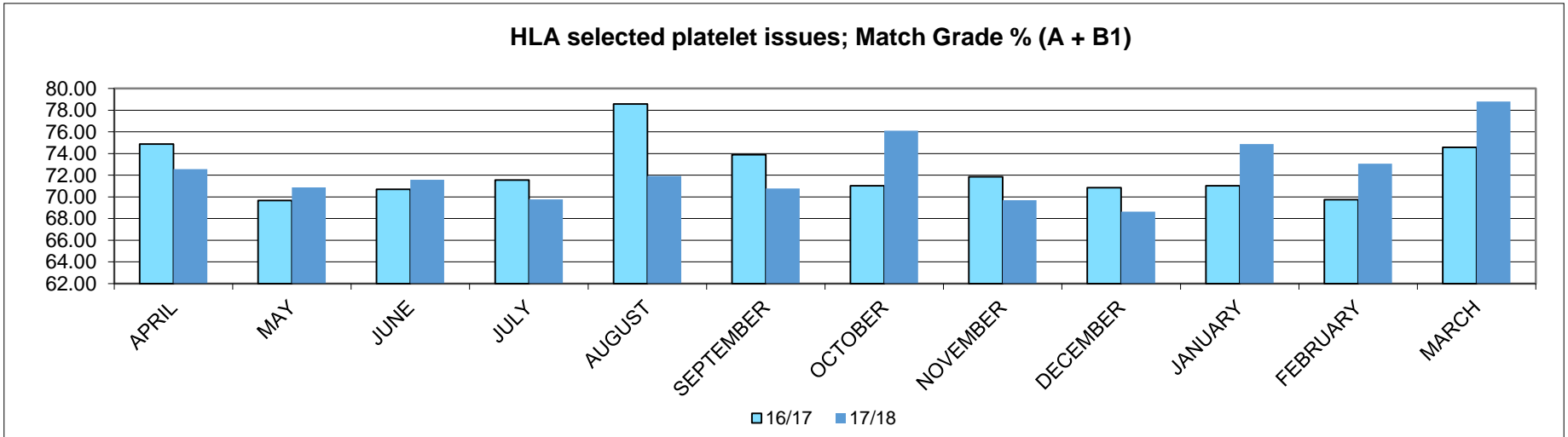
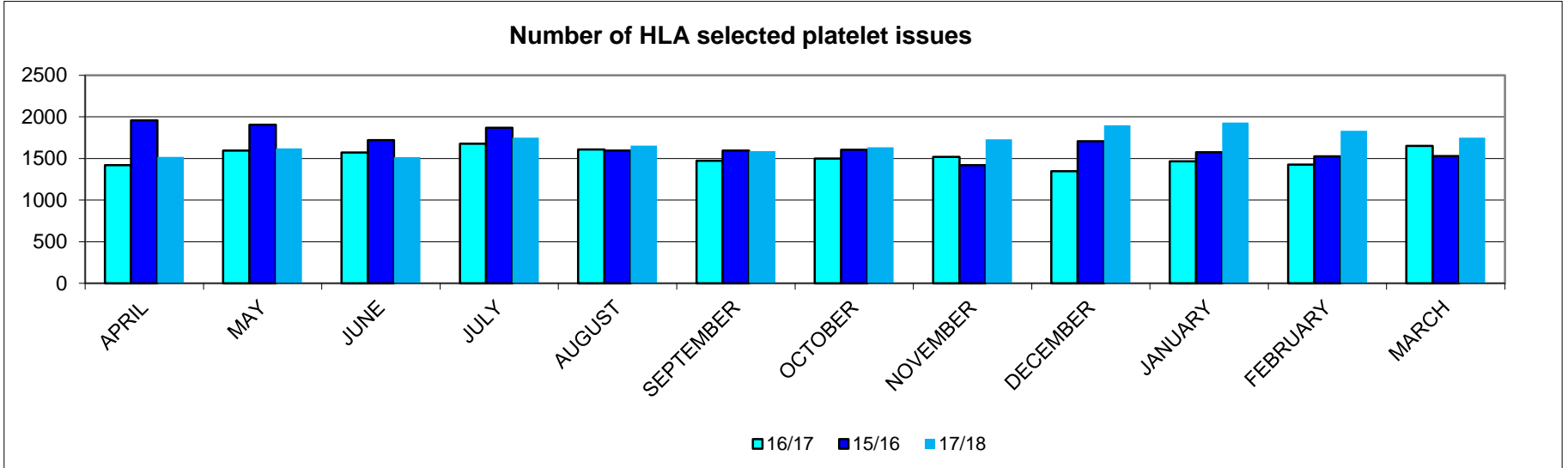
- Strategies for treating refractoriness due to HLA antibody
  - fully HLA match patient and platelet donor
  - select platelets lacking any antigens to which patient has antibody
- Patient's HLA type & antibody data
- Search platelets in stock for best available match
- HLA match grades
  - A - full match at HLA-A,B
  - B1 - single antigen mismatch
  - B2 - 2 antigen mismatches
  - B3 - 3 antigen mismatches
  - B4 - 4 antigen mismatch




# Matching

- Patient - HLA A2,A24 B44,B62
  - antibody specificity A1,A3,A11 B7,B27,B60,B61
- Donor 1 HLA A2 B44,B62 (A match)
- Donor 2 HLA A2,A68 B44,B62 (B1 match)
- Donor 3 HLA A1,A2 B44,B62 (B1 match)
- Donor 4 HLA A2,A31 B8,B44 (B2 match)
- Donor 5 HLA A2,A25 B7,B45 (B3 match)
- **Better responses to A and B1 mm vs B2-B4**

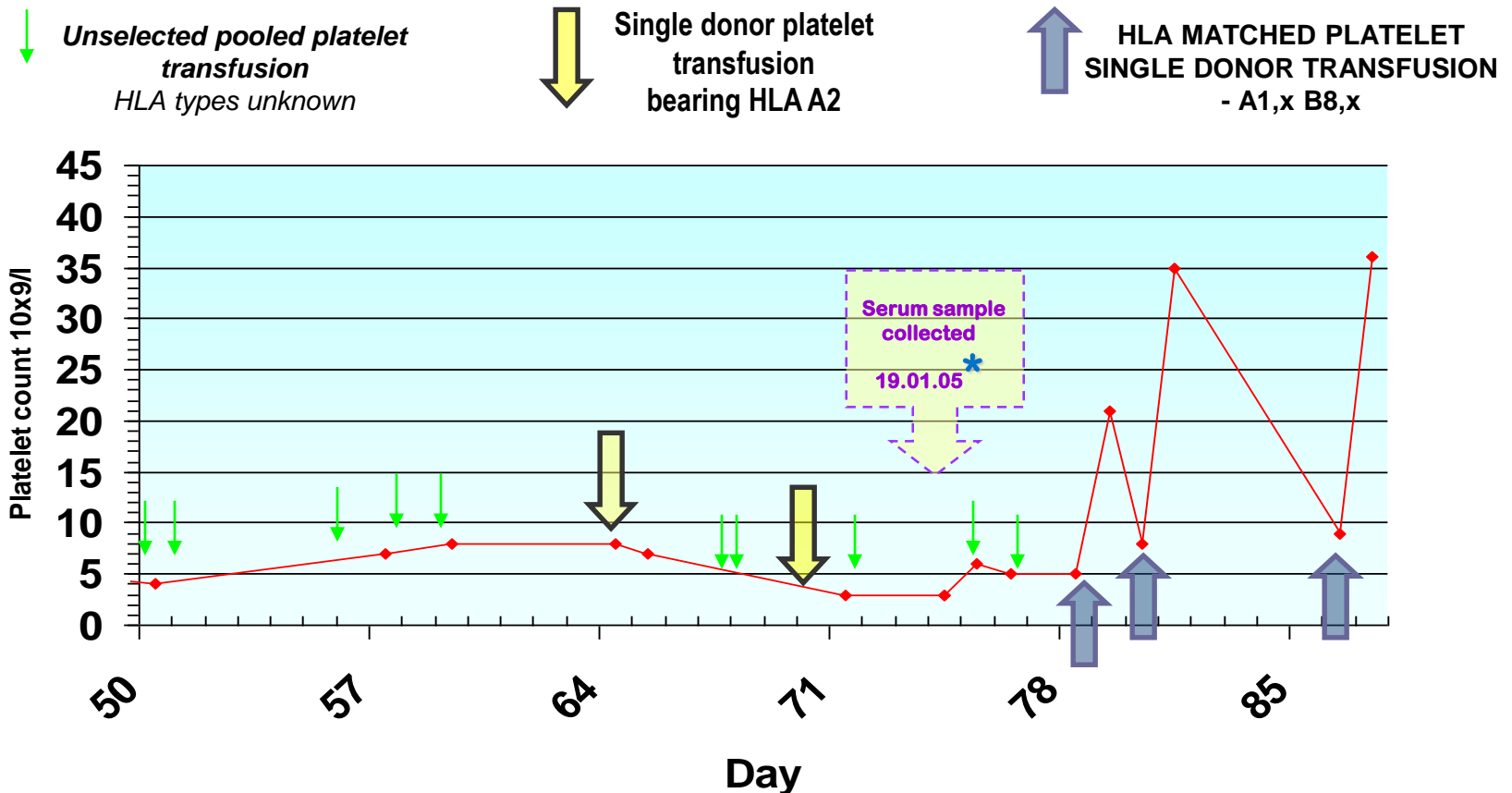
# Product Issue – HLA selected pts



# Important Factors When Ordering

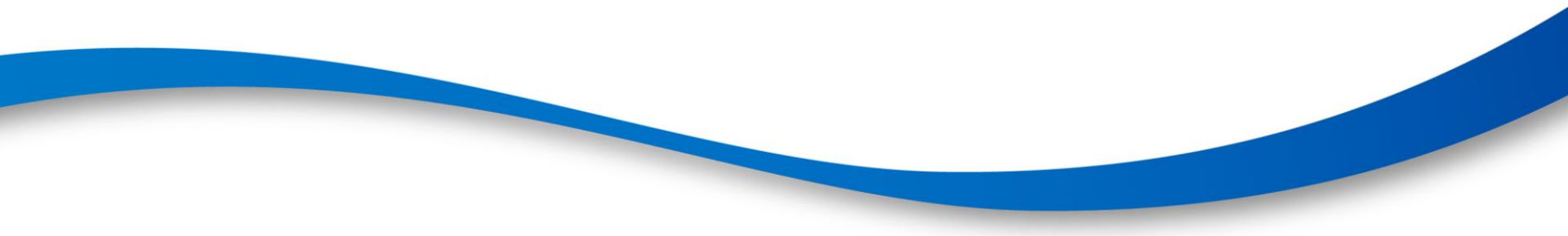
- Wherever possible 24 hrs notice required
    - so that the best possible match for the patient can be obtained
  - If only CMV Neg platelets are requested for patients
    - reduces the donor pool for matching and in some cases will result in a less well matched component being supplied than would be the case if CMV unselected was accepted
  - HLA platelets must be subject to ongoing increment measurement
    - informs future provision and fine-tuning of matching selected platelets for best outcome in patients
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# Case MJ - Platelet counts during unselected pooled and single donor apheresis and subsequent HLA matched platelet support



\* 19.01.05 = HLA A2 antibodies,  
Luminex also detected A68,B57,B58 PRA 46%

# Increment Data

- Required to aid in platelet selection
    - Identify unacceptable antigens
    - Identify acceptable antigen
    - Identify immune from non-immune refractoriness
  - National average return rate 2013 only 33.57%
    - Range 57.68 – 3.43%
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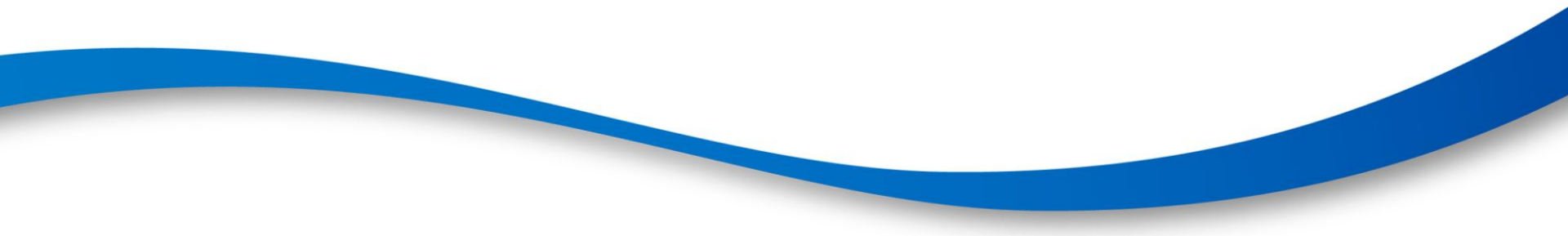
# Platelet increments

Patient WS

HLA type HLA-A2; B7 antibodies 96% A3++

Date	Donor type	Pre count	Post count
04/5/05	A2, A30; B7, B40	5	6
09/5/05	A2; B7, B27	7	33
11/5/05	A2; B40	9	30
17/5/05	A2, A24 B7, B39	6	3
18/5/05	A2; B7, B27	3	45
23/5/05	A2; B7	15	53
27/5/05	A2; B40	6	34

# Reasons for Incremental Data

- To aid in platelet selection
    - Identify unacceptable antigens
    - Identify acceptable antigen
  - To achieve better clinical response
  - To identify if HPA testing is required
  - To identify if further samples are required for HLA antibody testing
  - To not waste a precious resource
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# Service Level Agreement



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- Our SLA is to provide 24 hours notice (except for emergencies)

8.2 The Purchaser shall submit a purchase order for HLA and HPA-selected products at least one working day/24 hours (not including weekends) in advance of delivery unless its considered an emergency situation in which case the Purchaser shall submit a purchase order for HLA and HPA-selected products as soon as reasonably practicable to do so.

Requirement is for the benefit of the patient

- to source the most beneficial unit in the country
- time to transport the unit (without additional cost to the hospital) for the requested delivery time.

Helps to keep the cost of this product as low as possible as units can be moved around the country on routine NHSBT deliveries.



# Audit of orders for HLA selected platelets


- We performed a national audit of requests for HLA selected platelets
  - Period Jan 2016-March 2016
  - 46% of all orders were less than 24hours notice
    - Ad hoc charge may have been applied
    - Of these 23% were for same day delivery
    - A less well matched unit may have been provided
    - Risk of increasing the antibody profile of the patient

# Case Study G.O.


- HLA type A1,32 B7
- HLA Antibodies A11, A2, A23, A24, A25, A26, A29, A3, A30, A31, A33, A34, A43, A66, A68, A69, A74, A80, B13, B18, B35, B37, B38, B39, B41, B42, B44, B45, B46, B47, B48, B49, B50, B51, B52, B53, B55, B56, B57, B58, B59, B60, B61, B62, B63, B64, B65, B67, B71, B72, B75, B76, B77, B78, B8, B82

Date	Order type	Match Grade	DSA
11/9	Routine	A	N
19/9	On-call	B2	Y
20/9	On-call	B3	Y
20/9	On-call	B2	Y
25/9	Routine	B1	Y
27/9	Routine	B1	N
28/9	Routine	B1	N
30/9	Routine	B1	N

# Ordering HLA/HPA selected products

- Place orders for HLA/HPA selected products on OBOS (specialist stock module):
    - OBOS is available through your blood transfusion department
    - for planned procedures and emergencies
  - We will process orders, including transfusions planned for the weekend during core H&I laboratory hours:
    - **Monday to Friday 09.00 – 17.00 hours**
    - Orders for planned procedures should be placed during these hours
    - When placing an order **select a delivery time that provides at least 24 hours notice.**
    - If known, provide the transfusion date and time
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# Emergency Requests

- If a clinical emergency occurs outside of the core laboratory hours
    - after 17:00 hours and weekends
    - the emergency 'out of hours' service is available.
  - This service is for clinical emergencies only and not for routine or planned procedures
    - Not possible to provide optimally HLA matched platelets at short notice,
    - We will select a unit from local stock due to time constraints.
    - We will endeavour to provide a well matched unit, however finding a suitably matched unit at short notice may not always be possible for all patients.
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# NHSBT is reviewing this service



Blood and Transplant

- Developing new strategies to identify the most beneficial units for patients
    - clinical trial of epitope matched platelets
  - Reviewing Specialist stock management
    - to ensure stock is located at the most appropriate NHSBT sites to serve patients.
  - Reviewing our transport routes
    - to increase efficiency of transporting HLA/HPA selected products around the country.
  - These initiatives will continue to improve our ability to provide the most beneficial unit for your patient
  - And keep costs as low as possible for this product.
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- A thick, blue, wavy graphic that spans the width of the slide at the bottom, starting from the left edge and ending at the right edge, with a slight curve.

# Summary

- Not an 'off the shelf' product
  - Can be time consuming
  - Full matches not possible for majority of patients
  - For best patient response
    - Good planning needed to get best product
    - Increment data to inform selection
  - Patients with rare HLA types and/or multiple antibodies, especially those with HLA + HPA, may be difficult to support
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