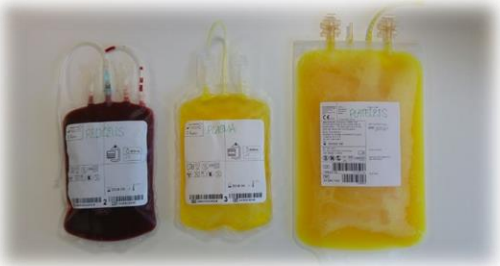
NHS
Blood and Transplant

NEW DEVELOPMENTS



TRANSFUSION BITES CONFERENCE

JANE DAVIES & MIKE WILTSHIRE

6TH NOVEMBER 2019

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Blood and Transplant

Whole Blood in Trauma (pre hospital)

Jane Davies

Whole Blood in Trauma

- Used widely in the military in cases of trauma.
- Phase 1 (whole blood without platelets). Study currently ongoing in conjunction with Royal London Hospital and London's Air Ambulance
    - To enable rapid transfusion of plasma as well as red cells
    - Logistical benefits over flying with & administering multiple bags/types of components

- Comparators.
    - Patients transfused RBC pre hospital (March 2015 – August 2018)
    - Trauma patients who received RBC and FFP pre hospital in Oxford and Newcastle.

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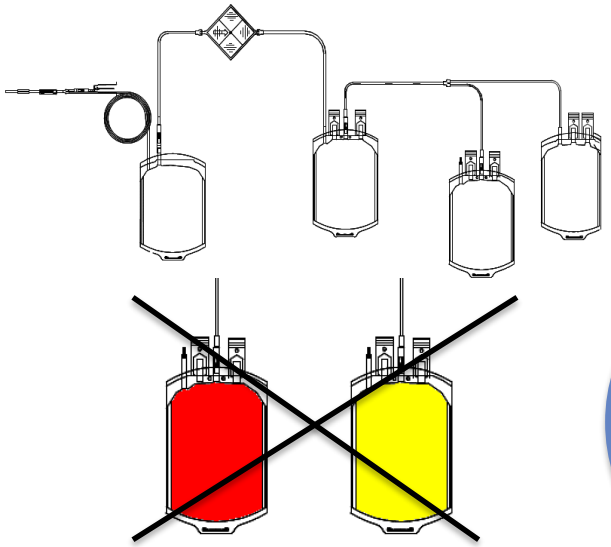
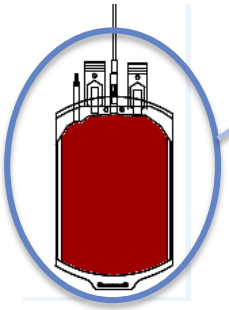
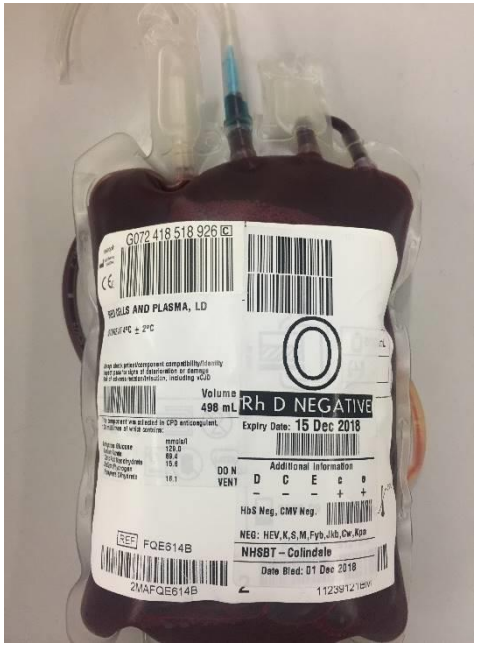
Whole Blood in Trauma - Phase 1.

Leucocyte depletion filter removes platelets



Red cells Plasma





- 14 day shelf life.
- Transfused Pre admission.
- Male donor / O neg / HT neg / Kell neg

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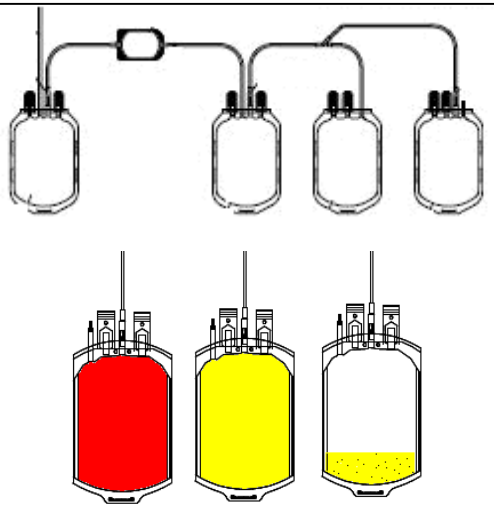
Whole Blood in Trauma - Phase 2.

Leucocyte depletion filter saves platelets (Terumo Imuflex)



Red cells | Plasma | ¼ unit of platelets

- Whole blood with platelets.
- Shelf life unknown as early validations are still ongoing (platelet studies)
- Hopeful for 14 days.
- Cold stored (including platelets)
  - Better for trauma
  - Bleeding time corrected more quickly.
- How novel is it ?
- Can we re-use it for anything if not required?

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Neonatal Platelets

Jane Davies

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Neonatal Platelets – Component Improvement.

- Currently suspended in plasma with a 7 day shelf life.
- Ongoing project to try to improve the quality of the platelet at the end of 7 days.
    - By the addition of an agreed volume of Platelet Additive Solution (SSP+) prior to splitting.
- Currently finalising validation and gaining approvals to proceed.

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Neonatal Platelets – Next steps.

- Complete change control
- Final Approvals
- Notify hospitals of go live date
- Go live

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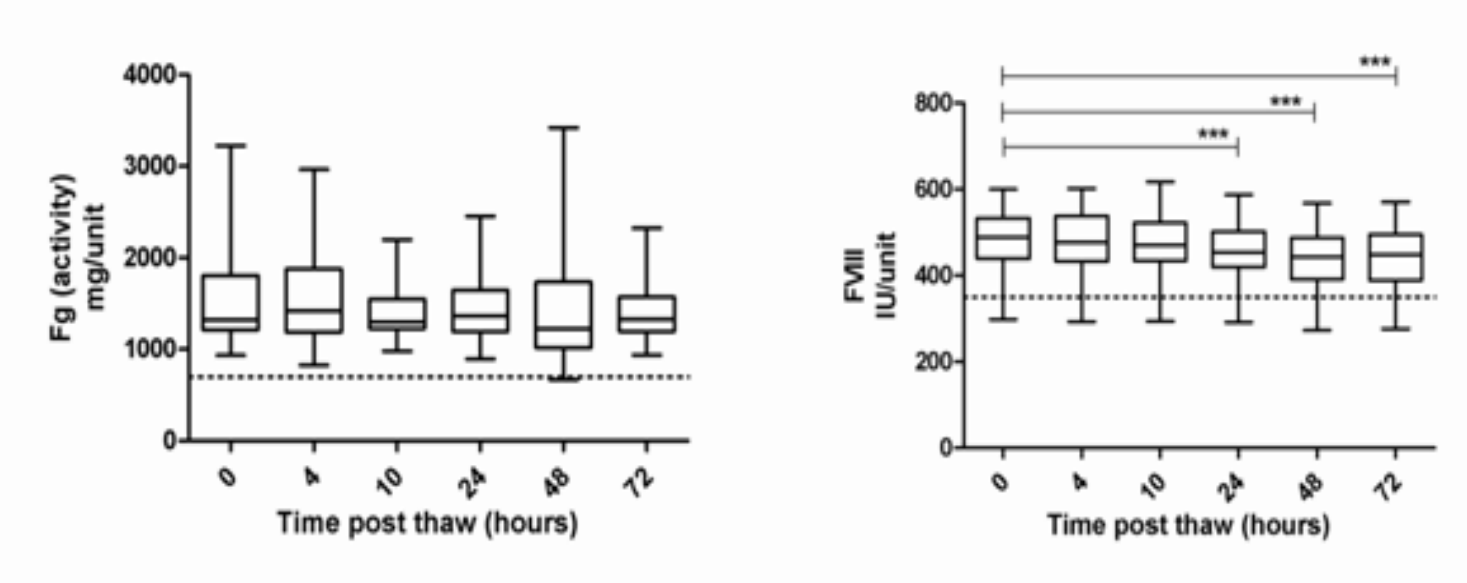
Can we improve speed of delivery / reduce wastage of cryoprecipitate?

Mike Wiltshire

Cryoprecipitate

Can we store it longer than 4h at ambient once thawed?



- Fibrinogen and FXIII stable for up to 72 hours
- Significant decrease in FVIII after 24 hours
- Bacteriology risk unquantified

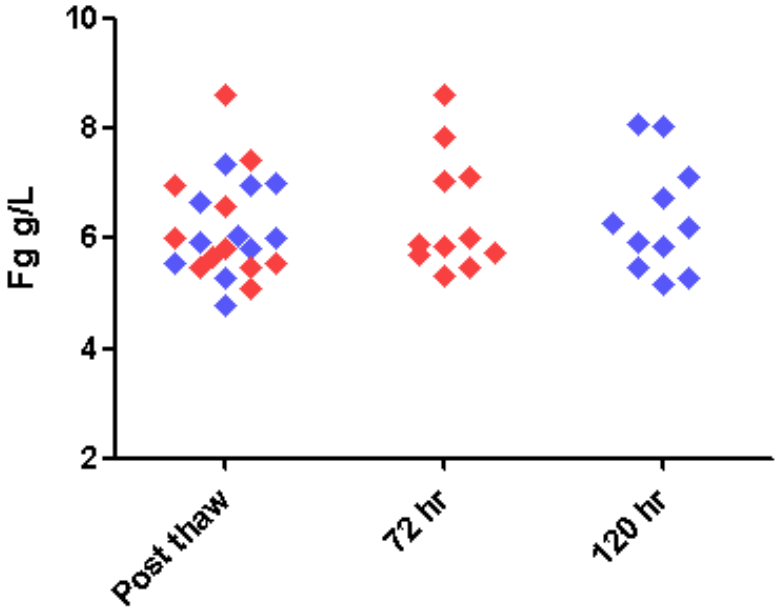
Green/Backholer et al. Transfusion 2016; 56:1356-1361

Cryoprecipitate – 4 °C storage

- Lower bacteriology risk
- FFP 5 day PT storage at 4°C for major haemorrhage
- Storage at 4°C causes reprecipitation of coagulation proteins
  - Reconstitute with a short 37°C warm step

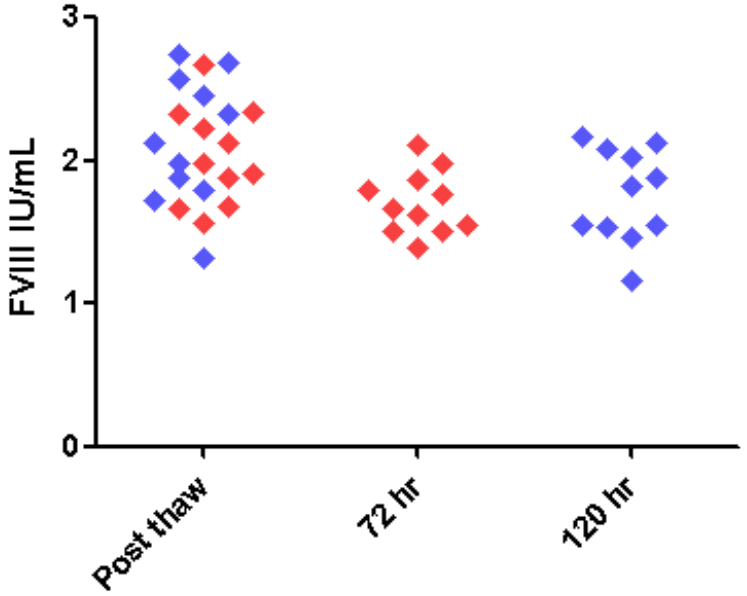
Cryoprecipitate – 4 °C storage

Fibrinogen



Storage	% of starting (post thaw)
72 hr	102.9
120 hr	104.1

FVIII



Storage	% of starting (post thaw)
72 hr	84.4
120 hr	82.4

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Can We Make Blood More ‘Universal’?

Mike Wiltshire

Universal Plasma

There is no licensed universal plasma product in UK or EU

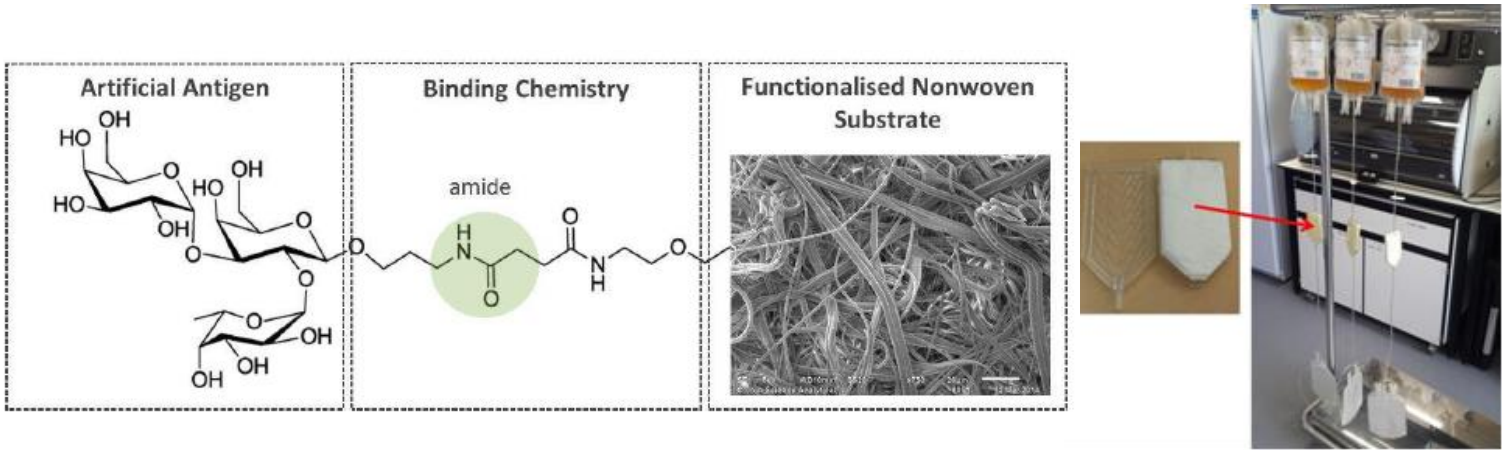
Options to make ‘universal’ plasma

- Pooling different blood groups to neutralise anti-A and B by binding to free A and B and residual red cells
  - Uniplas SD & Bioplasma FDP
  - FlyP (French Military)

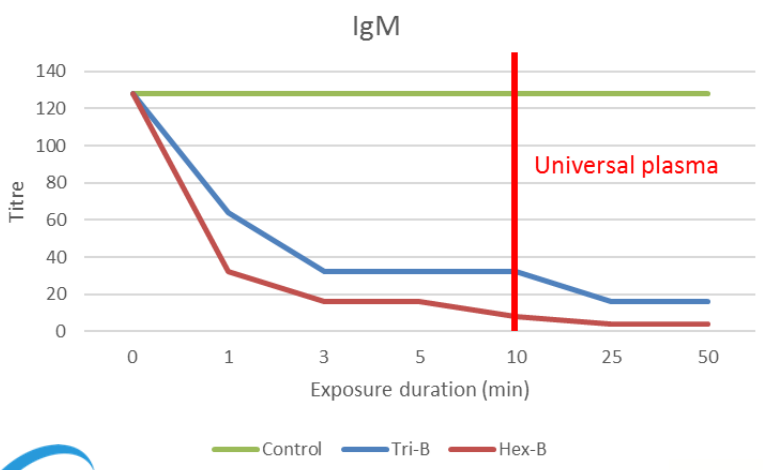
  Likely considered a medicine in UK
- Removal of anti-A and B
  - Concept used to remove anti-A and B prior to ABO incompatible transplant
  - Proof of concept performed for plasma

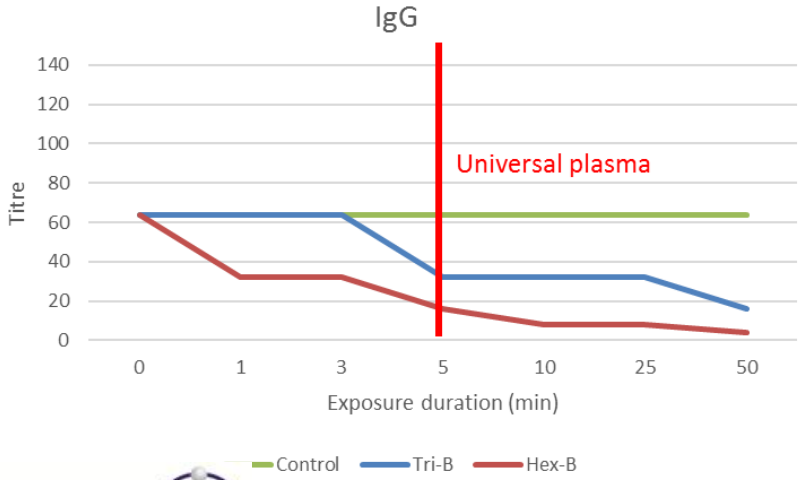
Universal Plasma Proof of Principle

We can incorporate artificial red cell substances into filter media



Filtration removes antibodies to levels we consider safe for patients





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More Universality for Platelets?

Platelets – what are the issues?

Challenges with supply

- Increasing demand in future?
- Short shelf-life (5-7d)
- Need to agitate (transport)
- Room temp storage (practicalities, bacteria)
- Have to take account of
  - ABO/RhD
  - HLA/HPA
  - CMV

Risks to the patient

- Acute and delayed haemolytic reactions
- Allergic and febrile non-haemolytic reactions
- Transfusion-related acute lung injury (TRALI)
- TTI: bacterial > viral > vCJD, emerging pathogens
- Transfusion-associated graft-versus host disease
- Post-transfusion purpura

The problem - Supply

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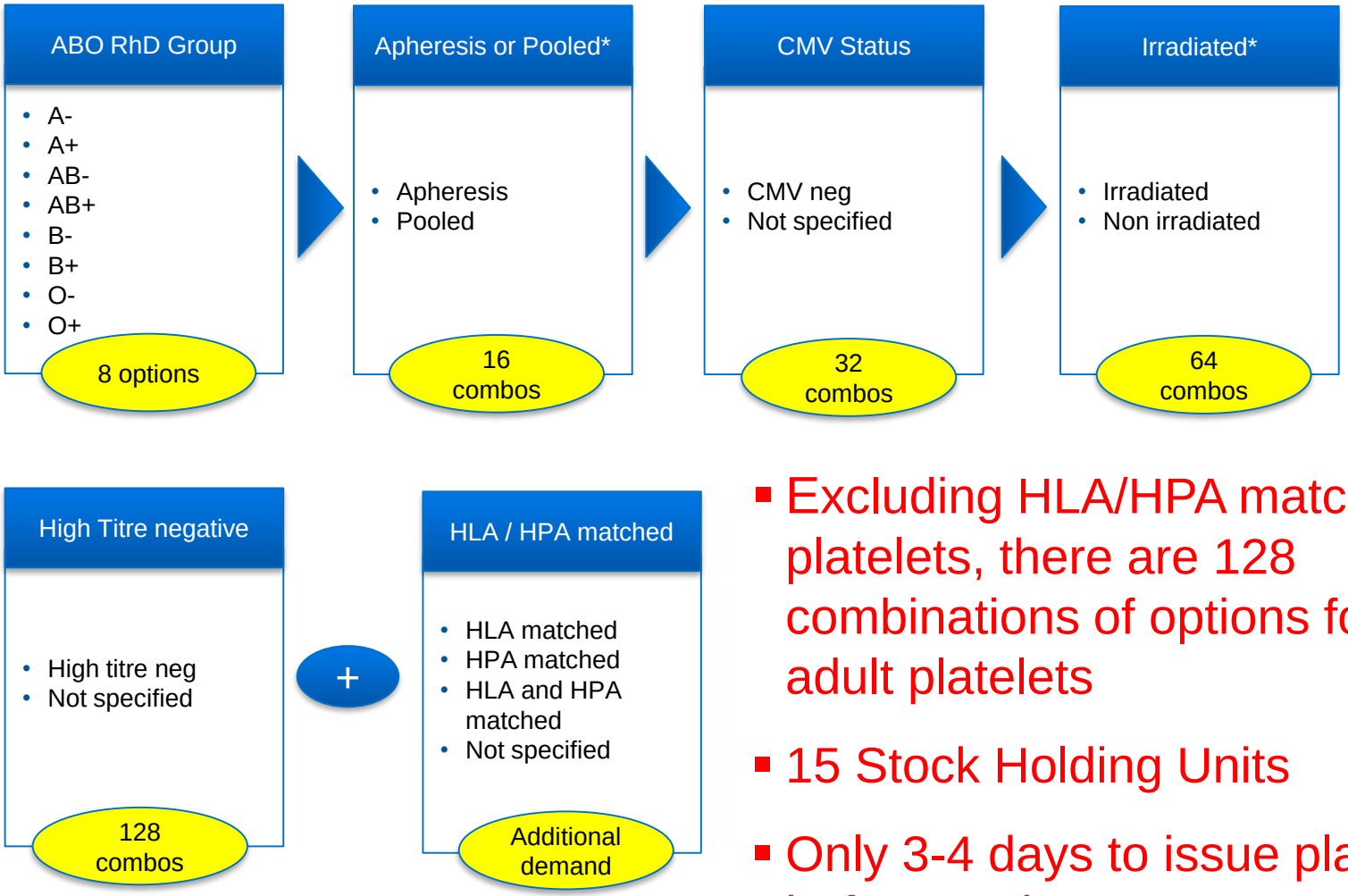


- Excluding HLA/HPA matched platelets, there are 128 combinations of options for adult platelets
- 15 Stock Holding Units
- Only 3-4 days to issue platelets before expiry

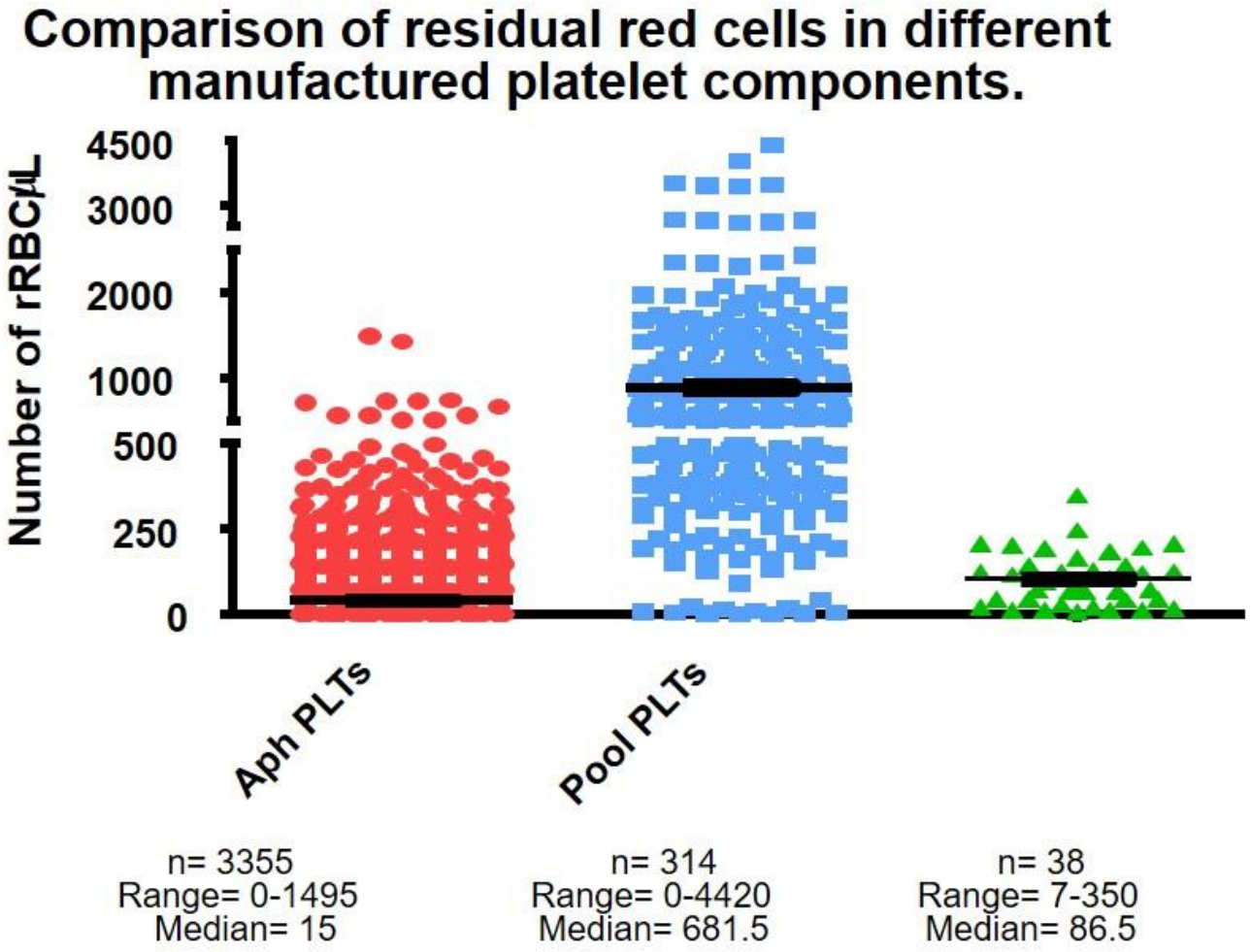
HLA / HPA matched platelets are all apheresis and irradiated

Could we do something about RhD?

- Can we transfuse out of group by reducing anti-A and B titres?
  - Unlike plasma we have options to dilute/re-suspend platelets in something other than plasma
  - Removal by ‘filtration’
- Unlike plasma we also have to consider A and B antigens on platelets
- Impact of ABO incompatibility on platelet count?

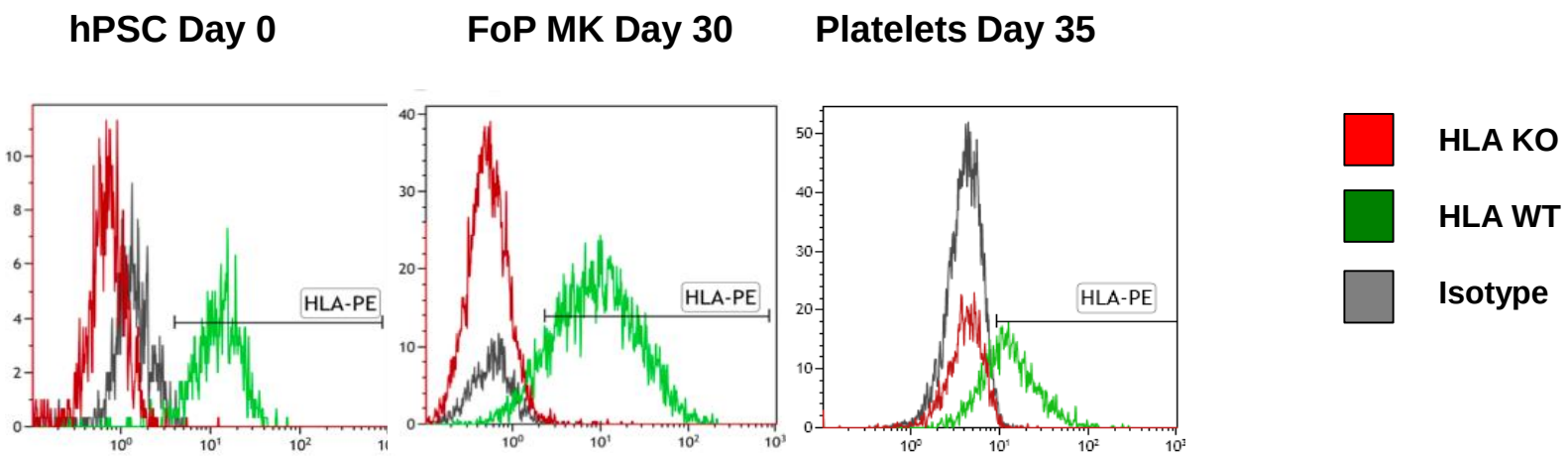
Could we do something about RhD?

Can we reduce red cell contamination of platelets?



Genome editing: ‘universal’ platelets

- 6% of all issued platelets units in England are HLA class I matched
- HLA Class I expression depends on expression of β2 microglobulin
- Using CRISPR-Cas 9 technology we can knock-out β2m expression and create iPSC lines from which universal HLA Class I null platelets can be derived



Slide courtesy of Ghevaert group University of Cambridge

More Universality for Platelets

- What else can be done:
  - CMV
    - Pathogen inactivation?
  - Irradiation
    - Pathogen inactivation?
    - 100% irradiation?

Universality for Platelets

- What data/trials would be needed to assure safety?
- What data/trials would be needed to enable change in policy?

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Any Questions ?