UK NEQAS 50 Years as World Leaders in EQA 1969–2019

International Quality Expertise

Histocompatibility and Immunogenetics

Annual Participant's Meeting 2018

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Director: Tracey Rees

Manager: Deborah Pritchard

Operations Manager: Amy De'Ath

Deputy Scheme Manager: Melanie Bartley

Healthcare Scientist Practitioner: Geraint Clarke

UK NEQAS Officers: Luke Gardner & Lucy Palmer

Welsh Blood Service

GIG CYMRU NHS WALES

Ymddiriedolaeth GIG Prifysgol Felindre

Velindre University NHS Trust

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Welcome and Introduction

Judith Worthington

Chair of UK NEQAS for H&I Steering Committee

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2018 Steering Committee

- Judith Worthington (Chair)
- Arthi Anand
- Patrick Flynn
- James Kelleher
- Anthony Poles
- Ruhena Sergeant
- John Smith – retired November 2018
- Helena Lee (BSHI Representative to UK NQAAP)
- Rommel Ravanan (Clinical Representative)

- Kathryn Robson (Lead Expert Advisor Scheme 5B)
- Alan Balfe (Expert Advisor Scheme 5B)
- Gavin Willis (Expert Advisor Scheme 5B)

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Notes

- Presentation focus on performance, interesting trends, discussion points, changes for 2019
- Labs 1-100 are from the UK and Ireland (UK&I)
- Labs 101 + are from the rest of the world (RoW)
- Please ask questions!

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Scheme Assessment

- Most Schemes assessed on a consensus basis using a 75% consensus level i.e. 75% of reports must agree on a result for it to be assessed
- Reference typing results are used for typing/disease schemes if consensus not reached and any educational/pilot schemes
  - Scheme 5B: Interpretative HFE
  - Scheme 8: HLA Genotyping for HLA Associated Diseases
  - Scheme 4A1: HLA Typing at 1st Field Resolution - DPB1 assessment using a reference result
  - Scheme 4A2: HLA Typing to 2nd/3rd Field Resolution, Scheme 7: HLA-B*57:01 Typing for Drug Sensitivity, Scheme 9: KIR Genotyping, Scheme 10: HPA Genotyping a reference result used for assessment if consensus is not reached
- All Not tested (NT) results excluded from assessment
- Equivocal result only accepted for Scheme 2B
- Labs that fail to return results, or provide valid reason for NT are assessed as unacceptable

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Unsatisfactory Performance (UP)

- Each scheme has minimum annual performance criteria
  - HLA Typing schemes 90%
  - Crossmatching 85%
  - Disease Association Schemes 100%
  - Antibody Specificity 75%
  - Antibody Detection 80%
- Participants that do not meet the minimum criteria are classed as unsatisfactory performers
- Must complete a root cause analysis and CAPA form

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Changes for 2019

- Steering Committee
  - Tim Clench and Marian Hill (Expert Advisor Scheme 5B)
  - John Smith Retired
  - Helena Lee replaced by Elizabeth Wroe
- NEQAS Operations Manager covering maternity leave
- Financial year operation has been implemented
- The 'Participant's Portal' bespoke EQA IT system has been introduced

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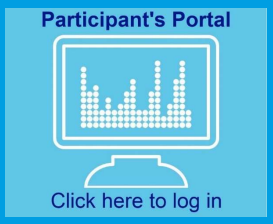
Participant's Portal



"Thank you for implementing this new on-line system for EQA.

I found it easy and logical to navigate."

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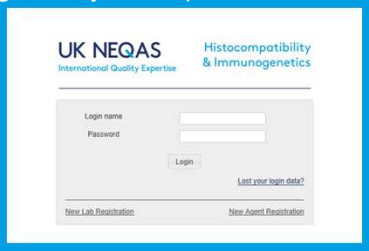
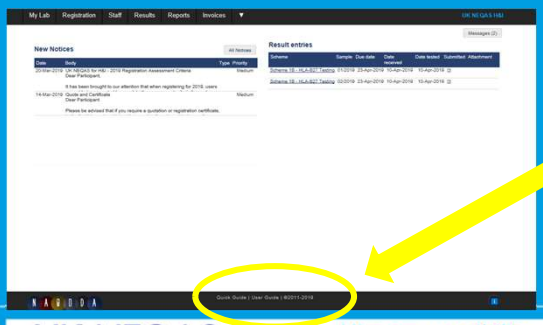
Participant's Portal

- A link to the system can be found on the UK NEQAS for H&I webpage (https://neqas.welsh-blood.org.uk) or by going directly to the portal website https://ukneqashandi.naqoda.cloud
- *Note: users will automatically be logged out of the system after 60 minutes of inactivity. Ensure any work, e.g. results entry is saved or submitted to prevent loss of data.*





- *Note: The System User Guide and the 'QuickGuide' are available in the footer section*

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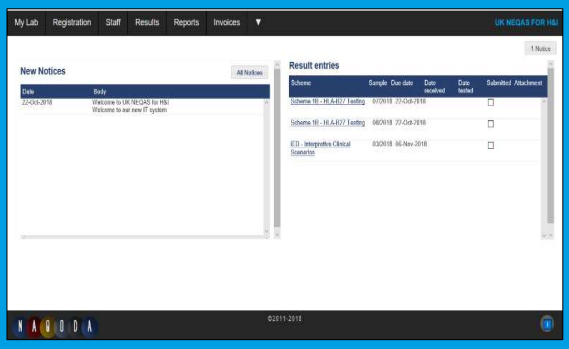
Participant's Portal



- New notices from UK NEQAS for H&I are displayed on the homepage when a user logs in to the system
- Click on a notice to mark it as 'read' and remove it from the homepage.
- To view previously read notices click on All Notices
- Notices may contain important information so please read them regularly and mark as 'read' when finished

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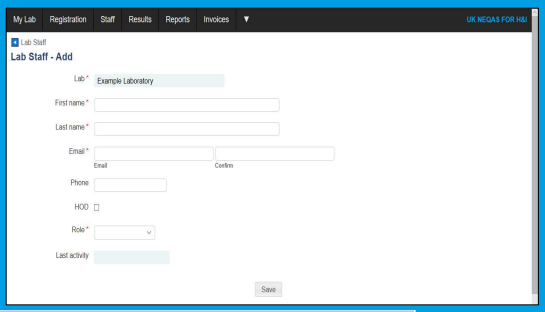
Participant's Portal: Users

- Click on the Add button in the top right corner of the 'Lab Staff' page
- Complete the required name and contact information and select the relevant user role
- Once all required information is complete, click save and the staff member will be sent an e-mail detailing how to access the system



	Participant System Function				
User Role	Administer Registration/Scheme assessment criteria	Manage Users	Enter results	View reports	View Invoices
Primary User	✓	✓	✓ All Schemes	✓ All Schemes	✓
Scheme User	×	×	✓ Assigned Schemes only	✓ Assigned Schemes only	×
Report Recipient	×	×	×	Assigned Schemes only	×

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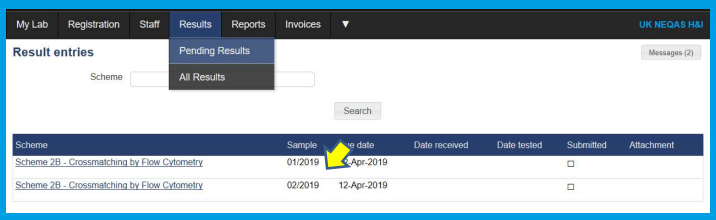
Participant's Portal: Result Entry



- Only Primary Users or Scheme Users linked to relevant scheme can enter results
- To enter results, select Results > Pending Results, samples that have results due/open for entry will be listed here
- Ensure you **do not** click on the highlighted Scheme name as this will take you to a summary of submitted results
- If relevant, the system will show you what assessment criteria you have chosen - this can be edited if incorrect in Registration > Scheme Entries
- Completion of selected assessment criteria is mandatory, denoted by *
- Only selected criteria will be assessed, however, other data can be entered for information only

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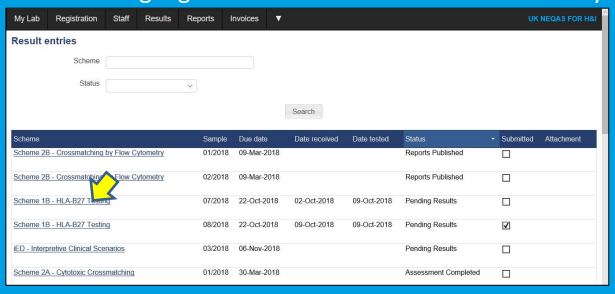
Participant's Portal: Result Entry

- **Method Pages**
  - Complete your laboratory testing methods by completing the methodology questions. This only needs to be completed once, you can then skip to results entry on subsequent samples.

- **View/Save/Print Entered Results**
  - Select Results from the main menu and Pending Results or All Results.
  - Click on the blue highlighted scheme name in the 'result entry' tables.



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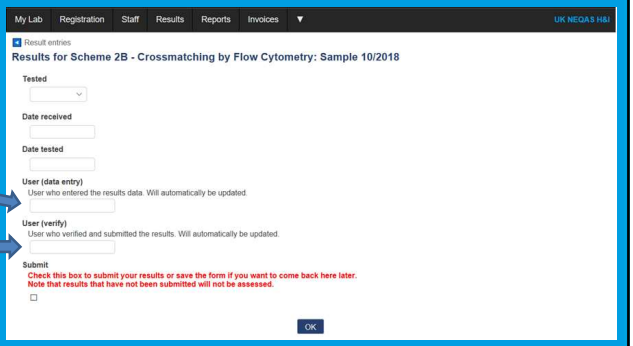
Participant's Portal: Result Submission



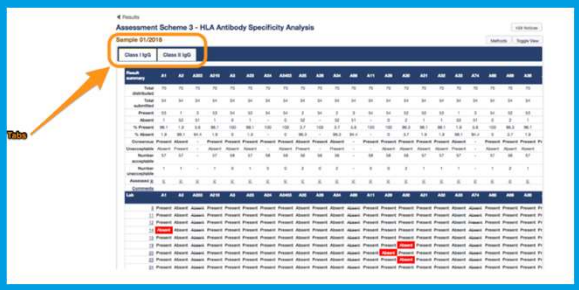
- The User that completes the initial data entry will be named here:
- The User that ticks the "Submit" box will be named here:
- If the initial User ticks the "Submit" box, they will be named in both fields

- If verification is required by a second staff member, leave the "Submit" button unticked and press "OK".
- When satisfied with the results, the second staff member can tick the "Submit" box to show verification has been completed, then press "OK".
- Results can be amended up until the deadline.
- A reminder will be issued 2 days before the deadline.
- **PLEASE NOTE: results must be formally submitted in order to be assessed. Failure to tick the "Submit" box before the deadline will result in Unsatisfactory Performance.**

Participant's Portal: View Assessed Results

- To view result summaries tables, select Reports > Performance Tables

PLEASE NOTE: all samples are separate entries in the system, even if in the same batch/distribution



The summary tables will highlight your lab

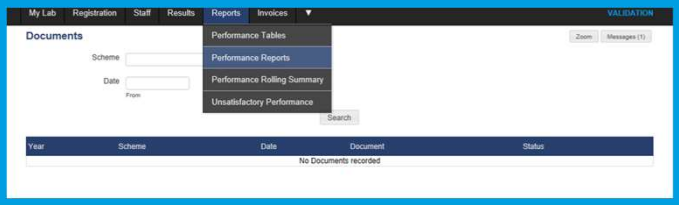
If you wish to know your lab ID this can be found in the My Lab menu

Participant's Portal: View Assessment Reports

Once assessment of samples is complete notification will be sent that your report is available to view in the Participant System.

- Click on Reports and Performance Reports to access all laboratory reports.

The table will display a list of available distribution reports. Unsatisfactory performance notifications, close-out letters and annual performance reports will also appear in this list.



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Participant's Portal

Please come and see us during breaks for specific questions

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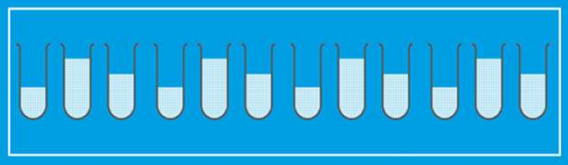
Scheme 2A

Cytotoxic Crossmatching



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Scheme 2A

- ***Purpose:*** To assess participants' ability to correctly determine cell/serum cytotoxicity crossmatch status
- 10 blood samples and 40 serum samples sent in five distributions
- ***Consensus***: determined by at least 75% agreement on a positive or negative result
- ***Satisfactory Performance***: Making 85% of reports in agreement with the consensus result in a distribution year for each cell/DTT type.

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Scheme 2A Performance

- 16 Unsatisfactory Performers (7 UK & Ireland)

All cells with and without DTT	2015 +DTT	2016 +DTT	2017	2018
Number of Participants (UK&I)	64 (18)	64 (18)	75 (19)	71 (18)
Number with Unsatisfactory Performance (< 85%) (UK&I)	9 (0)	13 (6)	16 (6)	16 (7)
% Unsatisfactory Performance (UK&I)	14.0% (0%)	20.3% (33.3%)	21.3% (31.6%)	22.5% (38.8%)

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UK&I 2018 Performance

	PBL	PBL +DTT	T Cell	T Cell +DTT	B Cell	B Cell +DTT
Crossmatches assessed (n=40)	37	38	34	39	23	33
% NT	7.9%	8.3%	6.8%	12.0%	14.7%	19.3%
NT	19	20	41	72	100	131
% incorrect assignments	5.0%	1.3%	6.9%	2.9%	13.0%	5.9%
False Positive	10	2	35	17	41	33
False Negative	1	1	0	0	10	0

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Unacceptable Performers 2018

	PBL -DTT	T -DTT	B -DTT	PBL + DTT	T + DTT	B + DTT	Lab Identified Error
25			82.6%				Cell viability
34			56.5%				Cell viability
38			78.3%				Unclear
39			75.0%				Cell viability
41		79.4%			84.6%	75.8%	Waiting for a response
51			78.3%			84%	Cell viability
54			81.3%			84%	Technical issues and cell viability
112	40%						No response
193			77.8%			81.8%	No response
197		69.6%	64.3%		66.7%	78.9%	No response
252			81.8%				No response
292			83.3%				Cell viability
293		0%	0%		0%	0%	Cell viability (transport)
351		0%	0%		0%	0%	No response
406	0%	0%	0%				No response
411		63.2%	50.0%		66.7%	55.6%	No response

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Cell Viability Issues

- Labs reporting issues with B cell viability or count

Sample 2A	UK&I Labs	% With an Issue (n=17)	RoW WB % With an Issue (n=18)	RoW PC % With an Issue (n=36)
01	9, 45, 54, 58	23.5%	16.7%	27.8%
02	9	5.9%	16.7%	25.0%
03	9, 34	11.8%	27.8%	13.9%
04	9, 20, 34	23.5%	27.8%	5.6%
05	9, 11, 12, 39, 51	29.4%	22.2%	16.7%
06	9, 11, 12, 24, 28, 39, 51	41.2%	11.1%	27.8%
07	51	5.9%	5.6%	41.7%
08	9, 11, 24, 28, 51, 54	35.3%	27.8%	36.1%
09	9, 25, 28, 38, 42, 51, 54, 58	47.1%	22.2%	38.9%
10	9, 24, 28, 42, 51, 54	35.3%	16.7%	33.3%

Key: Blue denotes B cell results were not submitted, green denotes B cell results were submitted, purple denotes some B cell results were submitted

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Cell Viability Issues

2018	2A01 Bcells	2A02 Bcells	2A03 Bcells	2A04 Bcells	2A05 Bcells	2A06 Bcells	2A07 Bcells	2A08 Bcells	2A09 Bcells	2A10 Bcells
9	80	70	90	60	60	60	70	60	70	60
11	75	60	70	70	-	-	-	-	65	50
12	85	90	75	85	60	70	95	95	95	98
20	95	80	80	40	90	90	85	85	90	90
23	90	90	80	30	80	-	80	80	80	90
24	90	90	90	95	80	70	95	90	95	95
25	99	99	95	99	99	99	100	100	40	99
28	85	95	99	85	80	50	90	65	20	60
34	90	90	80	85	85	85	80	80	97	97
38	85	-	85	97	85	87	90	80	-	85
39	98	98	95	90	100	100	90	90	98	98
41	90	95	90	90	98	90	95	90	90	90
42	95	90	95	85	95	85	90	95	-	90
45	80	85	95	90	85	85	85	85	80	90
51	90	90	95	90	80	90	-	-	90	90
54	50	80	95	85	95	80	95	80	60	70
58	20	90	-	-	85	85	90	90	20	95
101	-	-	99	-	-	-	-	-	-	-
114	-	-	95	70	-	-	-	-	-	-
116	45	55	-	-	50	80	85	90	95	95
117	-	-	-	-	-	-	-	-	-	-
136	95	98	-	80	95	95	99	85	98	98
145	80	80	90	-	100	90	100	100	100	100
149	-	-	100	100	-	-	-	-	-	-
162	45	100	99	98	-	-	100	100	90	100
181	100	100	95	99	90	92	95	85	100	100
186	99	99	80	95	99	99	99	99	99	99
204	80	80	60	90	80	85	-	-	90	90
206	100	100	15	50	80	80	90	85	90	90
223	70	45	90	90	50	50	95	90	20	20
227	98	98	-	80	98	90	98	98	90	90
268	90	90	80	85	85	80	80	90	90	80
284	85	95	-	-	97	97	90	90	60	50
311	95	80	-	80	90	90	70	60	80	80
315	-	80	-	-	80	80	-	-	80	80
351	-	-	-	-	-	-	80	80	90	90
406	-	-	-	-	-	-	-	-	-	-
411	-	-	-	-	70	65	-	-	-	-
415	-	-	-	-	-	-	60	60	70	65

Participant reports of B cell viability for Scheme 2A:

Average UK&I 83%

Average RoW 85%

Key (UK&I only):

Pink highlight any report of <90 cell viability,

Red labs reported more than 5 issues with B cells,

Orange labs reporting more than once on issue with B cells,

Yellow labs reporting one issue with B cell viability/count.

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Cell Viability Issues

Participant reports of cell viability for Scheme 2A in comparison to comments regarding poor viability and results submitted:

Labs	% Viable B Cells Reported by UK&I Labs									
	1	2	3	4	5	6	7	8	9	10
9	80	70	90	60	60	60	70	60	70	60
11	75	60	70	70					65	50
12	85	90	75	85	60	70	95	95	95	98
15	99	99	80	100	80	90	99		90	90
20	95	80	80	40	90	90	85	85	90	90
23	90	90	80	30	80		80	80	80	90
24	90	90	90	95	80	70	95	90	95	95
25	99	99	95	99	99	99	100	100	40	99
28	85	95	99	85	80	50	90	65	20	60
34	90	90	80	85	85	85	80	80	97	97
38	85		85	97	85	87	90	80		85
39	98	98	95	90	100	100	90	90	98	98
41	90	95	90	90	98	90	95	90	90	90
42	95	90	95	85	95	85	90	95		90
45	80	85	95	90	85	85	85	85	80	90
51	90	90	95	90	80	90			90	90
54	50	80	95	85	95	80	95	<80	60	70
58	20	90			85	85	90	90	20	95
Range	20-99	60-99	70-99	30-100	60-100	60-100	70-100	60-100	20-98	50-99
Average	83	88	88	81	85	82	89	84	74	85
Neqas Check	98	98	100	99	100	100	100	100	90	95
Consensus Reached	8/8	8/8	6/8	4/8	6/8	4/8	7/8	7/8	0/8	6/8

Key: Highlight denotes a comment on poor viability was made for that sample

Red Highlight = B cell results not submitted,

Yellow Highlight = some B cell results submitted,

Green Highlight = all B cell results submitted

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Cell Viability Issues

Lab	2B 01-10/2018 % Viable B Cells Reported by UK&I Labs														
	Date Bled:		19-Mar	Date Bled:		04-Jun	Date Bled:		10-Sep	Date Bled:		19-Nov	Date Bled:		22-Jan
	01	02	Age When Tested (Days)	03	04	Age When Tested (Days)	05	06	Age When Tested (Days)	07	08	Age When Tested (Days)	09	10	Age When Tested (Days)
9	80	70	3	90	60	3	60	60	3	70	60	3	70	60	2
11	75	60	3	70	70	3	N/A	N/A	2	N/A	N/A	4	65	50	2
12	85	90	2	75	85	2	60	70	2	95	95	2	95	98	1
15	99	99	2	80	100	2	80	90	2	99	N/A	3	90	90	1
20	95	80	4	80	40	3	90	90	3	85	85	2	90	90	2
23	90	90	2	80	30	2	80	N/A	2	80	80	2	80	90	1
24	90	90	3	90	95	3	80	70	3	95	90	3	95	95	2
25	99	99	2	95	99	2	99	99	2	100	100	2	40	99	1
28	85	95	2	99	85	2	80	50	2	90	65	2	20	60	1
34	90	90	2	80	85	2	85	85	2	80	80	2	97	97	1
38	85	N/A	2	85	97	2	85	87	2	90	80	2	N/A	85	1
39	98	98	2	95	90	2	100	100	2	90	90	2	98	98	1
41	90	95	2	90	90	2	98	90	2	95	90	2	90	90	1
42	95	90	3	95	85	3	95	85	2	90	95	2	N/A	90	1
45	80	85	2	95	90	3	85	85	2	85	85	3	80	90	3
51	90	90	3	95	90	3	80	90	3	N/A	N/A	4	90	90	2
54	50	80	3	95	85	3	95	80	3	95	<80	3	60	70	2
58	20	90	2	N/A	N/A	2	85	85	2	90	90	2	20	95	1

Key: Red Highlight = B cell results not submitted, Yellow Highlight = some B cell results submitted, Green Highlight = all B cell results submitted

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Cell Viability Issues

- NEQAS performed an investigation into cell viability and serum stability at different temperature ranges to establish whether whole blood and lymphocytes were stable when stored for up to 72 hours (3 days)
- The cells were stored at 4°C, 22°C, 37°C and 45°C then a FCXM was performed to check results were the same as testing on day 1 :

	Donor 1 Blood		Donor 1 Cells		Donor 2 Blood		Donor 2 Cells	
	Day 2	Day 3	Day 2	Day 3	Day 2	Day 3	Day 2	Day 3
4°C	✓	✓	✓	✓	✓	✓	✓	✓
22°C	✓	✓	✓	✓	✓	✓	✓	✓
37°C	✓	x	?	x	✓	x	x	x
45°C	x	x	x	x	x	x	x	x

- Serum stability was also assessed and no evidence of antibody degradation was found after 72 hours incubation at temperatures up to 45°C

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Participant Feedback on Viability

- The high percentage of serum / B cell samples Not Assessed due to labs reporting samples as Not Tested – laboratories frequently report poor cell viability as the stated reason for not reporting.
- Can NEQAS comment on the high percentage of B cell samples that are Not Assessed / Not Reported and whether this has changed over time?

2A Performance	No of Reports Assessed +DTT	B+DTT % NT	B+DTT % Incorrect	No of Reports Assessed -DTT	B-DTT % NT	B-DTT % Incorrect	%UP UK&I
2016	**27/40**	11.1%	4.2%	**34/40**	13.4%	5.1%	**19.25%**
2017*a	**29/36**	25.8%	5.4%	**27/36**	19.9%	5.1%	**31.6%**
2018	**33/40**	19.3%	5.9%	**23/40**	14.7%	13%	**38.8%**

*Excludes sample 2A 02/2017 which was not assessed due to poor sample quality [a] Higher number of B cell results not tested due to dynabead product recall

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Not Assessed Samples

- 15% of cell/serum combinations for 2018 were not assessed

2018 (n=36/240)	-DTT	+DTT
PBL	3	2
T cell	6	1
B cell	17	7
Total	**26**	**10**

- The percentage agreement for each cell type and whether the result was positive or negative usually falls at approximately 60% in NA samples:
- Is NA an indicator of cell viability??

PBL -DTT	PBL +DTT
71.4	66.7
57.1	50
50	
59.5	**58.35**

T-DTT	T+DTT
55.2	58.3
62.1	
61.3	
67.7	
56.7	
71	
62.3	**58.3**

B-DTT	B+DTT
70.4	50
65.4	73.1
64.3	52
53.6	71.4
50	***95.5***
57.1	***100***
52	***90.5***
53.8	
74.1	
66.7	
63.3	
76	
57.7	
60	
72	
68.8	
51.7	
62.2	**61.6**

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Participant Feedback: Splitting Assessment for UK&I from RoW

- 17 UK&I are assessed with 20 labs from the RoW that also receive whole blood.

	UK -DTT	RoW -DTT	UK +DTT	RoW +DTT
PBL	6	2	6	1
T Cell	15	20	15	17
B Cell	17	20	17	17

- Suggestion that UK&I labs should only be compared to other UK&I labs.

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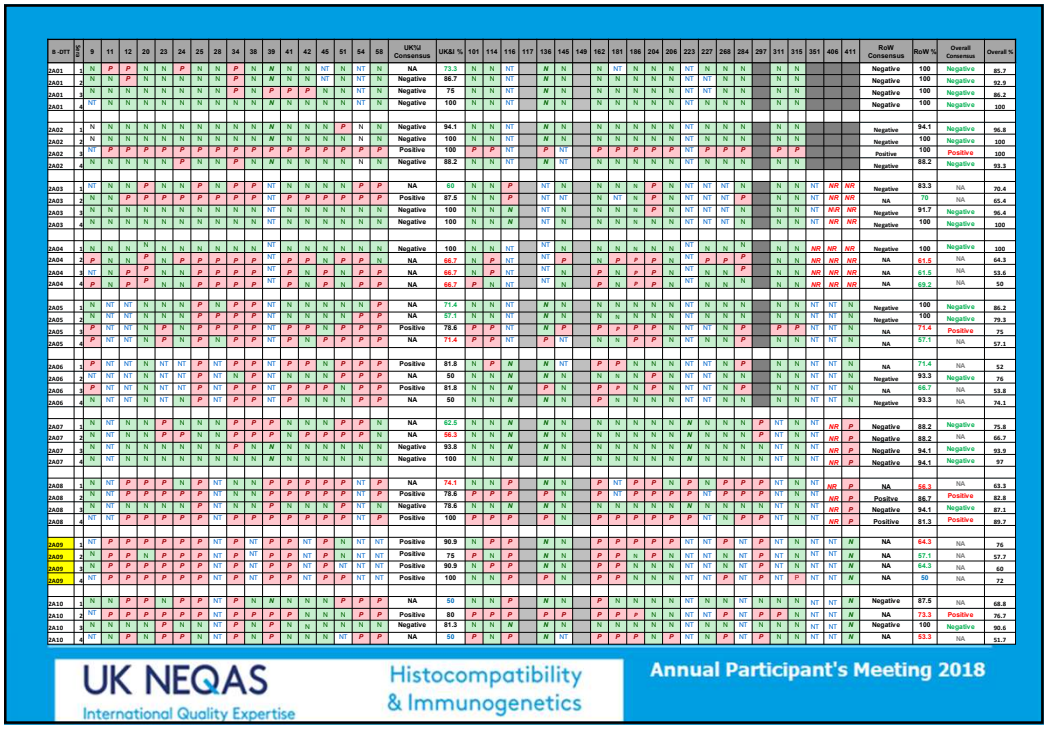

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Splitting Assessment

- Results were re-assessed from 2018 for UK&I and RoW independently
  - Less samples were 'not assessed' when split
  - UK&I had a greater tendency to agree on a positive result
  - RoW had a greater tendency to agree on a negative result

2018 Results	UK&I	RoW	Overall
Negative	13	22	18
Positive	12	3	5
Not Assessed	15	15	17

B - DTT	Sera	UK%I Consensus	UK&I %	RoW Consensus	RoW %	Overall Consensus	Overall %
2A01	1	NA	73.3	Negative	100	Negative	85.7
2A01	2	Negative	86.7	Negative	100	Negative	92.9
2A01	3	Negative	75	Negative	100	Negative	86.2
2A01	4	Negative	100	Negative	100	Negative	100
2A02	1	Negative	94.1	Negative	94.1	Negative	96.8
2A02	2	Negative	100	Negative	100	Negative	100
2A02	3	Positive	100	Positive	100	Positive	100
2A02	4	Negative	88.2	Negative	88.2	Negative	93.3
2A03	1	NA	60	Negative	83.3	NA	70.4
2A03	2	Positive	87.5	NA	70	NA	65.4
2A03	3	Negative	100	Negative	91.7	Negative	96.4
2A03	4	Negative	100	Negative	100	Negative	100
2A04	1	Negative	100	Negative	100	Negative	100
2A04	2	NA	66.7	NA	61.5	NA	64.3
2A04	3	NA	66.7	NA	61.5	NA	53.6
2A04	4	NA	66.7	NA	69.2	NA	50
2A05	1	NA	71.4	Negative	100	Negative	86.2
2A05	2	NA	57.1	Negative	100	Negative	79.3
2A05	3	Positive	78.6	NA	71.4	Positive	75
2A05	4	NA	71.4	NA	57.1	NA	57.1
2A06	1	Positive	81.8	NA	71.4	NA	52
2A06	2	NA	50	Negative	93.3	Negative	76
2A06	3	Positive	81.8	NA	66.7	NA	53.8
2A06	4	NA	50	Negative	93.3	NA	74.1
2A07	1	NA	62.5	Negative	88.2	Negative	75.8
2A07	2	NA	56.3	Negative	88.2	NA	66.7
2A07	3	Negative	93.8	Negative	94.1	Negative	93.9
2A07	4	Negative	100	Negative	94.1	Negative	97
2A08	1	NA	74.1	NA	56.3	NA	63.3
2A08	2	Positive	78.6	Positve	86.7	Positive	82.8
2A08	3	Negative	78.6	Negative	94.1	Negative	87.1
2A08	4	Positive	100	Positive	81.3	Positive	89.7
2A09	1	Positive	90.9	NA	64.3	NA	76
2A09	2	Positive	75	NA	57.1	NA	57.7
2A09	3	Positive	90.9	NA	64.3	NA	60
2A09	4	Positive	100	NA	50	NA	72
2A10	1	NA	50	Negative	87.5	NA	68.8
2A10	2	Positive	80	NA	73.3	Positive	76.7
2A10	3	Negative	81.3	Negative	100	Negative	90.6
2A10	4	NA	50	NA	53.3	NA	51.7

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B cell Without DTT

UK&I	Original 2018 Assessment (% Correct) 2A01&02	2A03&04	2A05&06	2A07&08	2A09&10	Total	UK only 2018 Assessment (% Correct) 2A01&02	2A03&04	2A05&06	2A07&08	2A09&10	Total
9	100.0%	100.0%	100.0%	80.0%	100.0%	**96.0%**	100.0%	75.0%	100.0%	80.0%	66.7%	***84.0%***
11	87.5%	100.0%	NT	NT	100.0%	**95.0%**	100.0%	75.0%	NT	NT	100.0%	**91.0%**
12	75.0%	100.0%	NT	100.0%	100.0%	**93.0%**	83.3%	100.0%	NT	100.0%	66.7%	**87.0%**
15												
20	100.0%	100.0%	75.0%	100.0%	100.0%	**95.0%**	100.0%	100.0%	0.0%	100.0%	66.7%	***73.0%***
23	100.0%	100.0%	100.0%	83.3%	50.0%	**86.0%**	100.0%	100.0%	100.0%	83.3%	66.7%	**90.0%**
24	75.0%	100.0%	66.7%	100.0%	100.0%	**88.0%**	83.3%	100.0%	0.0%	83.3%	66.7%	***66.0%***
25	100.0%	100.0%	25.0%	83.3%	100.0%	**81.0%**	100.0%	100.0%	100.0%	83.3%	66.7%	***90.0%***
28	100.0%	100.0%	66.7%	100.0%	NT	**91.0%**	100.0%	100.0%	100.0%	100.0%	NT	**100.0%**
34	50.0%	100.0%	50.0%	50.0%	50.0%	**60.0%**	66.7%	100.0%	100.0%	50.0%	33.3%	**70.0%**
38	100.0%	100.0%	25.0%	66.7%	100.0%	**78.0%**	100.0%	100.0%	100.0%	66.7%	100.0%	**93.0%**
39	87.5%	NT	NT	66.7%	50.0%	**68.0%**	100.0%	100.0%	NT	66.7%	66.7%	**83.0%**
41	87.5%	100.0%	100.0%	100.0%	100.0%	**97.0%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
42	87.5%	100.0%	100.0%	100.0%	50.0%	**87.0%**	100.0%	100.0%	100.0%	83.3%	66.7%	**90.0%**
45	100.0%	100.0%	75.0%	100.0%	50.0%	**85.0%**	100.0%	100.0%	33.3%	83.3%	66.7%	***76.0%***
51	87.5%	100.0%	75.0%	66.7%	50.0%	**76.0%**	83.3%	100.0%	66.7%	66.7%	33.3%	**58.0%**
54	100.0%	100.0%	50.0%	66.7%	100.0%	**83.0%**	100.0%	100.0%	100.0%	66.7%	66.7%	***86.0%***
58	100.0%	100.0%	25.0%	100.0%	100.0%	**85.0%**	100.0%	100.0%	100.0%	100.0%	66.7%	**93.0%**
RoW	Original 2018 Assessment						RoW only 2018 Assessment					
101	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
114	100.0%	100.0%	100.0%	100.0%	100.0%	**100%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
116	NT	100.0%	100.0%	100.0%	100.0%	**100.0%**	NT	100.0%	100.0%	100.0%	66.7%	**92.0%**
117												
136	100.0%	NT	75.0%	100.0%	100.0%	**94%**	100.0%	NT	100.0%	100.0%	100.0%	**100.0%**
145	100.0%	100.0%	100.0%	66.7%	100.0%	**94%**	100.0%	100.0%	100.0%	71.4%	100.0%	**94.0%**
149												
162	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%	100.0%	100.0%	100.0%	66.7%	**93.0%**
181	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
186	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
204	100.0%	66.7%	75.0%	100.0%	50.0%	**78%**	100.0%	66.7%	50.0%	100.0%	66.7%	***76.0%***
206	100.0%	100.0%	75.0%	100.0%	50.0%	**85.0%**	100.0%	100.0%	100.0%	100.0%	66.7%	**93.0%**
223	NT	NT	NT	100.0%	NT	**100.0%**	NT	NT	NT	100.0%	NT	**100.0%**
227	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**	100.0%	100.0%	100.0%	100.0%	100.0%	**100.0%**
268	100.0%	100.0%	75.0%	83.3%	100.0%	**91.0%**	100.0%	100.0%	100.0%	85.7%	100.0%	**97.0%**
284	100.0%	100.0%	100.0%	100.0%	NT	**100%**	100.0%	100.0%	100.0%	100.0%	NT	**100.0%**
297	NT	NT	NT	83.3%	100.0%	**91.0%**	NT	NT	NT	71.4%	100.0%	**85.0%**
311	100.0%	100.0%	100.0%	NT	100.0%	**100.0%**	100.0%	100.0%	100.0%	NT	100.0%	**100.0%**
315	100.0%	100.0%	100.0%	66.7%	50.0%	**87.0%**	100.0%	100.0%	100.0%	57.1%	66.7%	**85.0%**
351	NT	0.0%	0.0%	NT	0.0%	**0.0%**	NT	0.0%	0.0%	NT	0.0%	**0.0%**
406	NT	NT	0.0%	0.0%	0.0%	**0.0%**	NT	NT	0.0%	0.0%	0.0%	**0.0%**
411	NT	NT	75.0%	33.3%	50.0%	**42.0%**	NT	NT	100.0%	28.6%	66.7%	***48.0%***

Lab Performance

- **Original assessment:**

6 UK&I labs <75%

4 RoW labs <75%

- **Split assessment**

7 UK&I labs <75%

4 new labs now <75%

3 now >75%

2 still <75% but improved

1 still <75% but got worse

4 RoW labs <75%

same labs still <75%

1 still <75% but improved

1 still <75% but got worse

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Interesting Results: 2A01

- Query from UK lab regarding Sample 2A01 serum 3
  - Multiple UK&I labs called this B cell positive but the consensus was negative (all RoW labs reported negative): 86.2% negative –DTT, 76.9% negative +DTT
  - SAB testing performed by 5 labs:

- HLA PHENOTYPE OF BLOOD DONOR: HLA-A2, A3; B7, B60; Cw3, Cw7; DR4, DR15; DQ6, DQ8

SAB Defined 'DSA'	
A2	19,430
DR51	20,824
DQ6	21,559
Cumulative	61, 813

SAB Defined 'DSA'	
A2	15,281
DR4	5,103
DR51	15,825
DQ6	16,433
DQ8	1,221
Cumulative	53,863

SAB 'DSA' +EDTA	
A2	2,300
A3	9,600
B7	2,900
Cw7	1,100
Cumulative	15,900

SAB 'DSA' +EDTA	
A2	>10,000
DR51	14,000
DQ6	>8,000
Cumulative	32,000

SAB 'DSA' +EDTA	
A2	17,300
B56	1,300
B57	16,000
Cw1	1,700
DR1	21,000
DQ5	18,500
DR51	14,000
DRB1*04:01	5,300
Cumulative	~95,000

- Shouldn't a cumulative MFI of 61,813 cause a positive CDCXM????
  - Other labs reported that the PBL and T cell crossmatch was Negative although some reported PBL and T cell positives
  - Non-complement fixing antibodies?
  - Prozone effect? Not when PBLs tested in dilution:
    - Neat – Positive (4), 1:2 – Positive (4), 1:4 – Positive (2), 1:8 – Negative

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Discussion

- Not all Scheme 2A results will reach consensus (that's ok!)
- B-cells are difficult (transport, non-specific binding)
- Only partially emulates clinical practice
- 2A is a technical assessment of cytotoxic crossmatching and should not be 'interpreted'
- Lab's need to ensure that all test parameters and acceptance criteria are met prior to reporting NEQAS samples.
- CDC assays are not quantitative so reliant on subjective assessment.

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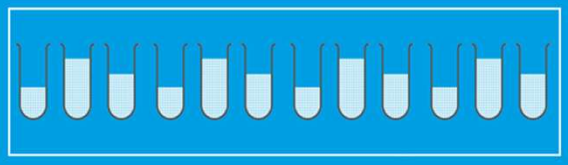
Scheme 2A

Discussion



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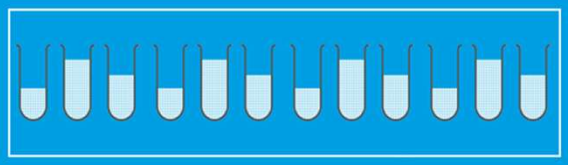
Scheme 2B

Crossmatching by Flow Cytometry



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Scheme 2B

- ***Purpose:*** To assess participants' ability to correctly determine cell/serum flow crossmatch status
- 10 blood samples and 40 serum samples sent in five distributions
- ***Consensus***: determined by at least 75% agreement on a positive, negative or equivocal result
- ***Satisfactory Performance***: Making 85% of reports in agreement with the consensus result in a distribution year for each cell type.

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Reporting of Equivocal Results

- In 2018 Equivocal results were assessed
  - i.e if 75% or more of participants report positive/negative, any laboratories reporting 'equivocal' were assessed as 'unacceptable'
  - If a 75% consensus result is not reached when including the equivocal reports, the sample was not assessed.
- Technical issues and invalid results (e.g control failures, replicate issues, sample quality issues) should be reported as 'Not Tested' with the reason stated.

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Scheme 2B Performance

- 15 Unsatisfactory Performers (2 UK & Ireland)

Scheme 2B	2015	2016	2017	2018
Number of Participants (UK&I)	73 (23)	76 (23)	85 (22)	83 (22)
Number with Unsatisfactory Performance (< 85%) (UK&I)	13 (3)	13 (1)	8 (1)	15 (2)
% Unsatisfactory Performance	17.8% (13.0%)	17.1% (4.3%)	8.7% (4.5%)	18.1% (9.1%)

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Scheme 2B Summary

	T Cells			B Cells		
	UK&I	RoW PC	RoW WB	UK&I	RoW PC	RoW WB
Number of participants	22	48	19	22	48	19
Number of XM assessed (>75% consensus)	34/40	32/40	34/40	36/40	36/40	30/40
Number of Positive XM	15	9	7	24	17	12
Number of Negative XM	19	23	27	12	19	18
Number of incorrect assignments	36 (4.8%)	64 (4.7%)	34 (4.7%)	32 (4.0%)	82 (6.9%)	36 (5.5%)
Number of False Pos	23	34	21	22	40	19
Number of False Neg	13	30	13	10	42	17
Number of equivocal assignments	22 (2.5%)	35 (2.0%)	10 (1.2%)	5 (0.6%)	24 (1.4%)	11 (1.3%)
Number of NT assignments	48 (5.5%)	230 (13.1%)	146 (17.4%)	83 (9.4%)	215 (12.2%)	147 (17.5%)

UK&I and RoW receive different blood samples

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Unacceptable Performers 2018

- 15 labs with UP (<85%)

Lab	T Cell	No. of results submitted	B Cell	No. of results submitted	Root Cause
28	69.2%	30/40	100%	25/40	Cell viability and reporting Equivocal
51	79.4%	40/40	88%	28/40	Cell viability and reporting Equivocal
139	84.2%	24/40	90.5%	24/40	No response
142	82.4%	40/40	93.3%	40/40	Technical issue
169	75%	32/40	61.1%	32/40	No response
189	75%	40/40	69.4%	40/40	Cell viability issue
218	81.0%	28/40	68.0%	28/40	No response
230	85.3%	40/40	76.7%	40/40	Technical issue
240	90.6%	40/40	66.7%	40/40	No response
271	94.4%	20/40	83.3%	21/40	Technical issue
315	47.1%	23/40	50.0%	23/40	Technical issue
351	83.3%	24/40	78.3%	24/40	No response
374	85.3%	40/40	73.3%	40/40	Technical issues
380	42.9%	8/40	38.5%	8/40	No response
392	0%	0/40	0%	0/40	No response

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Reporting of Equivocal Results

- 2018 Summary
  - 67 T cell equivocal results (from 3022 = 2.2%)
  - 42 B cell equivocal results (from 2809 = 1.5%)
  - 22 T cell equivocal results assessed as unacceptable (0.7%)
  - 20 B cell equivocal results assessed as unacceptable (0.7%)

2018	T cell Equivocal Results	Total Results	B cell Equivocal Results	Total Results	Equivocal Assessed as Unacceptable Result	
					T cell	B cell
1+2	23	608	11	550	3	7
3+4	9	648	13	587	5	1
5+6	14	632	6	578	4	4
7+8	9	553	7	569	3	5
9+10	12	581	5	525	7	3
Totals	**67**	**3022**	**42**	**2809**	**22**	**20**

2018	No of Labs Reporting Equivocal	No. of Labs Reporting >1 Equivocal Result
UK (n=22)	10 (45%)	6 (27%)
OS (n= 61)	34 (56%)	22 (36%)
Total (n=83)	**44 (53%)**	**28 (34%)**

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Reporting of Equivocal Results

- Compared to 2017 assessment criteria 4 sera changed consensus (3 T cell, 1 B cell - RoW only)

Sample	Serum	Lab	Consensus	No. Equivocal	Number Positive	Number Negative	2017 Result
T Cell							
2B01 2018 OS PC	serum 4	143 160 238 293 297	Not Assessed	5 (11.9%)	29 (69%)	8 (19%)	*Positive*
2B05 2018 OS PC	serum 2	154 159 167 218	Not Assessed	4 (9.5%)	9 (21.4%)	29 (69%)	*Negative*
2B09 2018 OS WB	Serum 1	142 176	Not Assessed	2 (11.8%)	12 (70.6%)	3 (17.6%)	*Positive*
B Cell							
2B09 2018 OS WB	Serum 4	315	Not Assessed	1 (6.7%)	11 (73.3%)	3 (20.0%)	*Positive*

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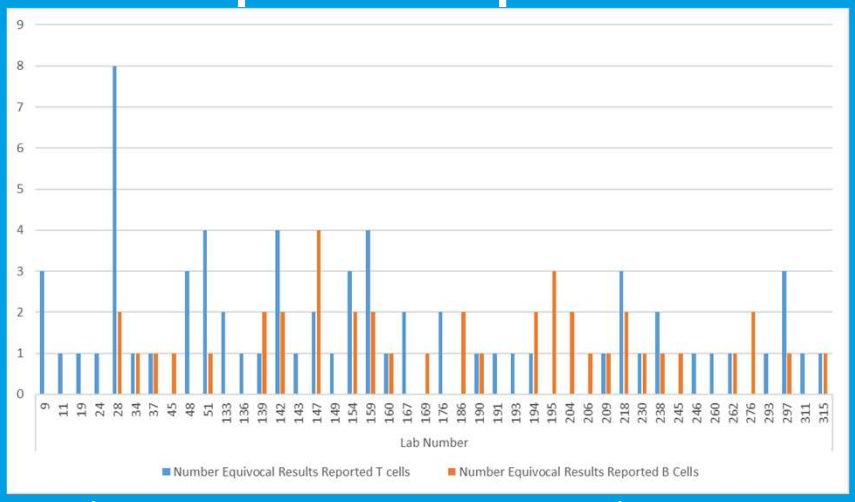
2018 Equivocal Reports Per Lab



- 44/83 labs reported an equivocal result (10/22 UK&I)
- 28/83 labs reported >1 equivocal result

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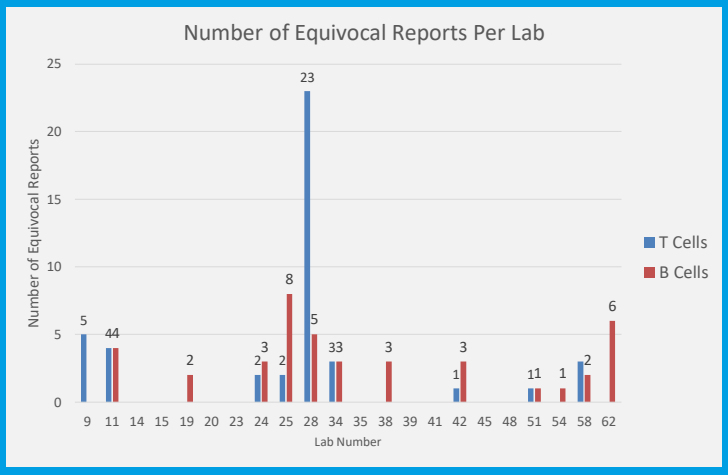
Equivocal Reports Per Lab 2017



- 13/22 labs reported ≥1 equivocal result

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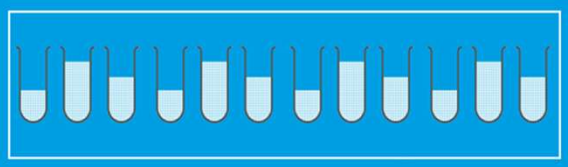
Scheme 2B

Discussion



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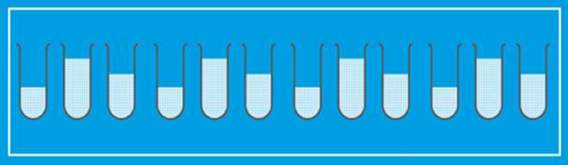
Scheme 6

HLA Antibody Detection



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Scheme 6

- ***Purpose:*** To assess participants' ability to correctly determine the presence of HLA antibodies
- 12 serum samples sent in two distributions
- ***Consensus***: determined by at least 75% agreement on a presence or absence of an antibody
- ***Satisfactory Performance***: Making 80% of reports in agreement with the consensus result in a distribution year.

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Scheme 6 Performance

- 5 Unsatisfactory Performers (0 UK & Ireland)

	2015	2016	2017	2018
Number of Participants (UK&I)	97 (24)	98 (24)	101 (24)	88 (25)
Number with Unsatisfactory Performance (< 80%) (UK&I)	6 (3)	18 (4)	21 (0)	5 (0)
% Unsatisfactory Performance	6.2% (12.5%)	18.4% (16.7%)	20.8% (0%)	5.7% (0%)

The 5 labs with unacceptable performance:

- 1 used Immucor kits only (1 mixed)
- 4 gave no information as to kit usage

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Not Assessed Samples

2018 Sample	Class I All Labs (n=90)	Class I UK&I (n=25)		Class II All Labs (n=88)	Class II UK&I (n=24)
601	92.9%	96%		97.5%	100%
602	90.5%	100%		98.8%	100%
603	90.4%	96%		91.3%	96%
604*	56.6%	52%		100%	100%
605	100%	100%		100%	100%
606	95.2%	100%		61.3%	60%
607	98.8%	100%		100%	100%
608	75.3%	100%		100%	100%
609	100%	100%		100%	100%
610	100%	100%		100%	100%
611*	70.2%	52%		100%	100%
612*	74.1%	56%		51.2%	62.5%

Green denotes agreement on negative result

* Denotes samples were sourced from non-transfused male donors

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Scheme 6 Errors

58/1573 (3.7%) results out of consensus (7 UK&I)

More false negative results in RoW but UK&I tendency for more false positive results

Non-specific binding an issue (sample 604, 611 612)

Error	UK&I	RoW
Class I only	5	43
Class II only	2	2
Class I & II	0	6

	Class I		Class II	
	False Pos	False Neg	False Pos	False Neg
UK&I	3	2	2	0
RoW	13	30	5	3

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Interesting Results: 608/2018

- Class I Consensus Positive (overall 75.3%, UK&I 100%)
  - 63 labs reported positive, 21 reported negative
- 18 Labs that use Immucor kits, 11 of them reported a Negative result
- 29 Labs use One Lambda kits all reported a Positive result

Sample 608/2018 Kit Breakdown			Pos	Neg	NT	Total
Not stated			29	9	3	41
Immucor	LM1	Class I ID Kit	3	0	0	3
	LMX	Lifecodes Lifescreen Deluxe Kit	2	11	0	13
	LSAI	Lifecodes Lifescreen SA Class I	1	1	0	2
One Lambda	LSM12	LS Mixed Class I&II	18	0	0	18
	LS1PRA	LABScreen PRA Class I	4	0	0	4
	LS12PRA	LABScreen PRA Class I&II	1	0	0	1
	LS1A04	LS SA Class I	6	0	0	6
		Totals	64	21	3	88

- Labs used numerous different kits to detect the presence/absence of antibodies
- Should we standardise?
  - Scheme 6 operates purely as a detection scheme. We do not state what detection methods have to be used to achieve this but it is important that the techniques used reflect clinical practice.

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Kit Differences Affecting Consensus

- Five 2018 non-consensus results were re-analysed by kit manufacturer.
- For labs reporting using One Lambda kits only (n=28)
  - 1/5 results reached consensus (sample 612 CII).
- For Immucor only users (n=15)
  - 3/5 results reached consensus (sample 611 CI, 612 CI and CII).
- In 3/5 results the consensus/majority result differed between the manufacturers
  - 604, 606, 612

2018 Samples	All Labs (n=CI 90, CII 88)	One Lambda (n=28)	Lifecodes (n=15)
604 Class I	56.6%	51.9%	60.0%
606 Class II	61.3%	64.3%	64.3%
611 Class I	70.2%	53.6%	78.6%
612 Class I	74.1%	64.3%	78.6%
612 Class II	51.2%	75.0%	84.6%

Green denotes agreement on negative result, red denotes agreement on positive result

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Mixed v Single Antigen

- Mixed kits have an 'undetermined' region
- Scheme requires 'positive' or 'negative' result
  - Test using additional kits
- Known sensitivity difference between mixed and SA beads
  - Could account for not-assessed results
  - Many labs reported testing using single antigen beads
- Result interpretation
- Samples containing marginal antibodies

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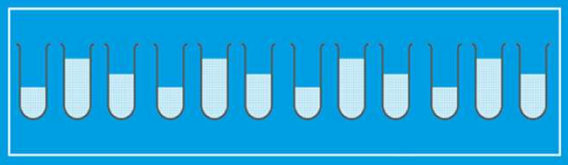
Scheme 3

HLA Antibody Specificity Analysis



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Scheme 3

- ***Purpose:*** To assess participants' ability to correctly determine the specificity of HLA antibodies
- 10 serum samples sent in two distributions
- ***Consensus***: Presence of a specificity is determined by at least 75% of labs agreeing, absence is determined by at least 95% of labs agreeing
- ***Satisfactory Performance***: Making at least 75% of specificities in agreement with the consensus result in a distribution year.

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Scheme 3 Performance

Class I		2015	2016	2017	2018
Number of Participants (UK&I)		81 (24)	85 (24)	72 (24)	73 (25)
Number with Unsatisfactory Performance (UK&I)	**Presence**	9 (1)	8 (0)	10 (0)	15 (1)
	Absence	2 (0)	3 (0)	3 (0)	5 (0)
% Unsatisfactory Performance	**Presence**	11.1%	9.4%	13.8%	20.5%
	Absence	2.5%	3.5%	4.2%	6.8%

Class II		2015	2016	2017	2018
Number of Participants (UK&I)		81 (24)	85 (24)	72 (24)	75 (25)
Number with Unsatisfactory Performance (UK&I)	**Presence**	4 (0)	5 (0)	5 (0)	12 (0)
	Absence	3 (0)	4 (0)	2 (0)	3 (0)
% Unsatisfactory Performance Presence/ Absence	**Presence**	4.9%	5.9%	6.9%	16.0%
	Absence	3.7%	4.7%	2.8%	4.0 %

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Unacceptable Performers 2018

- 17 labs (1 UK&I) with UP (<75%)

	Class I		Class II		Kit
Lab	Presence	Absence	Presence	Absence	
100	64.9%	98.8%	84.0%	95%	Lifecodes
133	73.3%	100%	96.0%	100%	Lifecodes
197	59.1%	94.6%	54.3%	84.9%	No Info
212	53.3%	72.5%	47.9%	89.1%	Lifecodes
214	47.1%	95.7%	76.6%	95.8%	Lifecodes
216	27.1%	98.4%	60.6%	99.2%	Lifecodes
218	69.3%	99.6%	76.6%	100%	Lifecodes
222	80.9%	59.7%	83.0%	73.9%	No Info
229	0%	0%	0%	0%	No Info
230	46.2%	83.7%	64.9%	100%	Lifecodes
242	56.4%	100%	51.1%	99.2%	One Lambda
252	22.2%	94.6%	40.4%	99.2%	Lifecodes
268	90.2%	100%	73.4%	100%	One Lambda
293	71.6%	95.7%	79.8%	94.1%	One Lambda
302	70.2%	76.0%	64.9%	75.6%	Lifecodes
392	0%	0%	0%	0%	No Info
401	0%	0%	0%	0%	No Info

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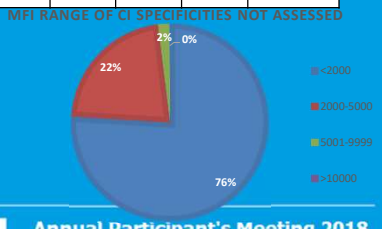
Class I Assessment

	Number of HLA Class I Specificities (n=89)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	33	13	7	23	12	5	23	37	27	45	225
Absent (<5%)	30	44	20	29	41	24	25	16	28	1	258
Absent 0%	11	27	52	17	19	44	18	8	13	4	213
Not Assessed (5-74%)	15	5	10	20	17	16	23	28	21	39	194

677 specificities reported over 10 samples
- 33.2% reached consensus presence
- 38.1% reached consensus absence
- 28.7% specificities were not assessed



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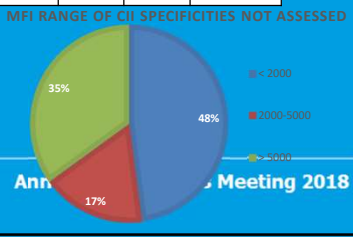
Class II Assessment

DPB included in assessment in 2018

	Number of HLA Class II Specificities (DR, DQ, DP) (n=46)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	13	14	4	7	5	1	11	20	0	19	94
Absent (<5%)	16	11	11	17	19	7	11	7	19	1	119
Absent 0%	10	8	27	18	19	29	15	12	24	0	162
Not Assessed (5-74%)	7	13	1	4	3	9	9	7	3	26	82

295 specificities reported over 10 samples
- 31.9% reached consensus presence
- 40.3% reached consensus absence
- 27.8% specificities were not assessed



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DPB only

	Number of HLA DPB Specificities (n=19)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	0	10	0	0	0	0	0	4	0	0	14
Absent (<5%)	10	1	1	4	7	1	5	4	6	1	40
Absent 0%	9	6	17	11	12	17	12	10	11	0	105
Not Assessed (5-74%)	0	2	1	4	0	1	2	1	2	18	31

2 samples had DPB1 specificities that reached consensus

85 specificities reported over 10 samples
- 16.5% reached consensus presence
- 47.1% reached consensus absence
- 36.4% specificities were not assessed

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DPA and DQA

- Labs reported DQA (=53) and DPA (n=44)
- Continue to report DQA and DPA, but these will not be assessed in 2019

	Number of HLA DQA Specificities										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	0	0	0	0	0	0	0	0	0	0	0
Absent (<5%)	2	6	4	5	3	2	2	0	1	0	25
Not Assessed (5-74%)	5	3	4	2	2	1	6	10	0	12	45

	Number of HLA DPA Specificities										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	0	0	0	0	0	0	0	0	0	0	0
Absent (<5%)	0	1	0	3	0	0	0	1	3	0	8
Not Assessed (5-74%)	1	4	0	0	0	0	0	6	0	7	18

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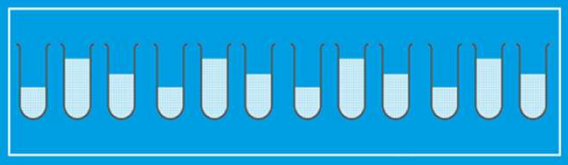
Schemes 3, 6

Discussion



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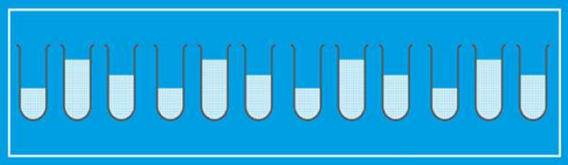
Scheme 9

KIR Genotyping



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Scheme 9

- ***Purpose:*** To assess participants' ability to correctly determine the presence or absence of specific KIR genes
- 10 blood samples sent in two distributions
- ***Consensus***: Genotype is determined by at least 75% of laboratories agreeing the presence/absence of each gene. Where consensus can't be reached a reference type will be used
- ***Satisfactory Performance***: Obtaining 9 or more full KIR genotypes in agreement with the consensus result in a distribution year.

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KIR Genotyping

- Participants able to report any of the following: KIR2DL1, KIR2DL2, KIR2DL3, KIR2DL4, KIR2DL5, KIR3DL1, KIR3DL2, KIR3DL3, KIR3DS1, KIR2DS1, KIR2DS2, KIR2DS3, KIR2DS4, KIR2DS5, KIR2DP1, KIR3DP1.
- Also able to report any other KIR polymorphisms they detected for information
- Participants can also report an 'A' or 'B' haplotype for each sample based on the gene content of the sample

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Performance 2018

- 3 Errors
- 1 Unsatisfactory Performer
  - 10 samples distributed, must make 9 or more full KIR genotypes in agreement with consensus

	2015 Pilot	2016 Pilot	2017	2018
Number of Participants (UK&I)	7 (1)	11 (2)	8 (3)	9 (1)
Number with Unsatisfactory Performance (UK&I)	N/A	N/A	0 (0)	1 (0)
% Unsatisfactory Performance (UK&I)	N/A	N/A	0%	11.1%

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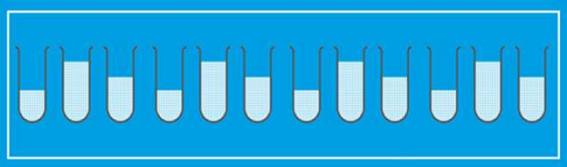
Scheme 10

HPA Genotyping



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Scheme 10

- ***Purpose:*** To assess participants' ability to correctly determine HPA polymorphisms
- 10 blood samples sent in two distributions
- ***Consensus***: determined by at least 75% of labs agreeing the presence/absence of each allele, a reference result is used for results failing to reach consensus
- ***Satisfactory Performance***: Obtaining 9 or more full HPA types in agreement with the consensus/reference result in a distribution year.

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HPA Genotyping

- Participants able to report any of the following: HPA-1, HPA-2, HPA-3, HPA-4, HPA-5, HPA-6, HPA-15
  - 25/37 reported HPA-1, 2 , 3, 4, 5 and 15
  - 30/37 labs reported HPA-4
  - 24/37 labs reported HPA-6
- Also able to report any other HPA polymorphisms detected, for information

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Performance 2018

- 3 Errors (RoW only)
- 1 Unsatisfactory Performer

	2015 Pilot	2016 Pilot	2017	2018
Number of Participants (UK&I)	14 (3)	12 (4)	15 (5)	37 (6)
Number with Unsatisfactory Performance (< 100%) (UK&I)	N/A	N/A	1 (0)	1 (0)
% Unsatisfactory Performance (UK&I)	N/A	N/A	6.7%	2.7%

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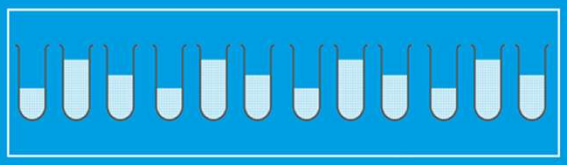
Scheme 11

HPA Antibody Detection/Specification



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Scheme 11

- ***Purpose:*** To assess participants' ability to correctly determine the presence and specificity of HPA antibodies
- 8 serum/plasma samples sent in two distributions
- ***Consensus***: Presence of a specificity is determined by at least 75% of labs agreeing, absence is determined by at least 95% of labs agreeing
- ***Satisfactory Performance***: Making at least 75% of specificities in agreement with the consensus result in a distribution year.

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Performance 2018

- 1 Unsatisfactory Performer (0 UK & Ireland)

	2017 Pilot	2018
Number of Participants (UK&I)	13 (3)	35 (4)
Number with Unsatisfactory Performance (< 75%) (UK&I)	N/A	1 (0)
% Unsatisfactory Performance (UK&I)	N/A	2.9%

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HPA Antibody Detection/Specification

- NIBSC no longer offering platelet genotyping or antibody schemes
- NIBSC participants offered to transfer to UK NEQAS for H&I

2018 Sample	HPA Detection	HLA Detection	HPA Antibody ID	
			Presence	Absence
1	100% Neg	100% Neg	100% Neg	
2	100% Pos	100% Pos	HPA-5b 96.9%	3.1% HPA-3b, 5a, 15a
3	Not Assessed (64.5% Pos)	100% Neg	Not Assessed	3.2% GPIIa/IIIb
4	90% Neg	100% Pos	96.7% Neg	
5	76.5% Neg	92.9% Neg	Not Assessed	77.1% HPA Neg
6	100% Neg	100% Pos	100% Neg	
7	100% Pos	100% Pos	HPA-5b 97.1%	HPA-15b 2.9%
8	94.1% Neg	89.3% Neg	Not Assessed	91.4% HPA Neg

Result for Sample 3	Method of HPA Detection	Number of Labs
Negative	MAIPA	11
Positive	Luminex	7
	MAIPA	5
	Luminex/MAIPA	8

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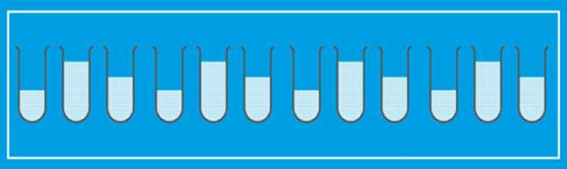
Schemes 9, 10, 11

Discussion



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Prof David Briggs

Quantitative Measurement of HLA Specific Antibodies

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Dr Martin Rutter

Islet Cell Transplantation: A Clinical Perspective

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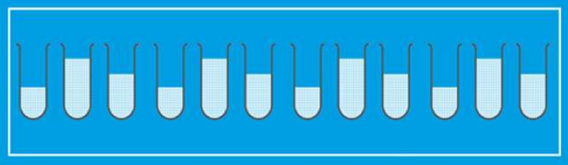
Scheme 1A

HLA Phenotyping



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Scheme 1A

- ***Purpose:*** To assess participants' ability to correctly use serological and supplementary methods to correctly identify HLA specificities
- 10 blood samples sent in two distributions
- ***Consensus***: Presence of a specificity is determined by at least 75% of labs in agreement
- ***Satisfactory Performance***: Making 9 or more complete HLA phenotypes in agreement with the consensus result in a distribution year.

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1A Performance 2018

- 6 labs with Unsatisfactory Performance (1 UK&I)

	2012	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	22 (10)	30 (10)	42 (9)	45 (9)	41 (7)	38 (6)	38 (6)
Number with Unsatisfactory Performance (< 90%) (UK&I)	1 (0)	0 (0)	8 (0)	4 (0)	3 (0)	1 (0)	6 (1)
% Unsatisfactory Performance	4.5%	0.0%	19.0%	8.9%	7.3%	2.6%	15.8%

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2018 Incorrect Assignments

Sample	Lab Number	Consensus	Report
1A 02	62	DQ2, DQ8	DQ2, ***DQ7***
1A 03	181	A2, A25; B51, B55; Cw9, Cw14; DR4, DR13; DQ6, DQ7	***DRB1*04:01, 13:01; DQB1*06:03, 03:01***
	286		***A*02:01:01:01, A*25:01:01:01; B*51:01:01:01, B*55:01:01; C*03:03:01:01, C*14:02:01:01; DRB1*04:01:01:02, DRB1*13:01:01:01; DQB1*06:03:01:01, DQB1*03:01:01:01***
1A 04	62, 163	A2, A68; B18, B57; Cw5, Cw6; DR1, DR103; DQ5, -	DR1, ***-***
	181		***DRB1*01:01, DRB1*01:03; DQB1*05:01, -***
	194		A2, ***A69***
	225		B18, ***B58***
	286		***A*02:01:01:01, A*68:02:01:01; B*18:01:01:02, B*57:01:01:01; C*05:01:01:02, C*06:02:01:01; DRB1*01:01:01, DRB1*01:03:01; DQB1*05:01:01:02, -***
	315, 401		DR1, ***-***

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2018 Incorrect Assignments

Sample	Lab Number	Consensus	Report
1A 05	159, 401	B7, B61	B7, ***B40***
1A 09	223	A2,A25; DR4, DR7; DQ2, DQ8	***A*02***, A25
	315		***A*02***, A25; ***DRB1*04, DRB1*07; DQB1*02, DQB1*03:02***
1A 10	223	A2, A3; B7, B38; DQ6, -	***A*02, A*03; B*07***, B38
	315		***A*02, A*03; B*07***, B38; ***DQB1*06, -***

17/380 (4.5%) incorrect HLA types in 2018 reported by 10 labs;
- 5 reports of incorrect broad/split specificity
- 8 reports of molecular based nomenclature
- 4 reports of missed specificity (i.e. reported blank)

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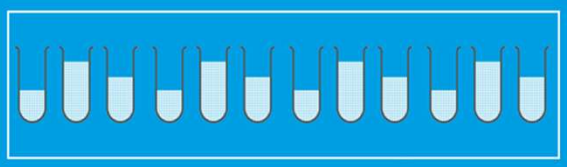
Scheme 4A1

DNA Typing at 1st Field Resolution



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Scheme 4A1

- ***Purpose:*** To assess participants' ability to correctly determine HLA types at the 1st field
- 10 blood samples sent in two distributions
- ***Consensus***: Presence of an allele is determined by at least 75% of labs agreeing, a reference result is used for those failing to reach consensus and for DPB1 assessment
- ***Satisfactory Performance***: Making at least 9 full HLA types in agreement with the consensus/reference result in a distribution year.

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Changes Introduced in 2018

- Participants can register for DPB1 assessment at low/medium resolution (i.e. SSP/SSO results)
- Assessed against a reference type
- Report DPB1 alleles at the resolution applicable to clinical need
- Strings of alleles not penalised if reference allele is present

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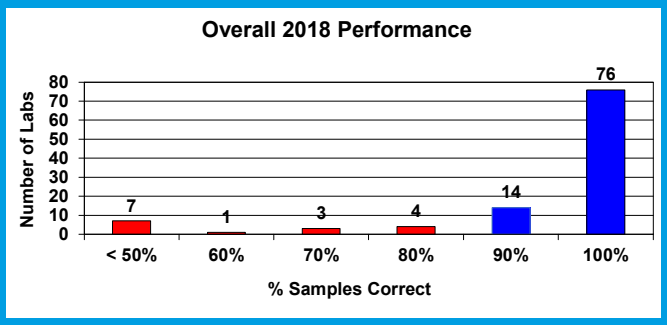
4A1 Performance 2018

	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	96 (30)	96 (30)	100 (29)	102 (28)	106 (28)	105 (28)
Number with Unsatisfactory Performance (< 90%) (UK&I)	5 (0)	9 (0)	7 (1)	21 (4)	11 (1)	15 (1)
% Unsatisfactory Performance	5.2%	9.4%	7.0%	20.6%	10.4%	14.3%



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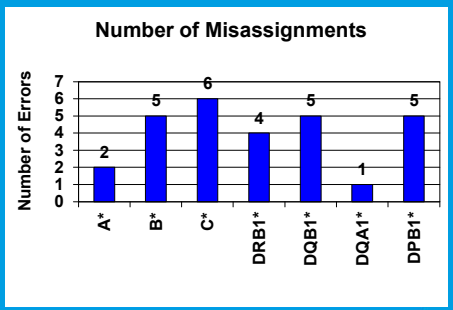
Incorrect Assignments

- 28/1014 (2.8%) incorrect HLA types reported by 22 labs (6 UK&I)
  - 13 incorrect assignments (e.g. A*26 instead of A*02)
  - 1 complete type error – sample mix-up (2 samples by 1 UK&I lab)
  - 9 missed assignments (e.g. reported homozygous/blank when hetero) – (5 UK&I)
  - 5 extra assignments (e.g. reported heterozygous when homozygous)
  - 28 other errors e.g. missed loci, DRB3/4/5 presence/absence errors

Methods for labs with errors

- 1 lab used SSP only
- 9 used Luminex only
- 6 used a combination (e.g.SSP&Luminex)
- 15 no info



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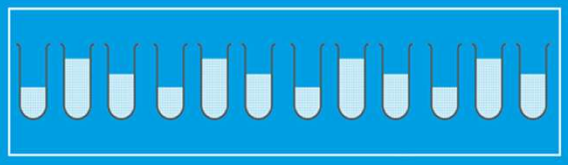
Scheme 4A1i

Interpretive HLA Genotype



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Scheme 4A1i

- ***Purpose:*** To assess participants' ability to correctly interpret their 4A1 result to the 'split' specificity level
- 10 blood samples sent in two distributions
- ***Consensus***: HLA type is determined by 75% of labs agreeing each specificity, a reference result is used for results failing to reach consensus
- ***Satisfactory Performance***: Making at least 9 full HLA types in agreement with the consensus/reference result in a distribution year.

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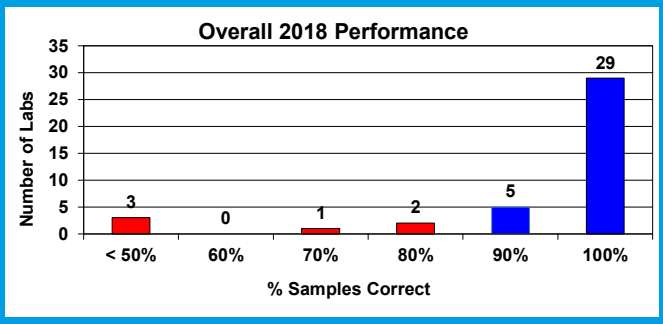
4A1i Performance 2018

	2017	2018
Number of Participants (UK&I)	36 (20)	40 (21)
Number with Unsatisfactory Performance (< 90%) (UK&I)	6 (1)	6 (0)
% Unsatisfactory Performance	16.7%	15.0%



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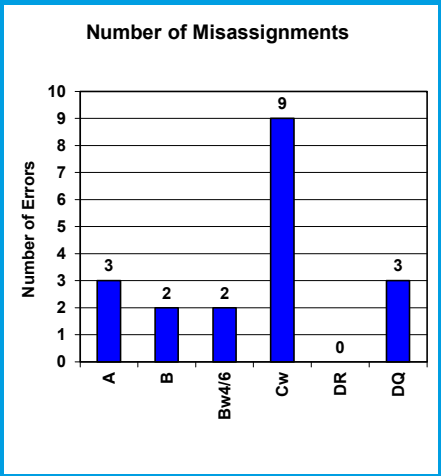
Interpreted DNA Results

- 12/380 (3.2%) incorrect HLA types reported by 8 labs (2 UK&I)
  - 2 reports with multiple errors in HLA type
  - 2 reports with an error at one loci
  - 2 reports of broad, not split specificity (e.g. Cw3 not Cw10) (1 UK&I)
  - 4 missed assignments (e.g. reported homozygous/blank instead of hetero)
  - 2 antigen mis-assignments (e.g. Bw4 and Bw6 instead of Bw6)



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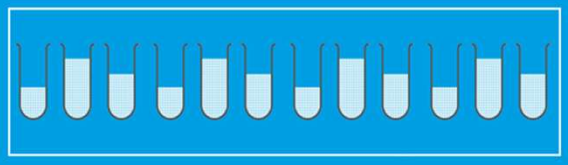
Scheme 4A2

DNA Typing to 2nd or 3rd Field Resolution



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Scheme 4A2

- ***Purpose:*** To assess participants' ability to correctly determine HLA type to the 2nd or 3rd field
- 10 blood samples sent in two distributions
- ***Consensus***: Genotype is determined by 75% of labs agreeing each allele. If consensus is not reached a reference result will be used
- ***Satisfactory Performance***: Making 9 or more full HLA types in agreement with consensus/reference genotype in a distribution year

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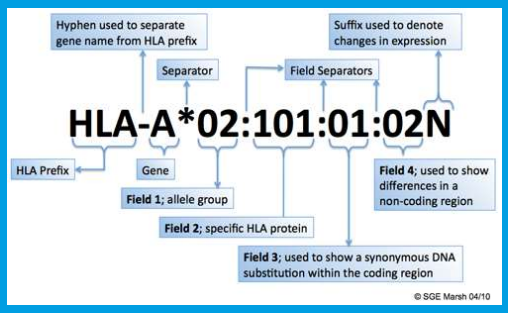
Introduced in 2018

- Participants can register for assessment of 3rd field results in Scheme 4A2



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4A2 Performance 2018

- 9 Unsatisfactory Performers (2 UK & Ireland)

	2014	2015	2016	2017	2018
Number of Participants (UK&I)	59 (21)	59 (20)	63 (21)	66 (21)	63 (20)
Number with Unsatisfactory Performance (< 90%) (UK&I)	5 (1)	7(1)	8 (2)	4 (0)	9 (2)
% Unsatisfactory Performance	8.5%	11.9%	12.7%	6.1%	14.3%

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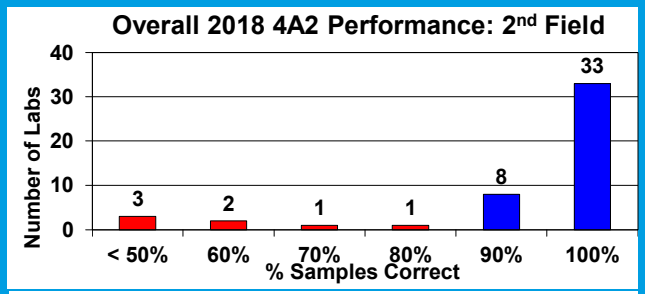
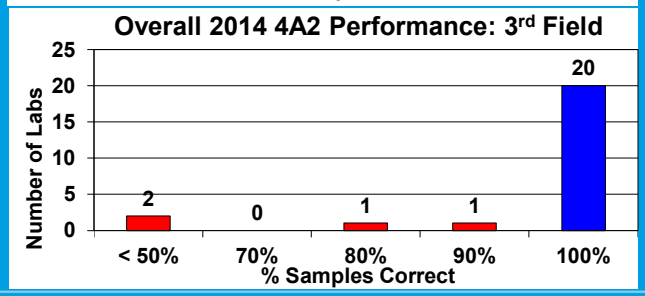
4A2 Performance 2018





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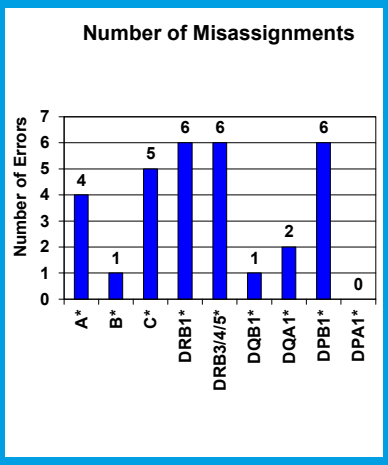
2018 Incorrect Assignments: 2nd Field

- 30/435 (6.9%) incorrect HLA types reported by 15 labs (6 UK&I)
  - 15 reports of alleles in a string that differ from the consensus allele (e.g. A*01:01/09) (4 UK&I)
  - 11 reports of incorrect allele (e.g. C*17:01 not C*17:03) (2 UK&I)
  - 2 reports of incorrect antigen (e.g. B*44:03 instead of B*40:01)
  - 1 report where a null allele was missed
  - 1 report where a null allele was included



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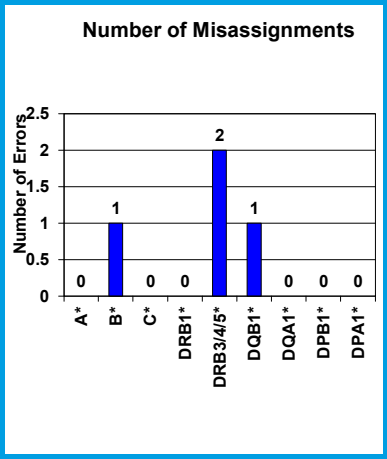
2018 Incorrect Assignments: 3rd Field

- 4/210 (1.9%) incorrect samples reported by 3 labs (1 UK&I)
  - 1 report of 2nd rather than 3rd field resolution
  - 2 reports of incorrect allele (e.g. DRB4*01:01:01 rather than 01:03:02)
  - 1 report with an error at 3rd field (e.g. DRB1*03:03:01 instead of 03:03:02)
  - 5 reports where not all loci reported



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Ambiguous 3rd Field Results

- The assessment of 3rd field results has been challenging.
  - Allowed all ambiguities at the 3rd field in 2018
  - Reporting should reflect clinical practice
  - All ambiguities at the 3rd field must be resolved in 2019

Lab	Sample(s)	Locus	Consensus Type	Type reported	2nd/3rd field ambiguity	CDS difference
42	02/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
42	02/2018	DQB1*	02:02:01	02:02:01/02:97	2nd	Yes – Exon 4
42	03/2018	DPA1*	02:01:01	02:01:01/02:08	2nd	Yes – Exon 4
42	04/2018	DQB1*	03:02:01	03:02:01/03:02:26	3rd	Yes – Exon 4
42	05/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
42	05/2018	DQB1*	02:02:01	02:02:01/02:97	2nd	Yes – Exon 4
130	02/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
130	03/2018	DPA1*	02:01:01	02:01:01/02:08	2nd	Yes – Exon 4
130	05/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
156	02/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
156	02/2018	DQB1*	02:02:01	02:02:01/02:97	2nd	Yes – Exon 4
156	03/2018	DPA1*	02:01:01	02:01:01/02:08	2nd	Yes – Exon 4
156	03/2018	DQB1*	05:01:01	05:01:01/05:01:24	3rd	Yes – Exon 1
156	05/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
156	05/2018	DQB1*	02:02:01	02:02:01/02:97	2nd	Yes – Exon 4
268	02/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4
268	05/2018	DRB1*	07:01:01	07:01:01/07:79	2nd	Yes – Exon 4

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Clinical Reporting

- Resolution being reported should reflect clinical practice
- NEQAS asked participants what level of resolution labs report at clinically 17 (27%) responses (5 from UK&I, 12 from RoW):
  - What clinical services do you provide and what's the highest resolution do you report at clinically?

	Solid Organ Transplant	HSCT	Disease Association	Specify
First Field	6	0	1	3 (HLA Selected Platelets)
Second Field	5	12	12	4 (Refractoriness to Platelet Transfusions and Special Requests)
Third Field	0	3	0	1 (Research Projects only)
No Response	6	2	4	9

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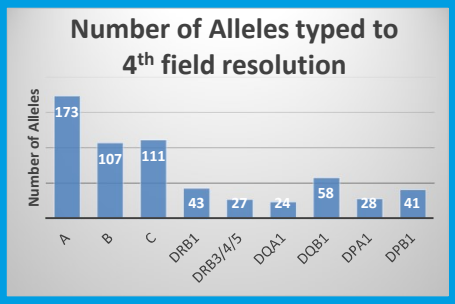
4th Field Results

- 7 labs reported results at 4th field resolution
- Total of 612 alleles

	UK&I	RoW
NGS	1	1
SBT/NGS	0	1
SSP/NGS	0	1
SSP/SBT/NGS	1	1
SSOP/SBT/LUM	1	0
SBT/LUM/RT-PCR	1	0
SBT	0	1
No response	0	6
Total	**4**	**11**

- 515 (84.2%) reported as unambiguous 4th field result (e.g. B*07:02:01:01)
- 97 (15.8%) contained 3rd or 4th field ambiguities (e.g. B*40:01:02:01/04)
- 1 error at 4th field: DRB4*01:01:01:01 instead of 01:03:02



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New for 2019

- More stringent assessment of 3rd field resolution
  - Participants must sequence all exons to resolve all ambiguities
    - E.g. DRB1*07:01:01/07:79 or DQB1*03:02:01/03:02:26 would be unacceptable as ambiguities in exon 4 have not been resolved
- Results at the 4th field can be reported, but will not be assessed

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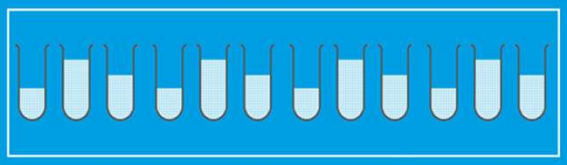
Schemes 1A, 4A1, 4A1i, 4A2

Discussion



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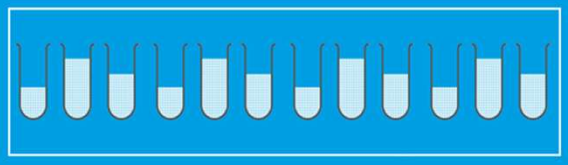
Scheme 1B

HLA-B27 Testing



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HLA-B27 Testing

- ***Purpose:*** To assess ability to correctly determine HLA-B27/2808/B*27 status
- 10 random donor samples sent in five distributions
- ***Consensus***: B27 status determined by at least 75% agreement on presence or absence of HLA-B27
- ***Satisfactory performance***: Making 10 reports in agreement with consensus in a distribution year

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2018 Incorrect Assignments

Sample	Result	Lab Number	Technique	HLA Type	Lab Identified Cause
1B01	False Neg	106*, 256, 279	Serological	B27, B47	No reply Low lymphocyte reactivity
1B02	False Neg	67, 83, 106*, 256, 279	Serological	B27, B60	Kit Ambiguity No response Transcription Error Low lymphocyte reactivity
1B05	False Neg	10*, 372	Serological	B27, B65	Delay in testing causing poor viability No response
1B06	False Pos	106*	*Unknown	B38, B50	No response
1B09	False Pos	10*, 372	Serological	B27, B65	Delay in testing causing poor viability No response
1B10	False Pos	106*	*Unknown	B38 B50	No response

6/10 samples distributed were HLA-B27 positive
14 errors: 10 False Neg, 4 False Pos

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Performance 2018

- 10 Unsatisfactory Performers (3 UK & Ireland)

	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	96 (47)	107 (51)	115 (54)	123 (54)	127 (52)	133 (54)
Number with Unsatisfactory Performance (< 100%) (UK&I)	4 (1)	4 (2)	8 (4)	15 (6)	7 (2)	10 (3)
% Unsatisfactory Performance (UK&I)	4.2% (2.1%)	3.7% (3.9%)	6.9% (7.4%)	12.2% (11.1%)	5.5% (3.8%)	7.5% (5.6%)

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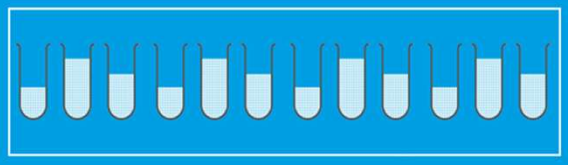
Scheme 5A

HFE Typing



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Scheme 5A

- ***Purpose:* To assess participants ability to correctly determine HFE mutations**
  - 3 mutations assessed:
    - Codon 63: Histidine63Aspartic acid (H63D)
    - Codon 282: cysteine282tyrosine (C282Y)
    - Codon 65: Serine63Cysteine (S65C)
- 10 random donor samples sent in two distributions
- ***Consensus***: determined by at least 75% agreement with the consensus/reference result
- ***Satisfactory Performance***: 10 reports in agreement with consensus in a distribution year

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Scheme 5A Performance

- No Unsatisfactory Performers

	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	58 (10)	59 (50)	60 (49)	58 (49)	56 (42)	58 (44)
Number with Unsatisfactory Performance (< 100%) (UK&I)	2 (2)	2 (2)	0 (0)	3 (2)	3 (2)	0 (0)
% Unsatisfactory Performance	3.9%	3.4%	0%	5.2%	5.3%	0%

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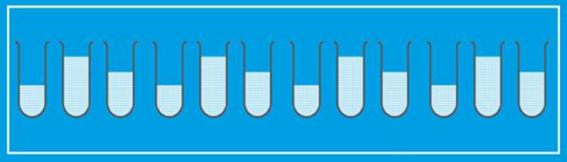
Scheme 5B

Interpretative HFE genotype
and hereditary haemochromatosis



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Scheme 5B

- ***Purpose***: to assess participants' ability to make an accurate, clear and concise clinical report
- Twice a year, 2 clinical scenarios:
  - HFE genotype provided, together with various pieces of clinical information
- Reports must be identical in format to that used for routine clinical reporting in participants' laboratories
- Interpretative criteria expected to be covered by the reports are identified and agreed by the expert assessors.
  - Penalty points awarded, if >50% of the available penalty points are awarded then performance is unacceptable

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Performance

2018 – all 4 scenarios

5 penalty points per scenario, 20 in total

3	labs got	1 penalty point
4	labs got	2 penalty points
7	labs got	3 penalty points
2	labs got	5 penalty points
2	labs got	6 penalty points
1	lab got	7 penalty points
1	lab got	8 penalty points
1	lab got	Multiple penalty points (sent wrong report)

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Scheme 5B Performance

- 1 Unsatisfactory Performer (1 UK&I)

	2012	2013	2014	2015	2016	2017	2018
Number of Participants	21	19	20	18	19	20	21 (18)
Number with Unsatisfactory Performance	3	3	5	0	0	0	1 (1)
% Unsatisfactory Performance	14.3%	15.8%	25.0%	0%	0%	0%	4.8%

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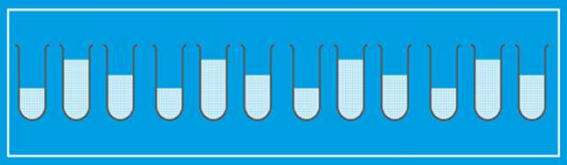
Scheme 7

*HLA-B*57:01 Typing for Drug Hypersensitivity*



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Scheme 7

- ***Purpose:*** To assess participants' ability to correctly determine HLA-B*57:01 status.
- 10 random donor samples sent in two distributions
- ***Consensus***: determined by at least 75% agreement with the consensus/reference result
- ***Satisfactory Performance***: Making ten sample reports in agreement with the consensus HLA-B*57:01 status in a distribution year.

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Scheme 7 Performance

- 7/10 samples distributed were HLA-B*57:01 positive
- 2 labs with unacceptable performance
  - Both did not return results

	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	47 (23)	56 (24)	62 (26)	62 (25)	64 (26)	67 (27)
Number with Unacceptable Performance (< 100%) (UK&I)	0 (0)	1 (0)	0 (0)	1 (1)	4 (1)	2 (0)
% Unsatisfactory Performance	0.0%	1.8%	0.0%	1.6%	6.3%	3.0%

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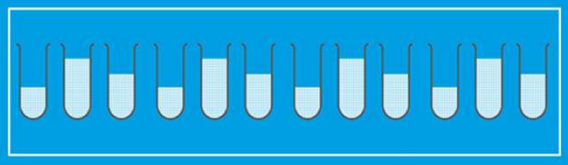
Scheme 8

HLA Genotyping for Coeliac
and other HLA Associated Disease



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Scheme 8

- ***Purpose:*** To assess participants' ability to correctly determine HLA type associated with various diseases e.g. coeliac disease and narcolepsy
- 10 blood samples sent in two distributions
- ***Consensus***: determined by assessment against the reference result
- ***Satisfactory Performance***: Making ten sample reports in agreement with the reference genotype in a distribution year.

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Scheme 8 Performance

- 14 Unsatisfactory Performers (4 UK & Ireland)

	2013	2014	2015	2016	2017	2018
Number of Participants (UK&I)	19 (8)	21 (9)	30 (8)	39 (8)	45 (9)	52 (10)
Number with Unsatisfactory Performance (< 100%) (UK&I)	2 (1)	3 (2)	8 (0)	8 (3)	15 (2)	14 (4)
% Unsatisfactory Performance	10.5% (12.5%)	14.3% (22.2%)	26.7% (0%)	20.5% (37.5%)	33.3% (22.2%)	26.9% (40%)

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2018 Unacceptable Performance by Disease

Disease	HLA Association	Number of Participants	No. of Participants with Unacceptable Performance
Coeliac	DQ2, DQ8, DQA	50	11
Narcolepsy	DQB1*06:02	21	3
Actinic Prurigo	DRB1*04:07	4	1
Birdshot Retinopathy	A*29	9	1
Behçet's	B*51	6	0
Rheumatoid Arthritis	DRB1*04	2	0
Diabetes	DR3, DR4	4	1

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2018 Incorrect Assignments

Sample	Lab	Result	HLA Type	Error
801	85	Negative for ***DQ2*** and DQ8	DRB1*04:01, DRB1*07:01/34/72; DQB1*02:02, DQB1*03:01; DQA1*02:01, DQA1*03:03	Interpretation issue
	185	DRB1*04, DRB1*07, DQA1*02:01, ***DQA1*03:02***, DQB1*02:02, DQB1*03:01		Transcription error
	255	***HLA-DQ2: NEG*** HLA-DQ8: NEG		Interpretation issue
	278	***Beta-subunit HLA DQ8, HLA DQ8 genotype***		No response
	279	DRB1 *04; *07, DQB1 *02:02; *03:01 DQA1 *02:01; ****03:01***		Technical issue
	319	***DQ2: NEG*** DQ8: NEG		Interpretation issue
802	78	***DQ2*** and DQ8 ABSENT	DRB1*03:01/124/132/137, DRB1*04:08; DQB1*02:01, DQB1*03:01; DQA1*03:03, DQA1*05:01	Technical issue
	185	DRB1*03, DRB1*04, ***DQA1*03:02***, DQA1*05:01, DQB1*02:01, DQB1*03:01		Transcription error
	279	DRB1 *03; *04 DQB1 *02:01; *03:01 DQA1 ****03:01***; *05:01		Technical issue
803	159	DQA1*01:01-05, *05:05 DQB1*03:01, ****05:01***	DRB1*11:01/97, DRB1*15:01/141; DQB1*03:01, DQB1*06:02; DQA1*01:02/11, DQA1*05:05	Kit issue
804	159	DQA1*01:01-05, *05:05 DQB1*03:01, ****05:01***	DRB1*01:03, DRB1*13:01/117/190/215; DQB1*03:01, DQB1*06:03; DQA1*01:03, DQA1*05:05	Kit issue

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2018 Incorrect Assignments

Sample	Lab Number	Result	HLA Type	Error
806	86	Coeliac disease-associated HLA alleles present: DQB1*03:01 DQA1*05:05 ***HLA DQ2: PRESENT*** - HLA-DQA1*05, HLA DQ8: ABSENT	DRB1*13:01, DRB1*13:03; DQB1*03:01, DQB1*06:03; DQA1*01:03, DQA1*05:05	Kit issue
808	123	***DQB1*07***, DQB1*03:03	DRB1*07:01, DRB1*09:01; DQB1*02:02, DQB1*03:03; DQA1*02:01, DQA1*03:02	No response
	319	***DQ2: NEG DQ8: NEG (A1*05: NEG, B1*02: POS, B1*0302: NEG)***		No response
809	129	DRB1*0401, -	DRB1*04:01, DRB1*07:01; DQB1*02:02, DQB1*03:02; DQA1*02:01, DQA1*03:01	Interpretation issue
	319	***DQ2:NEG, DQ8:POS (A1*05: NEG, B1*02: POS, B1*0302: POS)***		No response
810	17	***HLA-DQA1*05:01; DQB1*02:01 Positive HLA-DQA1*03;*** DQB1*03:02 Negative	DRB1*04:01, DRB1*15:01; DQB1*03:01, DQB1*06:02; DQA1*01:02, DQA1*03:03	Technical issue
	279	DRB1*04; DQB1*03:01,****05:01; DQA1*03:01***		Kit issue

- 18 incorrect assignments in 2018 (4 UK&I), 17/18 in Coeliac Disease
  - Also 2 labs did not report any results for samples 801-805/2018

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Participant Issues

- CAPA responses show some common problems:
  - sample handling or technical error - 2 labs (18%)
  - misinterpretation of a correct HLA type - 3 labs (27%)
  - ambiguous kit results or resolution issue - 4 labs (37%)
  - 2 labs (18%) did not respond

- Labs struggled with the interpretation of a correct HLA type
  - a lab reported that DQ2 was present or "*Half DQ2 positive*" when they had detected HLA-DQB1*03:01, DQA1*05:05 as they wanted to report they had detected the DQA1*05 subunit.

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Participant Issues

- Commercial kits also been to be the cause of some issues due to deficiencies in resolution and the interpretation of results:

Signal

Mix DQA1*05	Mix DQB1*02	Mix DQB1*03:02	HLA-Genotype
-	-	+	DQ8
-	+	+	DQ8
+	-	+	DQ8
+	+	+	DQ2 and DQ8
+	+	-	DQ2
+	-	-	A genetic predisposition for Coeliac Disease is unlikely
-	+	-	
-	-	-	

  - This table taken from a commercial kit insert shows how misleading it can be especially for labs with limited H&I experience

- Currently interpretative comments are collected but not assessed
- Examples from UK labs for the same sample:
  - *This patient is DQ2.2 positive, heterozygous. This patient is DQ2 positive which is associated with Coeliac Disease.*
  - *This individual does not carry the HLA-DQ variants associated with Coeliac Disease.*
  - *This patient is Heterozygous POSITIVE for HLA-DQ2 (but is DQA1*05 NEGATIVE) and NEGATIVE for HLA-DQ8 (DQA1*03, DQB1*03:02). Patients with this genotype have a LOW RISK of predisposition to Coeliac disease.*

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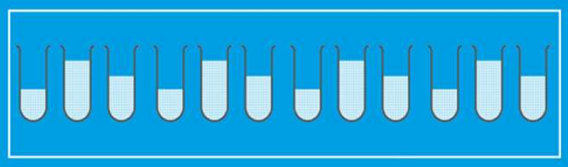
Coeliac Guidelines



Arthi Anand
Helena Lee

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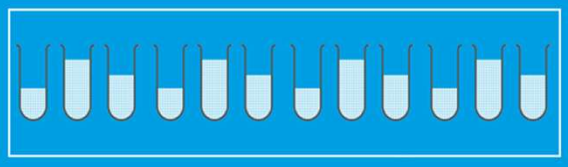
Schemes 1B, 5A, 5B, 7, 8

Discussion



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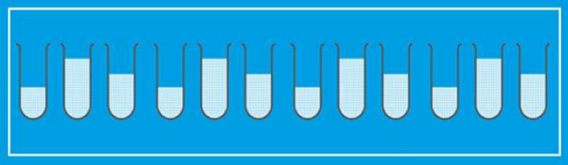
Steering Committee
Q&A Session



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Scheme Performance – UK&I

	2013	2014	2015	2016	2017	2018
Scheme 1A	0	0	0	0	0	1
Scheme 1B	1	2	4	6	3	3
Scheme 2A Without DTT Scheme 2A With DTT	2 N/A	6 N/A	2 0	3 6	6	7
Scheme 2B	0	2	3	1	1	2
Scheme 3 Class I Scheme 3 Class II	1 0	0 0	1 0	0 0	0 0	1 0
Scheme 4A1	0	0	1	4	1	1
Scheme 4A1i	N/A	N/A	N/A	N/A	1	0
Scheme 4A2	2	1	1	2	1	2
Scheme 5A	2	2	0	2	2	0
Scheme 6	0	1	3	4	0	0
Scheme 7	0	0	0	1	1	0
Scheme 8	1	2	0	3	2	4
Scheme 9	N/A	N/A	N/A	N/A	0	0
Scheme 10	N/A	N/A	N/A	N/A	0	0
Scheme 11	N/A	N/A	N/A	N/A	N/A	0
Total	**9**	**16**	**15**	**32**	**15**	**21**

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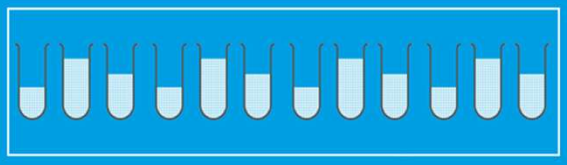
EDXM Scheme

Incorporating Crossmatching, HLA Typing and Antibody Detection/Specification



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'Whole Process' EQA

- UK NEQAS for H&I
  - Scheme 1A, 4A1, 4A2 – HLA Typing
  - Scheme 6 – HLA Antibody Detection
  - Scheme 3 – HLA Antibody Specification
  - Schemes 2A and 2B – Crossmatching
  - Solid Organ Interpretive Scenarios (Paper based)

"Schemes should relate more closely to clinical scenarios rather than testing individual test assays."

- Clinical decision making based on results from multiple assays
- Each assay only gives part of the picture
- Results from one assay can influence the interpretation of another
- Variation between centres
  - Sensitivity/cut offs
  - Assay repertoires

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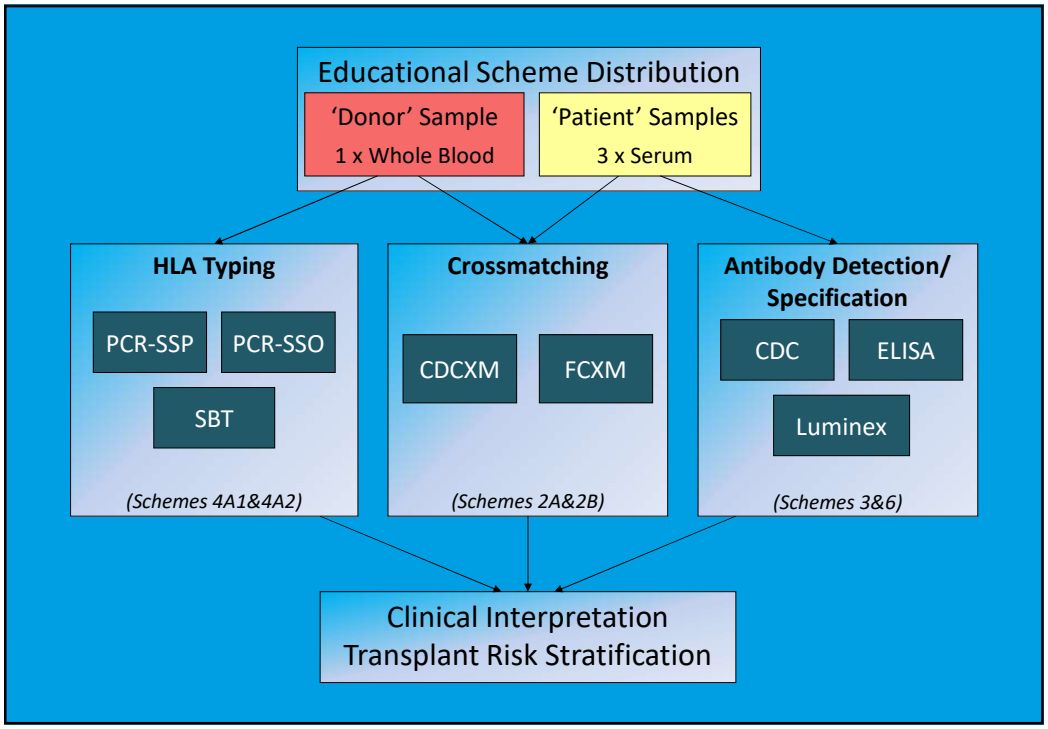

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2018 Results

- 32 participants
  - not all labs reported results for all tests
- 100% agreement on HLA type
  - except DRB4 with some labs reporting absence or no result

	A*	B*	C*	DRB1*	DRB4*	DQA1*	DQB1*	DPA1*	DPB1*
	24	**45**	**06**	**04**	**01**	**02**	**02**	**01**	**01:01**
	26	**40**	**03**	**07**	**-**	**03**	**03**	**02**	**04:02**
Number of reports	32	32	30	32	21	25	31	13	17[1]
% Labs in consensus	100%	100%	100%	100%	76%	100%	100%	100%	100%

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Serum 1 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	84%	5 labs reported negative (143, 190, 238, 260, 262)
HLA Class II Antibodies	Positive	100%	
DSA	Yes	97% (28/29)	Huge range in MFI reported e.g. DR4 3,287-17,567 DSA included A24, Cw6, DR4, DR7, DQ8, DR53 and DQA
CDC XM	Negative	100% (15/15)	
FCXM T Cell	Not Assessed	65.4% (17/26)	65.4% positive, 34.6% negative
FCXM B Cell	Positive	86.4% (19/23)	Lab 14, 112 reported negative, Lab 28, 54 reported equivocal
Transplant Risk	Contraindication /High	62% (18/29)	11 labs reported medium risk (9, 11, 24, 38, 48, 54, 62, 112, 149, 238, 262)

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Serum 2 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	100%	
HLA Class II Antibodies	Positive	100%	
DSA	Yes	96.6% (28/29)	Huge range in MFI reported e.g. DQ2 9,025-34,845 DSA included B45, DR7, DQ2, DQ8, DR53, DPB1*01:01, DPB1*04:02, DQA and DPA
CDC XM	B cell Positive T cell Negative	100% (15/15) 92.3% (12/13)	PBL –DTT 80% Positive, +DTT Not Assessed (57% Positive)
FCXM T Cell	Negative	84.6% (22/26)	4 Labs reported Positive (Lab 11, 19, 20 and 38), 1 reported Equivocal (Lab 122)
FCXM B Cell	Positive	100% (25/25)	
Transplant Risk	Contraindication /High	97% (28/29)	One Lab (195) reported medium risk

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Serum 3 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	94%	
HLA Class II Antibodies	Positive	100%	
DSA	Yes	86.2% (25/29)	DSA included A24, A26, B60, B45, Cw6, Cw10, DR4, DR7, DQ2, DQ8, DPB1*04:02, DQA and DPA
CDC XM	Negative	100%	
FCXM T Cell	Not Assessed	66.7% (18/27)	66.7% reported Negative, 33.3% Positive
FCXM B Cell	Not Assessed	58.3% (14/24)	58.3% reported Negative, 41.7% Positive
Transplant Risk	Medium Risk	55% (16/29)	5 labs reported a low risk (15, 23, 34, 39, 149, 194, 260), 3 a high risk (28, 48, 58) and 5 a contraindication (122, 162, 195, 220, 284)

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Summary of Crossmatch and DSA Detection Results

2018 Results		Serum 1		Serum 2		Serum 3	
DSA Defined by Luminex		Class I	Class II	Class I	Class II	Class I	Class II
MFI >10,000		Cw6 (90%)			DR7 (28%) DQ2 (28%) DQ8 (22%) DR53 (19%) DQA1*02:01 (8%) DQA1*03:01 (2%)		DQ8 (25%)
MFI 5,000-9,999			DR4 (97%)			A26 (9%)	
MFI 3,000-4,999				B45 (14%)	DPB1*01:01 (10%) DPB1*04:02 (16%)	B60 (15%) B45 (16%)	DPB1*04:02 (17%)
MFI 1,500-2,999			DR7 (14%) DQ8 (14%)		DPA1*01:03 (1%) DPA1*02:01 (1%)	A24 (14%)	DPA1*01:03 (1%) DPA1*02:01 (1%) DQA1*03:01 (1%) DQA1*02:01 (1%) DQ2 (1%)
MFI <1,499		A24 (14%)	DR53 (3%) DQA1*03 (3%)			Cw6 (2%) Cw10 (1%)	DR7 (2%) DR4 (1%)
CDCXM	No DTT	Negative		Positive		Negative	
	DTT	Negative		Negative (T cell) / Positive (B cell)		Negative	
FCXM	T Cell	Not Assessed		Negative		Not Assessed	
	B Cell	Positive		Positive		Not Assessed	
Risk		Contraindication/High (62%)		Contraindication/High (97%)		Medium (55%)	

The table shows the percentage of participants identifying a DSA and the most common MFI range it was reported in.

- DSAs with high MFI values have a noticeable affect on FCXM results but seem to affect labs differently in terms of the CDCXM

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Benefits

- Participants able to:
  - Monitor performance of multiple techniques within a single scheme
  - Make clinical interpretations based on their own results
  - Compare local policies for clinical assessment
- Educational
  - Monitor concordances
  - Review variations
  - Trainees
- Competency
  - Laboratory staff
  - Consultants

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Future Considerations

- Could the scheme form the basis of future formal EQA scheme design?
- Workload
  - Participants
  - UK NEQAS
- Assessment complexity
  - Consensus?
  - Incorrect result, correct interpretation?

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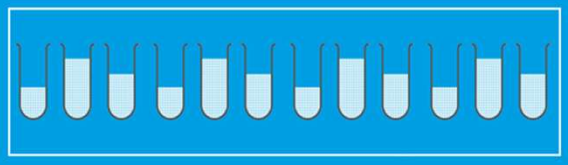
Interpretive Educational Schemes



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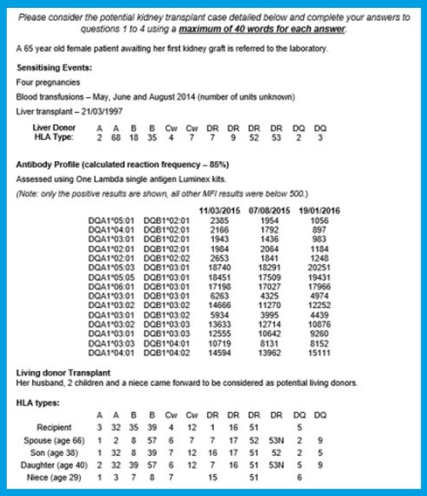
Interpretive Educational Scheme

- 3 Clinical Scenarios a year
  - Solid Organ, HSCT, Platelet/transfusion
- Based on patient cases
  - Provide relevant clinical details and test results
  - Questions on interpretation of results and clinical advice
- Not Assessed
- Provided free of charge



*Please consider the potential kidney transplant case detailed below and complete your answers to questions 1 to 4 using a **maximum of 40 words for each answer**.*

A 65 year old female patient awaiting her first kidney graft is referred to the laboratory.

Sensitising Events:

Four pregnancies

Blood transfusions – May, June and August 2014 (number of units unknown)

Liver transplant – 21/03/1997

Liver Donor HLA Type:	A 2	A 68	B 18	B 35	Cw 4	Cw 7	DR 7	DR 9	DR 52	DR 53	DQ 2	DQ 3

Antibody Profile (calculated reaction frequency – 85%)

Assessed using One Lambda single antigen Luminex kits.

(Note: only the positive results are shown, all other MFI results were below 500.)

		11/03/2015	07/08/2015	19/01/2016
DQA1*05:01	DQB1*02:01	2385	1954	1056
DQA1*04:01	DQB1*02:01	2166	1792	897
DQA1*03:01	DQB1*02:01	1943	1436	983
DQA1*02:01	DQB1*02:01	1984	2064	1184
DQA1*02:01	DQB1*02:02	2653	1841	1248
DQA1*05:03	DQB1*03:01	18740	18291	20251
DQA1*05:05	DQB1*03:01	18451	17509	19431
DQA1*06:01	DQB1*03:01	17198	17027	17966
DQA1*03:01	DQB1*03:01	6263	4325	4974
DQA1*03:02	DQB1*03:02	14666	11270	12252
DQA1*03:01	DQB1*03:02	5934	3995	4439
DQA1*03:02	DQB1*03:03	13633	12714	10876
DQA1*03:01	DQB1*03:03	12555	10642	9260
DQA1*03:03	DQB1*04:01	10719	8131	8152
DQA1*04:01	DQB1*04:02	14594	13962	15111

Living donor Transplant

Her husband, 2 children and a niece came forward to be considered as potential living donors.

HLA types:

	A	A	B	B	Cw	Cw	DR	DR	DR	DR	DQ	DQ
Recipient	3	32	35	39	4	12	1	16	51		5	
Spouse (age 66)	1	2	8	57	6	7	7	17	52	53N	2	9
Son (age 38)	1	32	8	39	7	12	16	17	51	52	2	5
Daughter (age 40)	2	32	39	57	6	12	7	16	51	53N	5	9
Niece (age 29)	1	3	7	8	7		15		51		6	

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Clinical Scenarios

	Solid Organ	HSCT	Platelet/ transfusion
2013	Live kidney transplant	Matched unrelated donor selection	N/A
2014	Deceased kidney transplant	Mismatched unrelated donor selection	N/A
2015	Cardiothoracic transplant	Paediatric cord blood donor selection	Platelet refractory
2016	Deceased donor virtual XM	Donor search for patient with unusual HLA type	Platelet refractory
2017	Cardiothoracic transplant	Haploidentical donor selection	TRALI
2018	Live kidney transplant	Unrelated donor selection permissive/non-permissive	NAIT

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Scenario 1- Kidney Transplant Case

Offer of kidney transplant to your centre and selection of recipients

Provided

- Patient HLA type and ABO (O)
- HLA antibody profile
- Information on potential recent sensitising events
- Crossmatching results

- 53 returns (22 UK&I)

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Would you recommend removing antibodies from the patient's profile?

HLA Antigen	01/2018	08/2017	02/2017	10/2016
A1	1105	793	1964	2697
A2	13071	12308	16756	18994
A23	654	922	1928	2640
A24	1062	1174	2138	1436
A69	721	1900	2015	2671
B44	1474	2413	2691	3248
B45	1369	1598	3365	4535
B13	1021	1845	2031	4461
B62	9204	6273	8333	10091
B63	1574	1308	3327	4112
B75	1246	1673	Negative	4238
B76	3675	3118	4494	6852
B77	Negative	Negative	1135	3241
B38	Negative	Negative	1340	1507
B39	1060	779	1395	1564
B57	12405	14011	18987	17756
B58	12008	11179	16947	17581
B49	6705	5387	5899	5698
B50	4752	5089	6357	6028
B27	1005	1062	Negative	Negative
B37	753	734	1379	1480
B41	5447	4968	5724	6937
B42	4218	3882	4185	4953
B55	2748	1540	2938	3337
B56	4619	4233	4703	4422
B59	1531	Negative	1135	1453
B67	3581	1890	4020	4321
B71	3168	2692	1960	1402
B72	7033	4305	4958	4510
Cw5	18465	18445	18993	18914
DR1	7298	6877	9665	12792
DR15	650	Negative	Negative	Negative
DR16	775	Negative	Negative	Negative
DR7	2580	2243	2330	4856
DR8	Negative	Negative	5006	Negative
DR9	3335	2728	3939	4590
DR10	2128	1709	2301	4291
DR103	6777	6717	9568	12323
DR51	4980	4367	6671	Negative

The patient currently has a cRF of 99%

Decision	UK&I		RoW		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Yes	22/22	**100%**	28/31	**90%**	50/53	**94%**
No	0/22	**0%**	3/31	**10%**	3/53	**6%**

94% recommended delisting antibodies. Reasons included:

- Temporal changes in ab level
- Some ab likely transfusion derived
- Increase threshold for listing to >3,000 as equates to a positive FCXM
- Delist from one loci at a time
- Only if patient medically fit to receive enhanced immunosuppression
- Perform C1q assay
- Remove only CDC negative ab
- Only include pregnancy derived ab as UAG

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Select Antibodies for Delisting

HLA Antigen	01/2018	08/2017	02/2017	10/2016
A1	1105	793	1964	2697
A2	13071	12308	16756	18994
A23	654	922	1928	2640
A24	1062	1174	2138	1436
A69	721	1900	2015	2671
B44	1474	2413	2691	3248
B45	1369	1598	3365	4535
B13	1021	1845	2031	4461
B62	9204	6273	8333	10091
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DR8	Negative	Negative	5006	Negative
DR9	3335	2728	3939	4590
DR10	2128	1709	2301	4291
DR103	6777	6717	9568	12323
DR51	4980	4367	6671	Negative

HLA Spec	Number of labs agreeing to remove Spec (n=50)		
	Total	UK&I	RoW
A1	41	20	21
A2	1	0	1
A23	39	19	20
A24	37	19	18
A69	36	17	19
B27	6	1	5
B37	7	1	6
B38	5	1	4
B39	7	1	6
B42	4	2	2
B44	10	4	6
B45	16	8	8
B49	2	0	2
B50	1	0	1
B56	5	2	3
B58	1	0	1
B59	6	1	5
B13	27	16	11
B62	1	0	1
B63	22	14	8
B67	5	2	3
B71	3	1	2
B72	1	0	1
B75	27	18	9
B77	27	15	12
B55	14	4	10
Cw5	1	0	1
DR7	12	4	8
DR8	30	16	14
DR9	7	2	5
DR1	1	0	1
DR10	13	5	18
DR15	33	14	19
DR16	34	15	19
DR51	9	4	5

The most frequency chosen antibodies for delisting are A1, A24, A24, A69, DR15 and DR16

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Would you perform additional testing or give recommendations to increase the chance of deceased donor transplantation?

Decision	UK&I		RoW		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
Yes	20/22	**91%**	28/31	**90%**	48/53	**91%**
No	2/22	**9%**	3/31	**10%**	5/53	**9%**

91% of respondents answered that they would perform additional testing.
Examples of which included:

- **EDTA treat serum samples**
- **Test using alternative method e.g. Lifecodes or C1q**
- **Perform 3rd party crossmatches**
- **Eplet study or HLA Matchmaker**
- **Consider live donor options**
- **Check ABO ab titres for ABOi transplant consideration**
- **Review local DCD/Fast Track local policy for priority allocation**
- **Plasma exchange/plasmapheresis**
- **Allow repeat mm to partner**
- **Perform an autologous crossmatch**

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Based on the results given what would you recommend?

Potential Donor	ABO	HLA type	Current CDC XM Result	Current FCXM Result
Niece	A	A2, A68; B44, B51; Cw5, Cw14; DR4, DR13; DQ6, DQ7	PBL Positive (scored "6" with and without DTT) B cell Positive (scored "4" with and without DTT)	T Cell (LCS 232) B cell (LCS 264) Strong Positives

LCS = Linear Channel Shift (T Cell >46 = Pos) (B Cell >63 = Pos)

Recommendations:

- **Discontinue transplant work up, high risk ABOi and HLAi**
- **Transplant veto as CDCXM and FCXM positive**
- **Perform autologous crossmatches, discuss at MDT meeting**
- **Repeat pregnancy haplotype mismatch with antibody, poor prognosis**
- **Patient unlikely to respond to desensitisation**
- **Enter pair into the Kidney Sharing Scheme**

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What antibody profile would you use to register the pair in the kidney sharing scheme?

		UK&I (n=22)		RoW (n=31)		Total (n=53)	%
		Number	Percentage	Number	Percentage		
Option 1	Same profile as original deceased donor profile	0	0%	4	13%	4	8%
Option 2	Modified deceased donor profile	16	73%	20	65%	36	68%
Option 3	Other	6	27%	7	22%	13	24%

Registration with the a reduced UAG profile was the most popular option (68%).
The reasons cited included:

- **To increase the chances of getting a match**
- **Use a conservative approach and delist in subsequent matching runs**
- **Local policy is to list of ab with MFI >3,000**
- **Patient has limited vascular access, may need to take additional risks and delist further**
- **Option to use pre and post transplant desensitisation**

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Predict the CDCXM and FCXM result for the new donor

Some antigens were removed from the patient's unacceptable antigen profile and a match was identified in the kidney sharing scheme (mm in red, patient DP type unknown)

ABO O **A1, A24; B8, B51; Cw1, Cw7; DR11, DR17; DR52; DQ2, DQ7; DPB1*02:01, -**

	Predicted Crossmatch Result								
	Positive			Negative			Other		
	UK&I	RoW	Total	UK&I	RoW	Total	UK&I	RoW	Total
CDC	0	0	0	22	30	32	0	0	0
Flow Cytometry	1	5	6	11	17	28	10	8	18

Most respondents predict the CDCXM and FCXM will be negative.
The reasons cited included:

- **Cumulative DSA MFI not expected to cause a positive result**
- **Possible historic positive, current negative crossmatch**
- **Patient has A1 and A24 DSA these antigens don't share any antibody-verified eplet with the sensitising event ab**
- **Wet crossmatch recommended**

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A crossmatch is performed. What level of immunological risk would you assign this transplant?

Serum Sample	03/2018	01/2018	08/2017	02/2017	10/2016
Donor directed antibody	A1, 24	A1, 24	A1, 24	A1, 24	A1, 24
Cumulative MFI of DSA	2867	2167	1967	4102	4133
LCS T cells (>46 = Pos)	40.1	38.1	35.6	68.1	88.2
LCS B cells (>63 = Pos)	58.5	59.7	55.5	71.1	82.1
FCXM result	T cell Neg B cell Neg	T cell Neg B cell Neg	T cell Neg B cell Neg	T cell Pos B cell Pos	T cell Pos B cell Pos
CDC XM result	Negative	Negative	Negative	Negative	Negative

LCS = Linear Channel Shift

Most respondents stated this would be a Intermediate risk transplant.

	UK&I (n=22)		RoW (n=30)		Total (n=52)	%
	Number	Percentage	Number	Percentage		
Standard	1	4%	0	0%	1	2%
Low	3	14%	4	13%	7	13%
Intermediate	18	82%	20	67%	38	73%
High	0	0%	5	17%	5	10%
Contraindication	0	0%	1	3%	1	2%
Other	0	0%	0	0%	0	0%

The reasons cited included:

- Following BTS/BSHI Guidelines
- Current negative, historic positive crossmatch, low level DSA

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A crossmatch is performed on a 2nd donor. What level of immunological risk would you assign this transplant?

ABO O **A1, A3; B7, B44; Cw7, -; DR4, -; DR53; DQ7, DQ9; DPB1*04:01, -**

Serum Sample	03/2018	01/2018	08/2017	02/2017	10/2016
Donor directed antibody	A1, B44	A1, B44	A1, B44	A1, B44	A1, B44
Cumulative MFI of DSA	2901	2579	3206	4655	5945
LCS T cells (>46 = Pos)	39.3	36.1	69.6	83.9	92.2
LCS B cells (>63 = Pos)	58.5	55.7	68.4	78.6	84.3
FCXM result	T cell Neg B cell Neg	T cell Neg B cell Neg	T cell Pos B cell Pos	T cell Pos B cell Pos	T cell Pos B cell Pos
CDC XM result	Negative	Negative	Negative	Negative	Negative

LCS = Linear Channel Shift

	UK&I (n=22)		RoW (n=30)		Total (n=52)	%
	Number	Percentage	Number	Percentage		
Standard	0	0%	1	3%	1	2%
Low	0	0%	2	7%	2	4%
Intermediate	18	82%	16	53%	34	65%
High	2	9%	8	27%	10	19%
Contraindication	0	0%	1	3%	1	2%
Other	2	9%	2	7%	4	8%

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What level of immunological risk would you assign this transplant?

Most respondents stated this would be a Intermediate risk transplant.

The reasons cited included:

- BSHI/BTS Guidelines categorise historic positive current negative T/B cell FCXM (CDCXM negative) due to current IgG class I DSA as intermediate risk.
- The risk of hyperacute rejection is low. However risk of accelerated antibody mediated rejection due to memory response is higher due to historically positive Flow crossmatch.
- DSA is due to a known sensitisation event, pregnancy.
- Transplant possible with augmented immunosuppression and post-transplant monitoring.
- Recent cumulative DSA is ~3,000MFI, historically ~6,000

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What clinical advise would you give?

Most common answers included:

- BSHI/BTS Guidelines state transplant is recommended given the anticipated loss of vascular access
- Clinical caution with proactive use of immunosuppression and post-transplant monitoring
- Discuss with MDT if sufficient time to enter another cycle of the sharing scheme

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Scenario 2 – HSCT Scenario

- 42 year old female with high-risk ALL
- Blood group: O Rh Positive
- CMV status: Negative
- HLA Type:

  A*02:01, A*24:02; B*07:02, B*51:01; C*02:02, C*07:02;
  DRB1*15:01, -; DQB1*06:02, -; DPB1*03:01, DPB1*04:01
- Patient only has half-siblings
- Unrelated donor search performed

37 responses received

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Comment on the likelihood of finding a donor

Summary of responses from UK and Ireland (UK&I)
Likely to find a 10/10 matched donor
There is a high likelihood of finding a matched unrelated donor - although maybe not an optimal donor for non-HLA reasons as the number found would be quite small. Would be a challenging search due to rare/intermediate B/C association and homozygous DRB1/DQB1.
HLA-B*51:01 is associated with several different HLA-C alleles (e.g. C*01:02, C*14:02, C*15:02 and C*16:02) and is less frequently associated with C*02:02, making it less likely a 10/10 match will be found, particularly if registry HLA-C data is not provided.
HLA-C typing can be missing from some donors, this makes it difficult to predict if these donors are potentially fully matched or mismatched at HLA-C.

Summary of responses from Rest of World (RoW)
The haplotype A*02:01 C*02:02 B*07:02 DRB1*15:01 DQB1*06:02 is not very frequent and it could represent a challenge in donor search.
The patient has a frequent HLA haplotype found in Caucasian populations with high probability to find an identical HLA 10/10 donor. The difficulty will be to find among the 30 donors 10/10 identified in the BMDW a rapidly available and CMV negative donor.
Identification of HLA matched unrelated donor could be challenging due to DRB1, -DQB1 homozygosity; HLA-B*51:01 that could be associated with different HLA-C alleles and therefore HLA-C allele MM could be expected.
The patient carries the variant HLA-B*51 that can be associated with several HLA-C alleles, but in this phenotypic context, the haplotype A24, B7, Cw7, DR15 and DQ6 is common.
Unusual HLA-B/C linkage disequilibrium (B*51:01/C*02:02): 8% (NMDP data for CAU ethnic code).

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An Unrelated Donor Search is Performed

10 available donors were identified

Respondents were asked to select 3 donors

							HLA genotype							
ID	M/F	Age	Blood group	CMV	Weight (kg)	Donor register	A*	B*	C*	DRB1*	DQB1*	DPB1*	Donor Choice	Reason
A	F	48	A Rh Pos	Unknown	Unknown	UK	02:01/01L 24:02/02L	51:01 07:02/61/ 161N	02:02 07:02	15:01	06:02/47/84/ 109/111/116/117 /127	-		
B	F	36	A Rh pos	Positive	65	UK	02, 24	51, 07	02, 07	15:01	06	-		
C	F	36	Unknown	Negative	98	UK	02, 24	51, 07		15:01	06:02	-		
D	M	24	Unknown	Unknown	58	UK	02;01 24:02	51:01 07:02	07:02 14:02	15:01	06:02	-		
E	M	28	O Rh neg	Negative	Unknown	UK	02, 24	51, 07	07, 15:44	15:01	06	04:01/ 126:01		
F	F	33	O Rh pos	Positive	Unknown	German	02:01 24:02	51:01 07:02	02:02 07:02	15:01	06:02	04:01 15:01	3rd (27%)	female., CMV positive, if transplant urgent give fully typed donors priority
G	M	31	O Rh pos	Negative	73	French	02:01 24:02	51:01 07:02	02:02 07:02	15:01	06:02	-	1st (89%)	10/10, CMV & ABO match, Young male, reliable registry
H	M	31	Unknown	Unknown	Unknown	German	02, 24	51, 07		15:01	06:02	-	3rd (22%)	Young male, likely HLA match
I	F	33	A Rh pos	Unknown	Unknown	US	02:01 24:02	51:01 07:02	02:02 07:02	15:01	06:02	02:01 03:01	1st (8%) 2nd (51%)	DPB permissive, 11/12 match, donor age, female to female, CMV unknown
J	M	55	Unknown	Negative	Unknown	German	2, 24	51, 7	2, 7	15:01	06:02	-	2nd (13.5%)	10/10 low resolution, CMV match, male, reliable registry

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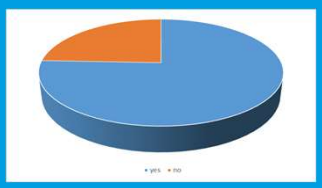
Does your laboratory test for HLA-DPB1 for HSCT patients and donors?



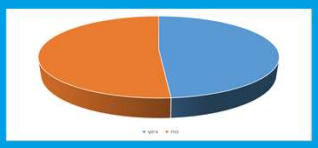
Most respondents stated they do perform DPB1 HLA typing.

Yes 76% (UK&I 67%), No 24% (UK&I 33%)

The reasons cited included:

- To get the best 12/12 match to see if permissive or non-permissive
- Routinely performed on all patients/donors but not used for donor selection/ranking unless a choice of well matched donors
- Aid to decide between well matched donors
- Published data on better outcomes for DPB permissive mismatch
- Only if DP antibodies are detected in the patient
- Not currently requested by clinicians

Does your Lab report permissive/non-permissive DPB1 mismatch information?



Yes 49% (UK&I 40%), No 51% (UK&I 60%)

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Using the additional information, rank donor K, L and M in order of preference and outline reasons

Donor Ref	Gender	Age	ABO matched/ mismatched	HLA-DPB1	Predicted Immunogenicity	Most common donor choice	Reason for selection
K	M	31	O Rh pos	09:01 13:01	Non-permissive HvG	2nd choice (51%)	Young male donor, ABO match preferred despite non-permissive mm
L	F	36	O Rh pos	05:01 13:01	Non-Permissive GvH	3rd choice (60%)	ABO match, older female (poss pregnancies), non-permissive GvH with possible GvL effect, increased risk of GvHD
M	F	33	A Rh pos	02:01 03:01	Permissive	1st choice (73%)	Young donor, 11/12, permissive, ABO mm

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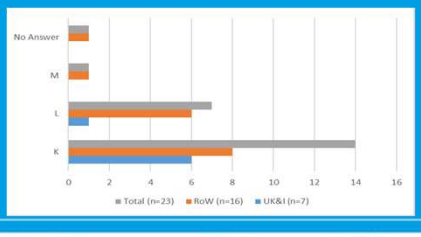
Does additional antibody screening data change your donor selection?

Antibody data provided (Potential DSAs):

HLA Allele	Specificity	MFI	HLA Allele	Specificity	MFI
DQB1*04:02	DQ4	24780	DRB1*12:02	DR12	14773
DQB1*04:01	DQ4	24455	DPB1*02:01	DP2	6428
DQB1*03:01	DQ7	22994	DPB1*18:01	DP18	4857
DQB1*03:01	DQ7	20935	DPB1*13:01	DP13	2532
DQB1*03:01	DQ7	20854	DPB1*06:01	DP6	2464
DQB1*04:02	DQ4	20158	DPB1*13:01	DP13	2385
DQB1*03:01	DQ7	18905	DPB1*14:01	DP14	2086
DQB1*04:01	DQ4	17499	DPB1*13:01	DP13	1986
DRB1*11:04	DR11	15762	DPB1*20:01	DP20	1796
DRB1*12:01	DR12	15458	DPB1*17:01	DP17	1432
DRB1*11:01	DR11	14865	DPB1*06:01	DP6	1305

Yes 62% (UK&I 47%), No 33% (UK&I 47%)
No response 5% (6%)

If yes, which donor would now be your first choice?



Most respondents stated they would now select donor K (61%) as first choice due to lower MFI of potential DSAs, ABO match and DP permissive.

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Scenario 3 – Neonatal Alloimmune Thrombocytopenia (NAIT)

- A suspected case of NAIT is referred for investigation.

- Maternal platelet count
- HPA type of mother, father and child
- Indirect MAIPA results

- 24 responses received (11 UK&I)

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Comment on the likelihood of NAIT, transfusion advice and potential risk to subsequent pregnancies

Question	Response	Total (n=24)
Likelihood of NAIT	*Highly Likely*	14 (56%)
	Likely	11 (44%)
Defined antibody	*HPA-1a antibody*	18 (90%)
	HPA-3a antibody	1 (5%)
	HPA-5b antibody	1 (5%)
Transfusion Advice	*HPA-1a negative platelets*	18 (75%)
	HPA-1a and 5a negative platelets	6 (25%)
Risk to Subsequent Pregnancies	*Yes*	22 (100%)
Patient Management in Subsequent Pregnancies	*Maternal IVIg*	17 (34%)
	Foetal HPA Typing	16 (32%)
	Ultrasound monitoring	5 (10%)
	Monitor Maternal HPA antibody levels	4 (8%)
	Caesarean	3 (6%)
	Transfuse HPA-1a negative platelets	3 (6%)
	Counselling	1 (2%)
	Transfuse HPA-1a 5b negative platelets	1 (2%)

Donor Cell Panel HPA –Type	1a, 1a 2b, 2b 3a, 3a 5b , 5b 15a, 15a	1b, 1b 2a, 2a 3b, 3b 5a, 5a$_1$ 15b, 15b	1a, 1a 2b, 2b 3a, 3a 5a, 5a 15b, 15b	1b, 1b 2a, 2a 3b, 3b 5b, 5b 15a, 15a	1a, 1b 2a, 2b 3a, 3b 5a, 5b 15a, 15b
GPIb/IIIa PAB 1	POS	N	POS	N	
GPIa/IIa	N	N			
GPIb/IX	N	N			
HLA W6/32 + P43					N

Mother - 1b:1b, 2a:2a, 3a:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

Father - 1a:1b, 2a:2b, 3a:3a, 4a:4a, 5b:5b, 6a:6a, 9a:9a, 15a:15b

Childs - 1a:1b, 2a:2a, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15a

- Most respondents agreed that NAIT was highly likely, due to a HPA-1a antibody.
- Advice would be to transfuse HPA-1a neg platelets. Subsequent pregnancies are at risk and treatment should be with IVIg.

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Comment on the likelihood of NAIT, transfusion advice and potential risk to subsequent pregnancies

A further case was referred to the lab

Question	Response	Total (n=24)
Consistent with NAIT	*Yes*	23 (96%)
	Unclear	1 (4%)
Reason	*HPA-3a antibody*	24 (60%)
	HPA-15b antibody	16 (40%)
Transfusion Advice	*HPA-3a negative platelets*	11 (46%)
	HPA-3a 15b negative platelets	6 (25%)
	HPA-1a and 5b negative platelets	3 (12.5%)
	Transfuse with maternal platelets	3 (12.5%)
	HPA-3b 15b platelets	1 (4%)
Risk to Subsequent Pregnancies	*Yes*	22 (92%)
	Undetermined	2 (8%)
Patient Management in Subsequent Pregnancies	*Maternal IVIg*	16 (47%)
	Close monitoring/desensitisation	6 (17%)
	Monitor Maternal HPA antibody levels	4 (12%)
	Foetal HPA Typing	4 (12%)
	Ultrasound monitoring	3 (9%)
	Caesarean	1 (3%)

Donor Cell Panel HPA –Type	1a, 1a 2b, 2b 3a, 3a 5b, 5b 15a, 15b	1a, 1a 2a, 2a 3b, 3b 5a, 5a 15a, 15b	1b, 1b 2b, 2b 3a, 3a 5a, 5a 15a, 15b	1b, 1b 2a, 2a 3b, 3b 5b, 5b 15a, 15a	1a, 1b 2a, 2b 3a, 3b 5a, 5b 15b, 15b
GPIIb/IIIa					
GPIa/IIa					
GPIb/IX					
HLA W6/32 + P43					
CD109					

Mother - 1a:1b, 2a:2a, 3b:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15a

Father - 1a:1a, 2a:2b, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15b

Child - 1a:1b, 2a:2a, 3a:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15a

- Most respondent agreed this case was NAIT, due to a HPA-3a antibody.
- Advice would be to transfuse HPA-3a neg platelets. Subsequent pregnancies are at risk and treatment should be with IVIg.

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Comment on the likelihood of NAIT, transfusion advice and potential risk to subsequent pregnancies

A further case was referred to the lab

Question	Response	Total (n=24)
Consistent with NAIT	*Yes*	11 (44%)
	Unclear	9 (36%)
	No	5 (20%)
Reason	*GPIIb/IIIa antibody*	19 (42%)
	Autoantibodies (ITP)	8 (18%)
	Possible Glanzmann's Thrombasthenia	7 (16%)
	HPA-5b antibody not detected	4 (9%)
	HPA-5b mismatch	4 (9%)
	HPA-5b antibody detected	2 (4%)
	HPA-3a antibody detected	1 (2%)
Transfusion Advice	*Transfuse random donor platelets*	10 (29%)
	Do not transfuse	5 (14.5%)
	IVIg	5 (14.5%)
	Maternal platelets	4 (12%)
	Crossmatch mother and father	3 (9%)
	HPA-1a and 5b negative platelets	3 (9%)
	Monitor neonatal platelet count	1 (3%)
	HLA matched platelets	1 (3%)
	HPA-3a negative platelets	1 (3%)
	Use medication to increase clotting	1 (3%)

Donor Cell Panel HPA –Type	1a, 1a 2b, 2b 3a, 3a 5b, 5b 15a, 15b	1a, 1a 2a, 2a 3b, 3b 5a, 5a 15a, 15b	1b, 1b 2b, 2b 3a, 3a 5a, 5a 15a, 15b	1b, 1b 2a, 2a 3b, 3b 5b, 5b 15a, 15b	1a, 1b 2a, 2b 3a, 3b 5a, 5b 15a, 15b
GPIIb/IIIa					
GPIIb/IIIa Alt.Mabs: PAB5					
GPIa/IIa					
GPIb/IX					
HLA W6/32 + P43					
CD109					

Mother - 1a:1b, 2a:2a, 3a:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

Father - 1a:1a, 2a:2b, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15b

Child - 1a:1b, 2a:2a, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15a

- Most respondents agreed this case was NAIT, due to a GPIIb/IIIa antibody.
- Advice would be to transfuse with random donor platelets.

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What tests would you recommend for this case and why?

A further case was referred to the lab

Question	Response	Total (n=24)
Further test	*CD109 MAIPA*	14 (22.5%)
	HPA typing	11 (18%)
	Crossmatch	7 (11%)
	Enquire whether mother used egg donor	5 (8%)
	Use extended panel MAIPA	4 (6%)
	Re-test after 4-6 weeks	4 (6%)
	Repeat MAIPA	4 (6%)
	Repeat MAIPA at double volume	3 (5%)
	Luminex screen for HLA antibodies	3 (5%)
	PIFT	3 (5%)
	Luminex screen for HPA antibodies	2 (3%)
	Investigate non-immune causes	2 (3%)
	Repeat MAIPA with dilute serum	1 (1.5%)
Reason	*HPA types do not suggest inheritance*	6 (40%)
	HPA-15 mismatch	6 (40%)
	HPA-15a alloantibody	3 (20%)
Immediate Transfusion Advice	*HPA-15a negative platelets*	7 (26%)
	Transfuse random donor platelets	4 (15%)
	HPA-5a 15b negative platelets	3 (11%)
	HPA-1a 5b negative platelets	3 (11%)
	Washed maternal platelets	2 (7.5%)
	IVIg	2 (7.5%)
	HLA matched platelets	2 (7.5%)
	HPA-5b negative platelets	1 (3.6%)
	Crossmatch mother and father	1 (3.6%)
	HPA-5b 15a negative platelets	1 (3.6%)
	Maternal HPA matched platelets	1 (3.6%)

Donor Cell Panel HPA –Type	1a, 1a 2b, 2b 3a, 3a 5b, 5b 15a, 15b	1a, 1a 2a, 2a 3b, 3b 5a, 5a 15a, 15b	1b, 1b 2b, 2b 3a, 3a 5a, 5a 15a, 15b	1b, 1b 2a, 2a 3b, 3b 5b, 5b 15a, 15b	1a, 1b 2a, 2b 3a, 3b 5a, 5b 15a, 15b
GPIIb/IIIa					
GPIIb/IIIa Alt.Mabs: PAB5					
GPIa/IIa					
GPIb/IX					
HLA W6/32 + P43					
CD109					

Mother - 1a:1b, 2a:2a, 3a:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15b:15b

Child - 1a:1b, 2a:2a, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15a

- Most respondents would perform a CD109 MAIPA due to a HPA-15 mm.
- Advice would be to transfuse with HPA-15a negative platelets.

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What tests would you recommend for this case and why? What transfusion advice would you provide?

A further case was referred to the lab maternal platelet count is 202 x 109/L, neonatal platelet count is 16 x 109/L, 38 weeks' gestation. MAIPA is negative.

Question	Response	Total (n=24)
Further test	*Crossmatch (PIFT or MAIPA)*	14 (22%)
	Repeat MAIPA with extended panel	11 (17%)
	Repeat MAIPA (double volume sera)	8 (12%)
	Luminex HPA antibody screen	7 (11%)
	Repeat test after 4-6 weeks	6 (9%)
	HLA antibody screen	5 (8%)
	HLA-DRB3 type mother	4 (6%)
	Indirect PIFT	3 (4.5%)
	HLA Typing	2 (3%)
	Type for other platelet antigens	2 (3%)
	Retest with dilute serum	1 (1.5%)
	Refer to reference lab	1 (1.5%)
	CD109 MAIPA	1 (1.5%)
Reason	*Rare low titre antibody*	4 (24%)
	Determine likelihood of HPA-1a alloimmunisation by DRB3 association	2 (12%)
	MAIPA not sensitive enough	2 (12%)
	Expression levels vary on platelets	1 (5.7%)
	Non-immune condition causing low platelet count	1 (5.7%)
	IgM blocking antibody present	1 (5.7%)
	Competition for binding site if antibody concentration high	1 (5.7%)
	Potential HPA-1a incompatibility	1 (5.7%)
	HLA antibodies causing thrombocytopenia	1 (5.7%)
	Other platelet antigens can cause NAIT	1 (5.7%)
	Antibodies not always detected on delivery	1 (5.7%)
	Patient antibodies absorbed on platelets	1 (5.7%)
Immediate Transfusion Advice	*HPA-1a 5b negative platelets*	15 (52%)
	Random donor platelets	6 (21%)
	HLA matched platelets	2 (6.75%
	HPA-1a negative platelets	2 (6.75%)
	IVIg	2 (6.75%)
	Washed maternal platelets	2 (6.75%)

Mother - 1b:1b, 2a:2a, 3a:3b, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

Father - 1a:1a, 2a:2b, 3a:3a, 4a:4a, 5b:5b, 6a:6a, 9a:9a, 15a:15b

Child - 1a:1b, 2a:2a, 3a:3a, 4a:4a, 5a:5b, 6a:6a, 9a:9a, 15a:15a

- Most respondents would perform a PIFT or MAIPA crossmatch due to a potential rare low titre antibody.
- Advice would be to transfuse with HPA-1a5b negative platelets.

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What tests would you recommend for this case and why?

A further case from a South East Asian family was referred to the lab. The MAIPA result is negative but the PIFT is positive with the mother's serum.

Question	Response	Total (n=24)
Further test	*Crossmatch*	10 (21%)
	GPIV/CD36 Typing/MAIPA	8 (17%)
	HLA antibody screening	6 (12%)
	Luminex HPA Antibody Screen	5 (10%)
	HLA Type	4 (8%)
	PIFT	3 (6%)
	HPA Type	3 (6%)
	NGS Sequencing	3 (6%)
	Investigate maternal auto-antibodies	3 (6%)
	Test for platelet disorder e.g. Glanzmann's	1 (2%)
	MAIPA with reduced serum volume	1 (2%)
	Platelet counts	1 (2%)
	Non-immune investigations	1 (2%)
Reason	*CD36 clinically relevant in Asian populations*	8 (35%)
	HLA Class I antibodies causing positive PIFT	4 (18%)
	Low frequency antibodies/antigens	4 (18%)
	Maternal auto-antibody	3 (13%)
	Anti-CD36 implicated in NAIT	1 (4%)
	Alloimmunisation to atypical HPA	1 (4%)
	Alloimmunisation to blood group antigens	1 (4%)
	Possible platelet disorder	1 (4%)

Mother - 1a:1a, 2a:2a, 3a:3a, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

Father - 1a:1a, 2a:2a, 3a:3a, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

Child - 1a:1a, 2a:2a, 3a:3a, 4a:4a, 5a:5a, 6a:6a, 9a:9a, 15a:15b

- Most respondents would perform a crossmatch as CD36 is clinically relevant in Asian populations.

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iED Discussion

- Questions / comments ?
  - Ideas for cases
  - Result feedback
  - Format of cases
  - Complexity level
  - Educational benefit
  - Number of questions

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Educational Scheme: Interesting Result

Sample ED03/18 probable HLA type

HLA-A*02:01, A*29:02; B*44:03, **B*44:221**; C*05:01, C*16:01; DRB1*11:04, DRB1*15:01; DRB3*02; DRB5*01; DQB1*03:01, DQB1*06:02; DPB1*02:01, DPB1*04:01

Allele 1		Allele 2	
Report	Number of Participants (n= 39)	Report	Number of Participants (n= 39)
B*44 homozygous	8 (21%)	B*44 homozygous	8 (21%)
B*44:02	6 (15%)	B*44:221	10 (26%)
B*44:03	10 (26%)	B*44:258	6 (15%)
B*44:02/03/...	11 (28%)	B*44:221/258	11 (28%)
B*44:02/221	2 (5%)	B*44:03/258	2 (5%)
B*44:104	1 (2.5%)	B*44:224	1 (2.5%)
B*35:01	1 (2.5%)	B*38:01	1 (2.5%)

- 10/39 (4/19 UK&I) labs correctly reported B*44:03, B*44:221
- 11/39 (6/19 UK&I) labs reported the correct type as part of a string e.g. B*44:02/03, B*44:221/258
- 6/39 (4/19 UK&I) labs reported B*44:02, B*44:258
- 2/39 (2/19 UK&I) labs reported B*44:02/221, B*44:03/258

Discrepancies in type caused by a cis/trans ambiguity

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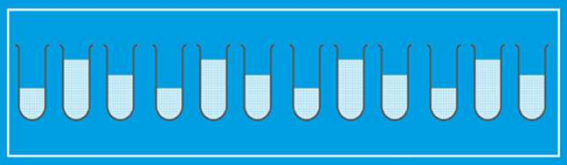
Thank you

Director: **Dr Tracey Rees**
Manager: **Deborah Pritchard**
Operations Manager: **Amy De'Ath**
Deputy Manager: **Melanie Bartley**
Healthcare Scientist Practitioner: **Geraint Clarke**
QA Officers: **Luke Gardner** & **Lucy Palmer**



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