UK NEQAS
International Quality Expertise

Histocompatibility and Immunogenetics

50 Years as World Leaders in EQA 1969–2019

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@UK_NEQAS

Annual Participant's Meeting 2019

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Director: Dr Tracey Rees

Deputy Director: Deborah Pritchard

Operations Manager: Amy De'Ath

Deputy Scheme Manager: Melanie Bartley

Healthcare Scientist Practitioner: Geraint Clarke

UK NEQAS Officer: Luke Gardner

Welsh Blood Service

GIG CYMRU NHS WALES
Ymddiriedolaeth GIG Prifysgol Felindre
Velindre University NHS Trust

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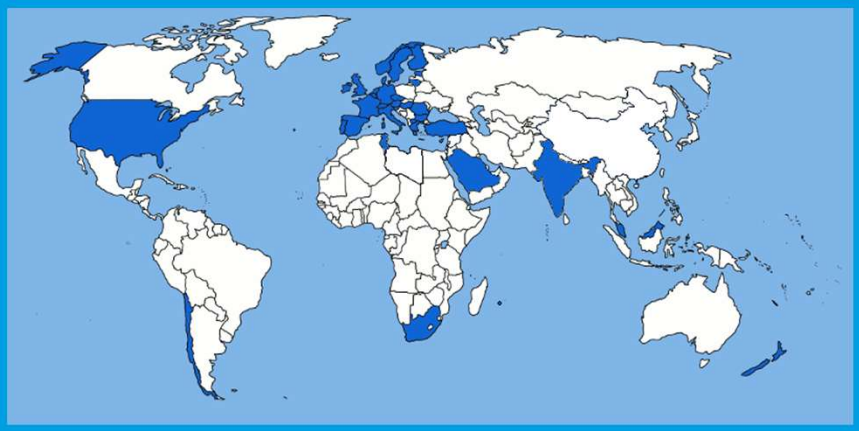
UK NEQAS for H&I: An Overview

- Over 350 participants
- Distribute to over 52 countries worldwide



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Welcome and Introduction

Judith Worthington

Chair of UK NEQAS for H&I Steering Committee

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2019 Steering Committee

- Judith Worthington (Chair)
- Arthi Anand
- Katy Derbyshire
- Patrick Flynn – retired 2020
- James Kelleher
- Sylvia McConnell
- Anthony Poles
- Rommel Ravanan (Clinical Representative)
- Ruhena Sergeant – retired 2019
- Elizabeth Wroe (BSHI Representative to UK NQAAP)

- Kathryn Robson (Expert Advisor Scheme 5B)
- Marian Hill (Expert Advisor Scheme 5B)
- Tim Clench (Expert Advisor Scheme 5B)

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Notes

- Presentation focus on performance, interesting trends, discussion points, changes for 2020
- Further detail on Schemes in handouts/available on NEQAS website
- 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 schemes
  - e.g.. Scheme 8: HLA Genotyping for Coeliac and Other HLA Associated Diseases and Scheme 4A1: HLA Typing at 1st Field Resolution - DPB1 assessment using a reference result
- Equivocal result only accepted for Scheme 2B
- All Not Tested (NT) results excluded from assessment
- Labs that fail to return results or do not a 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 2020-21

- Steering Committee
  - Patrick Flynn and Ruhena Sergeant retired and replaced by Sylvia McConnell and Katy Derbyshire
- Staffing
  - NEQAS Operations Manager secondment
  - Deputy Director position created
- The 'Participant's Portal' continues to be developed and improved
- Schemes
  - Scheme 4A1: users encouraged to report at intermediate resolution for DQA1
  - Schemes 5A, 7 and 8: distributed 3 times a year rather than 2
  - Scheme 8: Psoriasis and extracted DNA option
  - Scheme 4A2: reporting time has been extended to 4 weeks

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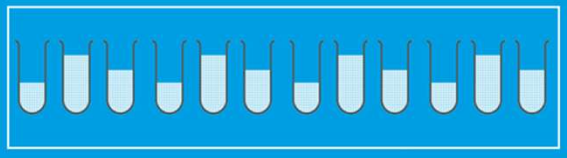
Scheme 2A

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

- 5 Unsatisfactory Performers (1 UK & Ireland)

All cells with and without DTT	2015 +DTT	2016 +DTT	2017	2018	2019
Number of Participants (UK&I)	64 (18)	64 (18)	75 (19)	71 (18)	71 (22)
Number with Unsatisfactory Performance (< 85%) (UK&I)	9 (0)	13 (6)	16 (6)	16 (7)	5 (1)
% Unsatisfactory Performance (UK&I)	14.0% (0%)	20.3% (33.3%)	21.3% (31.6%)	22.5% (38.8%)	7.0% (4.5%)

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UK&I 2019 Performance

	PBL	PBL +DTT	T Cell	T Cell +DTT	B Cell	B Cell +DTT
Crossmatches assessed (n=40)	36	38	39	40	33	32
% NT	12.9%	17.7%	6.7%	9.1%	14.5%	15.9%
NT	101	114	137	189	295	328
% incorrect assignments	2.9%	3.2%	1.4%	2.2%	3.8%	2.9%
False Positive	15	14	16	20	53	34
False Negative	8	7	14	25	24	26

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Unacceptable Performers 2019

	PBL -DTT	T -DTT	B -DTT	PBL + DTT	T + DTT	B + DTT	Lab Identified Error
23			83%				Waiting for a response
116			83%				Cell viability & delivery delay
189	67%			71%			Waiting for a response
204		72%	70%		72%	77%	Technical issues
351		0%	0%		0%	0%	No results returned
401		0%	0%				No results returned

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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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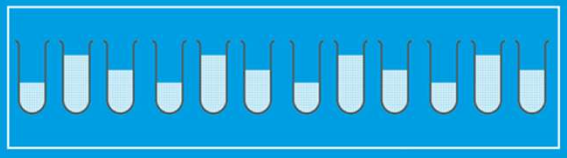
Scheme 2B

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 2019 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

- 12 Unsatisfactory Performers (1 UK & Ireland)

Scheme 2B	2015	2016	2017	2018	2019
Number of Participants (UK&I)	73 (23)	76 (23)	85 (22)	83 (22)	84 (23)
Number with Unsatisfactory Performance (< 85%) (UK&I)	13 (3)	13 (1)	8 (1)	15 (2)	12 (1)
% Unsatisfactory Performance	17.8% (13.0%)	17.1% (4.3%)	8.7% (4.5%)	18.1% (9.1%)	14.2% (4.3%)

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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	35	27	20	31	26
Number of XM assessed (>75% consensus)	33/40	36/40	33/40	32/40	31/40	32/40
Number of Positive XM	15	13	12	21	19	20
Number of Negative XM	18	22	17	11	12	10
Number of incorrect assignments	25 (3.9%)	48 (3.9%)	39 (4.6%)	26 (4.1%)	50 (5.3%)	46 (5.8%)
Number of False Pos	13	31	23	19	18	19
Number of False Neg	12	17	16	7	32	39
Number of equivocal assignments	1 (0.1%)	6 (0.5%)	8 (0.9%)	2 (0.3%)	6 (0.6%)	7 (0.9%)
Number of NT assignments	29 (4.5%)	124 (10.0%)	67 (7.9%)	30 (4.7%)	70 (7.4%)	78 (9.8%)

UK&I and RoW receive different blood samples

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Unacceptable Performers 2019

- 12 labs with UP (<85%)

Lab	T Cell	No. of results submitted	B Cell	No. of results submitted	Error
28	89%	35/40	83%	38/40	
139	92%	40/40	74%	40/40	
191	94%	40/40	81%	40/40	Cell count low
218	82%	19/40	31%	19/40	Technical issues
238	91%	40/40	80%	40/40	Technical issues
252	79%	38/40	83%	38/40	Cell viability low
260	72%	24/40	83%	24/40	Cell viability low
262	88%	39/40	84%	39/40	Technical issue
297	88%	39/40	81%	40/40	Sample mix up
351	48%	16/40	46%	16/40	Cell count low
374	73%	40/40	66%	40/40	Cell count low
401	43%	8/32	25%	8/32	Technical issues

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Reporting of Equivocal Results

- 2019 Summary
  - 29 T cell equivocal results (from 2784 = 1.0%)
  - 31 B cell equivocal results (from 2361 = 1.3%)
  - 17 T cell equivocal results assessed as unacceptable (0.6%)
  - 17 B cell equivocal results assessed as unacceptable (0.7%)

2019	T cell Equivocal Results	Total Results	B cell Equivocal Results	Total Results	Equivocal Assessed as Unacceptable Result	
					T cell	B cell
1+2	4	538	7	378	2	2
3+4	12	571	10	545	7	6
5+6	8	530	5	436	5	3
7+8	3	542	4	530	2	2
9+10	2	603	5	472	1	4
Totals	**29**	**2784**	**31**	**2361**	**17**	**17**

2019	No of Labs Reporting Equivocal	No. of Labs Reporting >1 Equivocal Result
UK (n=22)	2 (9.1%)	1 (4.5%)
OS (n= 62)	18 (29%)	4 (6.4%)
Total (n=84)	**20 (23.8%)**	**5 (5.9%)**

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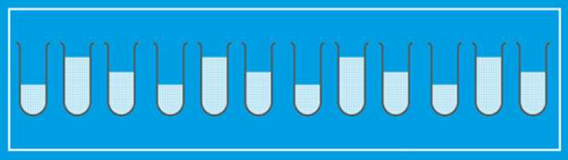
Scheme 6

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

- 8 Unsatisfactory Performers (0 UK & Ireland)

	2015	2016	2017	2018	2019
Number of Participants (UK&I)	97 (24)	98 (24)	101 (24)	88 (25)	82 (25)
Number with Unsatisfactory Performance (< 80%) (UK&I)	6 (3)	18 (4)	21 (0)	5 (0)	8 (0)
% Unsatisfactory Performance	6.2% (12.5%)	18.4% (16.7 %)	20.8% (0%)	5.7% (0%)	9.7% (0)

The 8 labs with unacceptable performance:

- 2 used Immucor kits and 3 used Labscreen
- 3 gave no information as to kit usage

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Not Assessed Samples

59/1587 (3.7%) results out of consensus (11 UK&I)

2019 Sample	Class I All Labs (n=88)	Class I UK&I (n=25)	Class II All Labs (n=84)	Class II UK&I (n=25)
601	98.6%	100%	77.9%	92%
602	100%	100%	98.5%	100%
603	93%	100%	97.1%	100%
604*	100%	100%	70.6%	88%
605*	98.6%	100%	66.2%	56%
606	100%	100%	100%	100%
607	100%	100%	100%	100%
608*	97.5%	96%	96.1%	100%
609	93.8%	100%	85.5%	92%
610	100%	100%	100%	100%
611	98.8%	100%	100%	100%
612*	85%	76%	100%	100%

Green denotes agreement on negative result

* Denotes samples were sourced from non-transfused male donors

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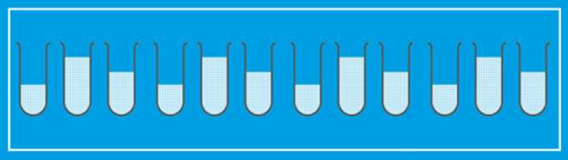
Scheme 3

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

- CI 5 Unsatisfactory Performers (0 UK&I), CII 7 UP (0 UK&I)

Class I		2015	2016	2017	2018	2019
Number of Participants (UK&I)		81 (24)	85 (24)	72 (24)	73 (25)	70 (25)
Number with Unsatisfactory Performance (UK&I)	**Presence**	9 (1)	8 (0)	10 (0)	15 (1)	3 (0)
	Absence	2 (0)	3 (0)	3 (0)	5 (0)	2 (0)
% Unsatisfactory Performance	**Presence**	11.1%	9.4%	13.8%	20.5%	4.2%
	Absence	2.5%	3.5%	4.2%	6.8%	2.6%

Class II		2015	2016	2017	2018	2019
Number of Participants (UK&I)		81 (24)	85 (24)	72 (24)	75 (25)	69 (25)
Number with Unsatisfactory Performance (UK&I)	**Presence**	4 (0)	5 (0)	5 (0)	12 (0)	5 (0)
	Absence	3 (0)	4 (0)	2 (0)	3 (0)	2 (0)
% Unsatisfactory Performance	**Presence**	4.9%	5.9%	6.9%	16.0%	7.2%
	Absence	3.7%	4.7%	2.8%	4.0 %	2.8%

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Unacceptable Performers 2019

- 6 labs (0 UK&I) with UP (<75%)

	Class I		Class II		Kit
Lab	Presence	Absence	Presence	Absence	
216	46%	95%	56%	92%	Lifecodes
218	98%	62%	80%	100%	No info
252	35%	96%	58%	88%	No Info
293	88%	99%	95%	55%	No info
302	86%	35%	68%	95%	Lifecodes
351	73%	47%	77%	32%	No info

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Class I Assessment

	Number of HLA Class I Specificities (n=69)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	3	2	13	8	15	9	43	5	24	28	150
Absent (<5%)	17	18	40	19	31	9	26	17	19	38	234
Absent 0%	66	55	27	60	19	61	8	51	5	4	356
Not Assessed (5-74%)	3	14	9	2	23	9	12	16	41	20	149

533 specificities reported over 10 samples
- 28.1% reached consensus presence
- 43.9% reached consensus absence
- 27.9% specificities were not assessed

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Class II Assessment

DPB included in assessment in 2019

	Number of HLA Class II Specificities (DR, DQ, DP) (n=68)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	14	2	7	0	0	16	7	16	31	15	108
Absent (<5%)	6	18	10	17	17	2	9	8	1	5	93
Absent 0%	20	55	28	27	25	26	26	11	1	19	238
Not Assessed (5-74%)	6	14	1	2	4	2	4	11	12	7	63

264 specificities reported over 10 samples
- 40.9% reached consensus presence
- 35.2% reached consensus absence
- 23.9% specificities were not assessed

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DPB only

	Number of HLA DPB Specificities (n=68)										
	301	302	303	304	305	306	307	308	309	310	Total
Present (≥75%)	10	0	0	0	0	0	0	11	10	0	31
Absent (<5%)	4	1	2	6	6	0	1	0	0	1	21
Absent 0%	2	17	17	12	10	19	18	2	1	15	113
Not Assessed (5-74%)	3	1	0	1	3	0	0	6	8	3	25

3 samples had DPB1 specificities that reached consensus

77 specificities reported over 10 samples
- 40.2% reached consensus presence
- 27.3% reached consensus absence
- 32.5% specificities were not assessed

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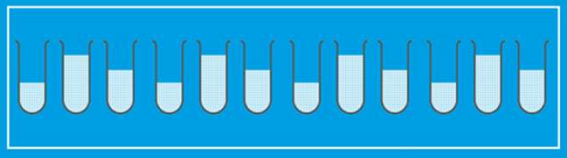
Participant Satisfaction Survey 2019

Results and Analysis



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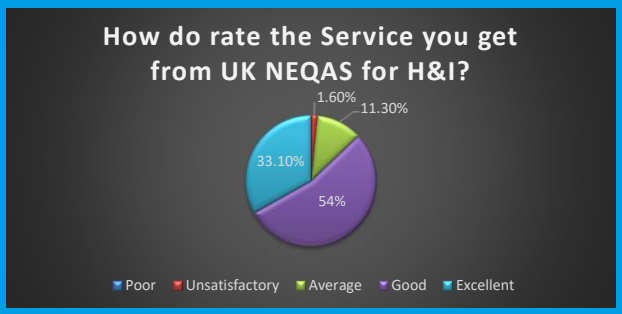
Participant Satisfaction Survey 2019

- 35.4% (125/353) participants completed the survey
- Addressed all aspects of the service and the schemes provided across 55 questions



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Participant Satisfaction Survey 2019

- The good points
  - **Communication** **"Answer all our questions and solve our problems"**
    - 85.3% users have accessed our website and 75.7% rated it good/excellent
  - **Customer Service** **"Staff are helpful and responsive"**
    - 81.8% of users have interacted with NEQAS office and 84.9% rated the customer service as good/excellent
  - **Unacceptable Performance** **"The process mirrors our own internal investigation procedure, no additional work is required"**
    - 79.5% of user rated the process as good/excellent
  - **Sample Quality** **"Samples received on time and properly packaged"**
    - The quality of blood, sera and DNA samples provided was rated 4.5 stars out of 5 stars
  - **Scheme Design**
    - The design and sample selection of all scheme was rated 4.5/5 stars
    - The reporting times for all schemes classed as just right
  - **Data Analysis and Reports**
    - Reports rated 4.5/5 stars
    - 87.4% rated the end of year reports good/excellent

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Participant Satisfaction Survey 2019

- Areas for improvement

Participant's Portal	1 (Poor)	2	3 (Average)	4	5 (Excellent)	n
How do rate the Portal overall?	1.8%	4.5%	22.5%	**55.0%**	16.2%	111
How do you rate the ease of use?	4.5%	5.4%	35.1%	**40.5%**	14.4%	111
How do you rate the functionality?	3.6%	7.2%	28.8%	**45.0%**	15.3%	111
How do you rate the registration process?	2.0%	9.8%	27.5%	**39.2%**	21.6%	102
How do you rate result entry?	3.7%	12.1%	24.3%	**43.9%**	15.9%	107
How do you rate accessing reports?	6.5%	10.2%	27.8%	**34.3%**	21.3%	108
How do you rate the process for scheme registration?	1.0%	5.2%	24.0%	**49.0%**	20.8%	96

  - **Participant's Portal**
    - **Ease of use of the system**
    - **Accessing reports**
    - **Accessing result summary tables**
    - **Data entry of results – 2B, 3, 4A1i and 4A2**
    - **System generated notices**

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Participant Satisfaction Survey 2019

- Areas for improvement
  - **Engagement with the Participant Manual**
    - only 68.1% have read it
  - **Value for money**
    - 53.3% rated us good/excellent value for money
  - **Engagement with Steering Committee**
    - only 35.5% aware of SC and just 6% have engaged with a suggestion (83.4% rated the response good/excellent)
  - **Sample quality of isolated cells**
    - rated 3 out of 5 stars, too few cells, poor viability
  - **Report format**
    - difficult to interpret
  - **Sample delivery**
    - expensive and can take too long
  - **Uptake of Educational Schemes**
    - less than a third of user said these schemes were worthwhile

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Participant Satisfaction Survey 2019

- **Action Plan** created to address improvements
  - Make the Participant's Manual more interactive
  - Continue to improve and develop the Portal
  - Address the quality of the samples provided to users
  - Improve information and analysis provided to participants

- Feedback to Participants
  - Individual responses provided when requested
  - Q&A session to main issues in Newsletter
  - AGM discussion
  - BSHI/EFI 2020 exhibitors

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Participant's Portal

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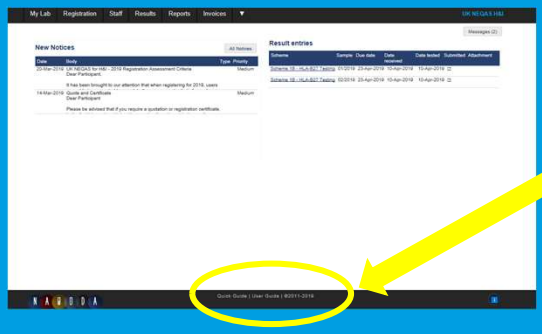
Participant's Portal

- **Participant's Portal**
  - Ease of use of the system
  - Accessing reports
  - Accessing result summary tables
  - Data entry of results – 2B, 3, 4A1i and 4A2
  - System generated notices



- *The System User Guide and the 'Quick Guide' are available in the footer section*

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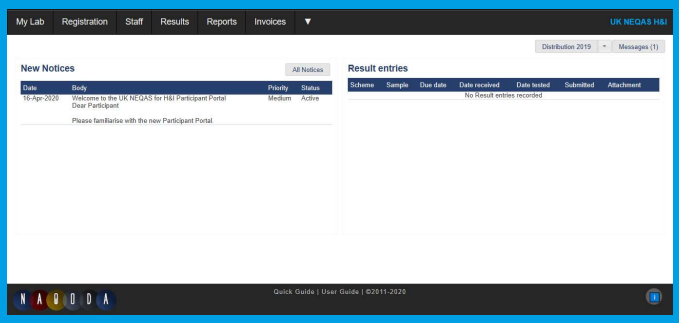
Participant's Portal



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

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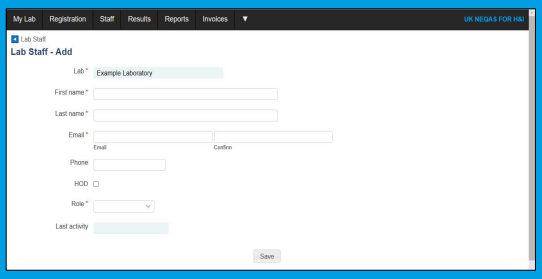
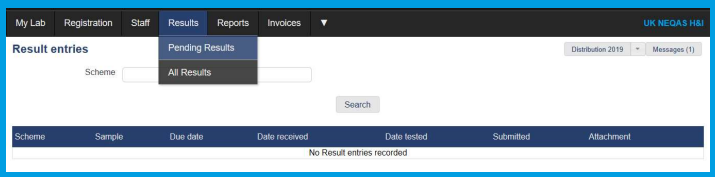
Participant's Portal: Users

- 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
- 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	×

Participant's Portal: Result Entry

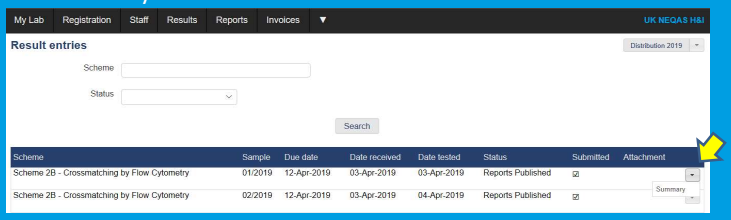


- Only Primary Users or Scheme Users linked to relevant scheme can enter results
- To enter results, select Results > Pending Results, samples that have results due/open for entry will be listed here
- If relevant, the system will show you what assessment criteria you have chosen - this can be edited 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

Participant's Portal: Result Entry

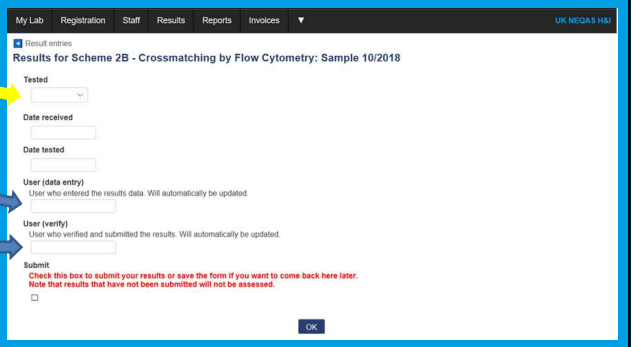
- **Method Pages**
  - Complete your laboratory testing methods by completing the methodology questions. This only needs to be completed once, you can then skip to results entry on subsequent samples.

- **View/Save/Print Entered Results**
  - Select Results from the main menu and Pending Results or All Results.
  - Click on the drop down arrow on the right of the 'result entries' table and select "Summary"



Participant's Portal: Result Submission

- Enter here if results were not tested and include a reason



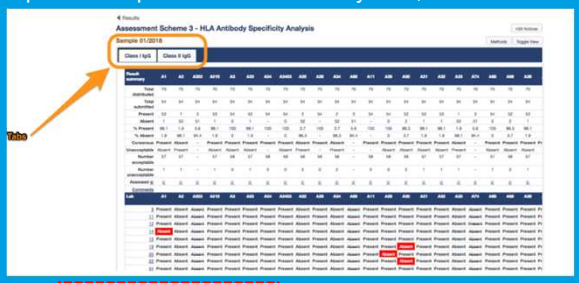
- The User that completes the initial data entry will be named here:
- The User that ticks the "Submit" box will be named here:
- If the initial User ticks the "Submit" box, they will be named in both fields

- 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 distribution



The summary tables will highlight your lab

- Performance tables can be downloaded as .xlsx files
- PLEASE NOTE: lab numbers in the Performance tables/downloaded spreadsheets are random for anonymity and therefore do not correlate to your UK NEQAS reference number

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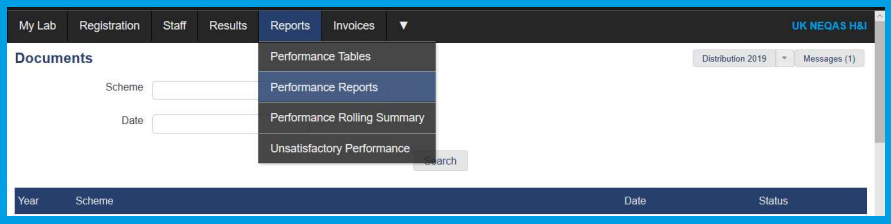
Participant's Portal: View Reports

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.



To view and print/save a copy, click the relevant row and on the next screen click on the document hyperlink (e.g.. SAMPLE_REPORT_X_XXXX-XX-XX_XX_XXXX.pdf)

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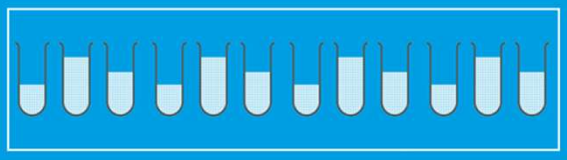
UK NEQAS
International Quality Expertise

Histocompatibility and Immunogenetics

Participant's Portal

Please come and see us during breaks for specific questions



Annual Participant's Meeting 2019

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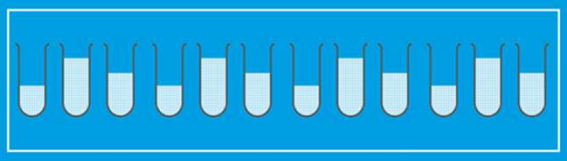
UK NEQAS
International Quality Expertise

Histocompatibility and Immunogenetics

Interpretive Educational Schemes



Deborah Pritchard

Annual Participant's Meeting 2019

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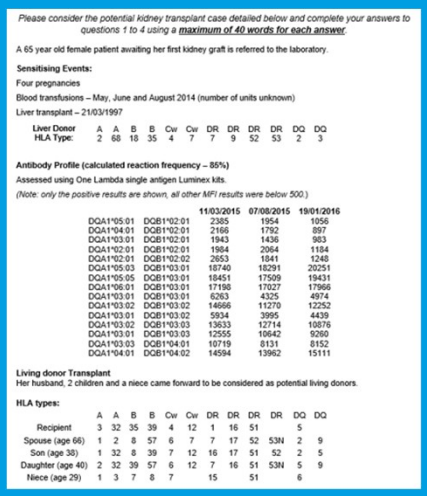
Interpretive Educational Scheme

- 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
2019	Kidney after heart transplant	Haploidentical donor selection with ab	Platelet refractory

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Scenario 1- Kidney After Heart Transplant

53 returns (23 UK&I)

- Information provided
  - A sensitised patient currently on dialysis
  - Patient HLA type and ABO (O)
  - Patient has had multiple blood transfusions
  - HLA antibody profile
  - Previous heart transplant and donor HLA type
  - Previous live kidney transplant and donor HLA type

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The patient transfer to your centre. What testing do you perform prior to activation?

Response	Number of Labs (n=53)
Perform additional/repeat antibody testing	46
Confirm patient HLA type/perform additional typing/higher resolution	38
HLA type previous donors/additional loci/higher resolution	20
Request antibody test results / sera from other centre	17
Perform autologous crossmatch	7
Confirm ABO	6

Other selected comments
• Accept previous typing and antibody results if EFI accredited lab
• Request previous sera from other centre and retest Luminex single antigen as MFI values/cut offs vary between centres.
• 2x HLA antibody screening; given the unusual antibody profile which includes allelic and auto antibodies
• Full HLA type of patient's wife (confirm unusual associations of DR4 with DQ9 & B7 & B8 with Cw2 & Cw3)

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What Antibodies Would you Select as Unacceptable?

HLA Spec	Number of labs agreeing to list Spec			Reason(s) for listing as unacceptable antigen
	Total (n=53)	UK&I (n=23)	RoW (n=30)	
None	5	4	1	No unacceptable antigens
DR9 / DRB1*09:01	37	16	21	MFI >1000/>1500/>2000/>2500/>3000/>4000/ Previous Mismatch
DR7 / DRB1*07:01	37	18	19	MFI >1500/>2000/>3000 Previous Mismatch
DR15 / DRB1*15:01	31	9	22	MFI >1000/>2000 Previous mismatch
DR17 / DRB1*03:01	29	11	18	MFI >1000/>2000 Previous Mismatch
DP23 / DPB1*23:01	27	15	12	MFI >1000/>1500/>2000
DP14 / DPB1*14:01	26	13	13	MFI >1000/>1500/>2000
DR10 / DRB1*10:01	26	11	15	MFI >1000/>1500/>2000 Previous Mismatch
DR8 / DRB1*08:01	22	8	14	MFI >1500/>2000
DP4 / DPB1*04:01	21	10	11	MFI >1000/>1500/>2000
DR13 / DRB1*13:01	21	7	14	MFI >1000/>1500/>2000
DR51 / DRB5	20	7	13	MFI >2000 Previous mismatch
DR12 / DRB1*12:01	19	6	13	MFI >1000/>1500/>2000 Previous Mismatch
DR103 / DRB1*01:03	18	11	7	MFI >1000/>2000 Previous mismatch
DR14 / DRB1*14:01	17	4	13	MFI >1000/>1500/>2000
DR1 / DRB1*01:01	17	3	14	MFI>2000
DR16 / DRB1*16:01	16	2	14	MFI >1500/>2000
DR52 / DRB3	14	5	9	MFI >1500/>2000
B8	11	6	5	MFI>2000 Previous mismatch
A30	9	6	3	MFI>2000 Previous mismatch
DQ9	7	4	3	Previous mismatch
DQ2	7	4	3	Previous mismatch
DQ6	6	3	3	Previous mismatch
Cw3	6	4	2	MFI>2000 Previous mismatch
A1	6	3	3	Previous mismatch
A11	3	0	3	MFI > 1000
DR4	3	0	3	MFI >2000
DR3	2	1	1	Previous mismatch
DR18	2	0	2	Associated with DRB3*01:01 MFI >2000 Previous mismatch
DQ1	1	1	0	Previous mismatch
DR2	1	1	0	Previous mismatch
DRB4	1	0	1	MFI
All MFIs >1000	1	0	1	
All with consistently raised MFIs	1	0	1	

The antibodies presented included mismatches to previous transplants, reactions against self and antibodies to DRB3/4/5

The nomenclature used selecting unacceptables differed
- some listing DR17 whilst others used DRB1*03:01

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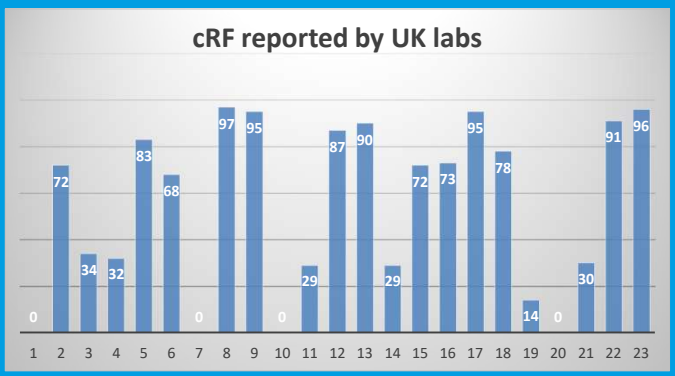
What Antibodies Would you Select as Unacceptable?

There was a huge difference in antibodies selected:

- 5 centres would list no unacceptable antigens
- The other centres would list between 2-24 (mean 9.7)
  - resulting in a range of cRF between 0-97%!



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Comments regarding unacceptable antigen selection

- Investigate alternative living donors and Kidney Sharing Scheme
- Investigate reactivity: DSA pre-adsorption, EDTA, denatured antigen reactivity, use an alternate antibody detection kit
- Increase MFI threshold for listing or consider delisting previous mismatched antigens
- Supplementary typing of previous donors
- Perform third party crossmatches
- Enhance patient's immunosuppression
- Perform autologous XM

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Would this transplant proceed based on a virtual XM?

Patient's HLA Type:
HLA-A*03:01, A*31:01; B*07:02, B*27:03; C*02:02, C*07:02; DRB1*04:01, -; DRB4*01:01, -; DQB1*03:01, DQB1*03:02; DPB1*04:02 , -

Potential Donor Type:
A3, -; B27, -; Cw2, Cw7; DR4, -; DQ7, -; DPB1*04:01, -

Decision	Total (n=53)	UK&I (n=23)	RoW (n=30)
Yes	8 (15.1%)	2 (8.7%)	6 (20.0%)
No	45 (84.9%)	21 (91.3%)	24 (80.0%)

If not vXM, what prospective testing do you perform?

Pre-Transplant Testing Performed	Total (n=53)	UK&I	RoW
CDC XM & FCXM	26 (49.1%)	11	15
CDC XM only	12 (22.6%)	0	12
FCXM Only	12 (22.6%)	11	1
Luminex AB Screen	21 (39.6%)	9	12
HLA Type	24 (45.3%)	7	17
Other – C1q, ABO, Serologic HLA Typing	8 (15.1%)	3	5

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What criteria do you use to assess whether a transplant can proceed with a vXM?

	Examples of vXM Policies
UK&I	Negative (<1000) SAB in last 12 months with no sensitising events, current sample tested within 90 days, minimum 6 months screening on 2 samples.
	Pre-tx antibody screen performed on day of transplant. No XM performed unless indicated by pre-tx screening results.
	Latest serum sample within 14 weeks, fully Luminex tested and no subsequent sensitising events. No Luminex DSA, DP or DQA antibodies with MFI >1000.
	Criteria for VxM: 1-non-sensitised patients, 2- sensitised patients with stable Ab profile and no DSA. Consider previous transplants, transfusions and other sensitising events. Previous transplant mismatches are not a contraindication to virtual crossmatch, we would ensure no DSA as part of pre-transplant testing.
	No DSA in all known testing and up to date testing (<3months) or day of Tx testing results for a patient sensitised by previous Tx.
	Virtual crossmatch criteria: recent single antigen results (within 3 months), No sensitising events in previous 4 months, No unacceptable antigens against the donor HLA type, No allele-specific reactivity against the donor HLA type.
	Recipient must have no donor directed antibody in current or historic samples (MFI>2000 and > self antigens). > 12 month screening history, sample within 4 weeks screened by Luminex Single antigen beads, and no antibodies to untyped donor antigens.
	VXM - samples in date, patients with no HLA antibodies, cRF<85% with consistent antibody profile
	A transplant would be cleared to proceed on the basis of a virtual crossmatch, if the patient had not previously transplanted, had screened negative for HLA antibodies on three samples in the last 12 months, a sample had been screened within 3 months of the offer and no sensitisation events had been reported after the last screen.
RoW	To performed VCM we recommend at least 2 sera analysed by Luminex assay included one in Single antigen. The last tested serum must be less than 6 months without immunizing events. It is positive in case of antibodies >2000 MFI on historical sera.
	Criteria for transplantation with a virtual cross match: first transplantation, non sensitised, low sensitised (calculated PRA < 85%) without DSA > 2 000 and without more than 2 DSA <2000, no sensitised event until the last sample tested for antibody screening and identification

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State the predicted XM result and immunological risk

PREDICTED RESULT		Total	UK&I	RoW
CDCXM	Positive	1 (1.9%)	0	1 (3.3%)
	Negative	46 (86.8%)	18 (78.3%)	28 (93.3%)
	Other	3 (5.7%)	3 (13.0%)	0
	N/A	3 (5.7%)	2 (8.7)	1 (3.3%)
FCXM	Positive	9 (17.0%)	1 (4.3%)	8 (26.7%)
	Negative	21 (39.6%)	10 (43.5%)	11 (36.7%)
	Other	17	10	7

RISK	UK&I (n=23)	RoW (n=30)	Total (n=53)
Standard	8 (34.8%)	1 (3.3%)	9 (17.0%)
Low	3 (13.0%)	3 (10.0%)	6 (11.3%)
Intermediate	8 (34.8%)	17 (56.7%)	25 (47.2%)
High	1 (4.3%)	3 (10.0%)	4 (7.5%)
Contraindication	0	4 (13.3%)	4 (7.5%)
Other	3 (13.0%)	2 (6.7%)	5 (9.4%)

- Labs seems to have a good understanding of how results correlate to expected outcomes and risk stratification

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Follow-up

- The scenario was based on a real case
- Selected to determine how labs deal with patients with a complex transplant history and an antibody profile that includes self-reactivity
- It is interesting to note the divergent approaches to
  - listing unacceptable antigens
    - Inclusion of previous mm
  - Use of vXM in sensitised patients
  - Pre-transplant testing differences in UK (approx. half use CDCXM and FCXM) and RoW (12 labs use only CDCXM). 40% perform ab screening on-call.

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Scenario 2 – HSCT

50 responses received

- Information provided
  - 52 year old CMV negative female patient with AML
  - 4 potential related donors
    - 2 children
    - 2 half-siblings
  - Unrelated search initiated

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What aspects of the patient's HLA type make this a challenging unrelated donor search?

Patient's HLA Type:
HLA-A*34:02, A*68:02; B*14:03, B*51:01; C*08:02, C*16:01;
DRB1*11:04, DRB1*15:03; DRB3*02:02, DRB5*01:01;
DQB1*05:02, DQB1*06:02; DQA1*01:02, DQA1*-;
DPB1*11:01, DPB1*18:01

Responses included:
Likely African descent, which is underrepresented on donor registries
Low frequency alleles e.g.. B*14:03, DRB1*15:03, A*34:02
Uncommon DR-DQ association (DRB1*11:04-DQB1*05:02, would expect DQB1*03)
B*51:01 has a number of HLA-C associations, reducing the chance of a C match
Rare haplotypes

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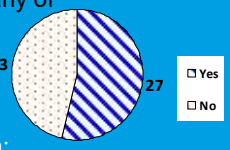
An Unrelated Donor Search is Performed

Donor ID	A*	B*	C*	DRB1*	DQB1*	DPB1*	Registry	Age	Sex	CMV	ABO
Patient	34:02 68:02	14:03 51:01	08:02 16:01	11:04 15:03	05:02 06:02	11:01 18:01		52	F		
A	34:XX 68:XX	(07:XX) 14:XX		11:XX 15:XX			BR - Redome	28	Male		B
B	(30:02) 68:XX	14:03 51:XX		11:XX 15:XX			US-NMDP	39	Male	Neg	
C	(30:XX) 34:XX	14:XX 51:XX	08:XX 16:XX	11:XX 15:XX			BR - Redome	46	Male		A
D	34:XX 68:XX	14:XX (15:XX)		11:XX 15:XX			BR - Redome	48	Male		
E	28 34	14 51		15:XX (04:XX)			US-NMDP	57	Female		A
F	(02:XX) 68:XX	14:XX 51:XX		11:XX 15:XX			BR - Redome	32	Female		
G	(02:XX) 68:XX	14:XX 51:XX		11:XX 15:XX			BR - Redome	37	Male		
H	34:XX 68:XX	(15:XX) 51:XX		11:XX 15:XX			BR - Redome	38	Female		
I	28 34	(44) 51		11:04 15:XX			US-NMDP	47	Male		
J	34:XX 68:XX	(44:XX) 51:XX		11:04 15:03			US-NMDP	47	Male		
K	(01:XX) 68:XX	14:XX 51:XX		11:XX 15:XX			DE-ZKRD	52	Male		
L	(23:XX) 68:XX	14:XX 51:XX		11:XX 15:XX			DE-ZKRD	55	Female		

Would you select any of the donors listed?



- Reasons for decision:
- No
  - All donors likely to have >1 HLA mm due to patient's low frequency alleles/linkage.
  - Would need to carry out too much additional testing to consider MUDs with the likelihood of finding a match unlikely. Donors aged >25 years.
- Yes
  - All sub-optimal on age, registry, resolution, ethnicity and ABO/CMV data. However, depending on patient disease status and clinical input we would select a 8/10 or 9/10.
  - If the urgency of the case required it but would simultaneously look at other options.
  - No guarantee there is not a match so we would attempt to type donors but communicate to clinical team that a match is unlikely.
  - Potential for 9/10 which is preferable over a haplo

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If you would select a donor from the search which would you select?

Donor	UK&I	RoW	Total	Reasons for Selection
First Choice Donor:				
B	12	7	19	Potential 9/10 Has B*14:03 allele CMV Neg Age ok Male Reputable registry
C	0	4	4	Already typed for HLA-C 1 antigen mismatch at HLA-A Male
A	0	3	3	Male Age HLA-B mismatch
G	0	1	1	HLA A*02 mismatch and this allele has shared epitopes to HLA A*68
I	0	1	1	If this is a B*44:03 there is a LD with -C*16:01
J	0	1	1	Identity for HLA DRB1*, A and one B

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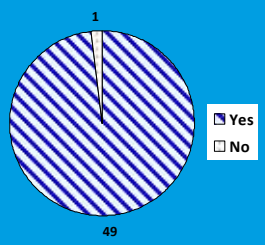
Would you perform additional testing or require further information to inform selection of a related donor?



	Responses included:
Donor	CMV
	ABO
	Donor Weight
	KIR Typing
	DPB1 Permissive mismatch tool
	Virology screening
	Confirmatory HLA typing
	PIRCHE
Patient	HLA Antibody testing
	Weight
	Confirmatory HLA typing
	ABO

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Rank the top two related donors

Patient	HLA-A*34:02, A*68:02; B*14:03, B*51:01; C*08:02, C*16:01; DRB1*11:04, DRB1*15:03; DRB3*02:02, DRB5*01:01; DQB1*05:02, DQB1*06:02; DQA1*01:02, DQA1*-; DPB1*11:01, DPB1*18:01
Son (20 yrs)	A*34:02, A*74:01; B*42:01, B*51:01; C*16:01, C*17:01; DRB1*13:01, DRB1*15:03; DRB3*03:01; DRB5*01:01; DQA1*01:02, -; DQB1*05:01, DQB1*06:02; DPB1*01:01, DPB1*18:01
Daughter (17 yrs)	A*30:02, A*34:02; B*45:01, B*51:01; C*16:01, -; DRB1*15:03, -; DRB5*01:01 DQA1*01:02, -; DQB1*06:02, -; DPB1*18:01, DPB1*105:01
Half Sibling 1 (male 36 yrs)	A*32:01/05/08/12/14/27N, A*36:01/05/06/07/08; B*40:06/70/103/127/131/361N, B*53:01/10/18/20/25 C*04:01/04/05/07/09N, C*15:02/02N/03/08/10/13 DRB1*11:01/12/15/24/27/169N, DRB1*15:02/104; DRB3*02:02/10/28/29N/30; DRB5*01:02; DQA1*01:02/08/09/11/16N, DQA1*01:03/10/14/15N/17; DQB1*06:01/43/99/100/101/102N, DQB1*06:02/46/47/84/107/216N
Half Sibling 2 (male 32 yrs)	A*68:02, A*74:01; B*14:03, B*41:02; C*03:04, C*08:02; DRB1*11:01, DRB1*11:04; DRB3*02:02, DRB3*03:01; DQA1*01:02, -; DQB1*05:02, DQB1*06:02; DPB1*11:01, DPB1*105:01

Donor	UK&I	RoW	Total	FIRST CHOICE DONOR - Reasons for Selection
Son	8	13	21	Young male Haploidentical Benefit of NIMA effect Permissive DP mismatch Likely to provide good cell dose
Half Sibling 2	8	8	16	Haploidentical Male Likely to provide best cell dose Reduced chance of pregnancy induced DSA Permissive DP mismatch Sibling preferred over parent or child donor
Daughter	3	10	13	8/10 match Young donor More likely to be CMV Negative due to age Haploidentical Homozygous Few mismatches in GvH direction Permissive DP mismatch

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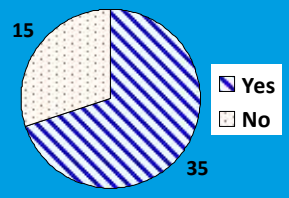
Would the results HLA antibody testing alter your ranking of related donors?

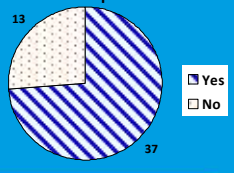
Potential DSA	MFI	Donor ID
B42	6017	Son
B45	2397	Daughter
B61	5540-5554	Half Sib 1
B41	2832	Half Sib 2



If yes, what is your preferred new donor?

Donor	UK&I	RoW	Total	Reasons for Selection
Half Sibling 2	7	13	20	Lower risk DSA to B41 MFI 2832
Daughter	4	8	12	Low risk B45 DSA (2396) than Son
Son	0	2	2	No HLA antibodies detected

Does your lab routinely perform haplo-id tx?



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Follow up

- The son was excluded due to sickle cell trait
- Half sibling 2 ruled out due to DSA (B41 – 2800)
- Half sibling 1 HLA mismatch
- Daughter selected as haplo-identical and lower MFI (B45 - 2400)
  - Patient underwent plasma exchange and was DSA neg the day before transplant
- Local policy to select haplo over mm unrelated
- HLA antibody status evaluated for all haplo tx on two samples and patients given plasma exchange until neg

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Scenario 3 – Platelet Refractoriness

- 37 responses received (20 UK&I)
- A patient failing to increment after random donor platelet transfusion is referred for investigation.
- Multiparous female
- HLA type of patient, CMV result and ABO blood group provided
- Summary of SAB Luminex results given

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Identify three optimal donations from the options provided

Donation	ABO	HLA	HLA	HLA B	HLA B	HLA C	HLA C	CMV
A	A+	A2		B44		Cw5		Negative
B	O+	A24		B7		Cw7		Positive
C	A+	A2		B18	B55	Cw9	Cw7	Negative
D	O+	A2		B18	B44	Cw5	Cw7	Positive
E	A+	A2		B44		Cw5		Positive
F	O+	A2	A25	B18		Cw5	Cw12	Negative
G	O+	A1		B8		Cw7		Negative
H	A-	A2	A30	B7	B18	Cw5	Cw7	Negative
I	A+	A3		B7		Cw7		Negative
J	O+	A3	A30	B62	B18	Cw4	Cw7	Positive
K	O+	A1		B41	B57	Cw6	Cw17	Positive
L	O+	A1	A30	B60	B18	Cw10	Cw5	Negative
M	AB+	A33	A68	B65	B18	Cw7	Cw8	Negative
N	A+	A26	A30	B13	B64	Cw6	Cw8	Negative
O	O+	A1		B7		Cw7		Positive
P	A+	A2	A30	B44	B18	Cw5		Positive
Q	O+	A31	A30	B49	B18	Cw5	Cw7	Positive
R	A+	A26	A30	B44	B18	Cw5		Positive
S	A-	A24	A31	B7	B18	Cw7		Positive
T	A+	A3	A31	B7	B18	Cw5	Cw7	Negative
U		A1	A31	B57		Cw6		Negative
V	A-	A3	A24	B51		Cw14		Positive
W	B+	A30		B57		Cw6		Positive
X	O+	A3		B8		Cw7		Positive
Z	A-	A1		B8	B44	Cw7	Cw5	Negative

- Three most popular donors selected as 1st Choice and reason:
  - G (38%) B2 match, no DSA, ABO compatible, CMV neg
  - W (32%) B1 match, no DSA, ABOi, CMV pos
  - S (21%) B2 match, ABO compatible, no DSA, CMV pos
- Three most popular donors selected as 2nd Choice and reason:
  - G (26%) B2 match, no DSA, CMV neg
  - K (21%) B2 match, no DSA, ABO compatible, CMV pos
  - M/B (14%/14%) B2 match, no DSA (M ABOi, CMV-/B ABOc, CMV+)
- Three most popular donors selected as 3rd Choice and reason:
  - K (24%) B2 match, no DSA, ABOc, CMV pos
  - O (22%) B2 match, no DSA, ABOc, CMV pos
  - B (16%) B2 match, no DSA, ABOc, CMV pos

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Based on increment data provided would you suggest any additional testing for this patient?

ABO	HLA	HLA	HLA B	HLA B	HLA C	HLA C	Pre Count	Post Count
O+	A1		B8		Cw7		3	58
A+	A1		B52	B57	Cw1	Cw6	11	50
B+	A30		B57		Cw6		8	53
A+	A1		B41	B57	Cw6	Cw17	7	44

Answer	Reasons for Decision	UK&I (n=20)	RoW (n=17)	Total (n=37)
Yes	Patient is incrementing but levels are decreasing.	7	9	16 (43%)
	Recommend HPA and ABO antibody titre testing.			
	Perform HLA antibody monitoring.			
	Test for autoantibodies.			
	Consider anti-D prophylaxis,			
No	Acceptable increment post transfusion.	13	8	21 (57%)
	Review HLA antibody status.			

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Comment on the suitability of the following platelet units in light of the patient's HSCT

- Potential HSCT donor HLA-A1, A30

Allele	Specificity	MFI
B*51:01	B51	12016
B*51:02	B51	11580
B*53:01	B53	10747
B*38:01	B38	10461
B*15:13	B77	10377
B*15:18	B63	10225
B*59:01	B59	9843
B*52:01	B52	9756
B*49:01	B49	9537
B*57:03	B57	9469
B*13:02	B13	9440
B*57:01	B57	9393
B*58:01	B58	9237
A*25:01	A25	8527
B*37:01	B37	7931
B*44:03	B44	7560
B*27:05	B27	7512
B*13:01	B13	7506
B*44:02	B44	7310
B*78:01	B78	6819
B*15:02	B75	6737
B*35:01	B35	6389
B*15:11	B75	5182
B*15:10	B71	4474
A*03:01	A3	4092
B*47:01	B47	3811
B*18:01	B18	3648
A*02:01	A2	2967
A*02:06	A2	2905
A*02:03	A2	2696
B*14:01	B64	2411
A*32:01	A32	1397
A*23:01	A23	1251
B*14:02	B65	1070
B*15:01	B62	942
B*46:01	B46	904
A*24:02	A24	832
A*24:03	A24	808
B*15:03	B72	698
B*56:01	B56	669

ID	ABO	HLA	CMV	Comments	Reason
1	A-	A30, A24; B35, B41; Cw4, Cw17	Neg	Not suitable (89%)	DSA to B35 (MFI 6389) and A24 (MFI 832). Unlikely to increment. Risk of immunising patient against A30 in the potential HSCT donor.
				Could be considered (11%)	ABO and CMV matched. DSA but Patient's own type is positive in SAB test. Local policy would be to adjust cut off for positivity to level of self-reactivity.
2	O+	A1, -; B7, -; Cw7, -	Pos	Not suitable (68%)	Only provide CMV matched plts as patient requires HSCT. Could sensitise patient to A1.
				Could be considered (16%)	B2 match, no DSA. CMV pos, could sensitise patient to A1. Give post-transplant if required.
				Suitable (16%)	No DSA, CMV pos.
3	A+	A11, -; B8, B18; Cw7, -	Neg	Not suitable (19%)	DSA, potential allelic (B*18:01) or self reactive antibody. Risk of failure to increment.
				Could be considered (22%)	B2 match, ABO and CMV matched. Potential allelic antibody. Perform high resolution typing before deciding use.
				Suitable (59%)	ABO and CMV match, no DSA, B2 match. Acceptable risk of sensitising patient.

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The issuing centre are unable to gamma irradiate the selected platelet unit. What advice would you give?

Advice for platelet selection	Reasons
Use CMV Negative Platelets	• Patient is CMV negative. • Avoid primary CMV infection.
Select HLA matched units in the graft v host direction	• To avoid the risk of transfusion induced graft vs host disease. • High risk of TA-GVHD in homozygous platelets which are matched in the HvG direction but potentially mismatched in the GvH direction.
Select HLA mismatched platelet units	• The patient is immunocompromised, therefore, supplying HLA mismatched platelets is the best way to avoid Transfusion Associated GVHD (TA-GVHD). Non-irradiated, HLA selected platelets would need to be issued under medical concession. • Avoidance of homozygous donors will minimise the risk of TA-GVHD as the patient will be able to recognise the donor lymphocytes as non-self. However, this may be associated with poor increments.
Select irradiated units from another source/ Send platelets to another centre for irradiation	• The patient will be at high risk of graft versus host due to; • The patient being immunocompromised as a result of the HSCT transplant • The HLA disparity in the platelet units available and the HSCT transplant. • BCSH guidelines state that all HLA selected products should be irradiated prior to transfusion to avoid TA-GvHD. • Leukocyte reduction filters are not considered adequate to remove enough white cells to guarantee prevention of GVHD. Residual leukocytes in a platelet unit could cause GvHD in patients who are immunosuppressed as a result of their HPCT conditioning regimen. • To avoid the risk of transfusion induced graft vs host disease. • Cannot issue platelets that have not been irradiated. • Current guidelines state that HLA selected platelets issued to HSCT patients (especially if immunocompromised) should be gamma irradiated to prevent the risk of engraftment causing TA-GvHD which has a >90% fatality rate.

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The issuing centre are unable to gamma irradiate the selected platelet unit. What advice would you give? *Continued…*

Select units towards end of shelf life	• Viable lymphocytes will be reduced.
Use vironinactivated platelets	• The patient is CMV-, so there is a risk of CMV infection.
Transfuse non-irradiated platelets	• Treat patient with intercept to cause inactivation of nucleated cells.
Use platelets treated with Amotosalen	• If platelets treated with amotosalen then do not require irradiation to prevent transfusion graft host disease which could occur in immunosuppression recipient.
Transfuse irradiated or not, if patients platelet count <10 G/L or <20G/L + bleeding	• Bleeding risk is higher than Graft versus Host disease risk (if low patients platelet count at the moment).

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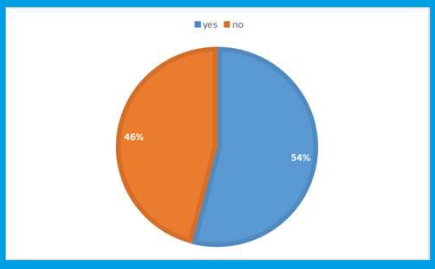
Does your laboratory provide a clinical platelet service?



Platelet Service	UK&I (n=20)	RoW (n=17)	Total (n=37)
Yes	7	14	21 (46%)
No	13	3	16 (54%)

- The lab does antibody testing and HLA typing for platelet refractory patients, but we do not select and issue platelet units. Clinical advice is given by our consultant if needed.
- In France treatment by amotosalem of all platelet units allows us not to take care of CMV status and not to irradiate units before transplantation.
- We only look for HLA Ab. Platelet donors are chosen by another service of our Blood Centre.

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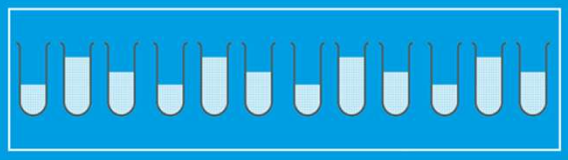
Scheme 1A, 4A1, 4A1i, 4A2

HLA Typing



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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 2019

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

	2012	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	22 (10)	30 (10)	42 (9)	45 (9)	41 (7)	38 (6)	38 (6)	38 (5)
Number with Unsatisfactory Performance (< 90%) (UK&I)	1 (0)	0 (0)	8 (0)	4 (0)	3 (0)	1 (0)	6 (1)	8 (1)
% Unsatisfactory Performance	4.5%	0.0%	19.0%	8.9%	7.3%	2.6%	15.8%	21.1%

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2019 Incorrect Assignments resulting in UPs

Sample	Lab Number	Consensus	Report
1A 01	41	A3, A11; B7, B35; Cw4, Cw7; DR103, DR-; DQ5, DQ7	**A03**, A11; **B07**, B35; **Cw04**, **Cw07**; **DR01:03**, DR-; **DQ05**, **DQ03:01**
1A 01	159	DR103,-; DQ5, DQ7	**DR01:03**, -; **DQ05**, **DQ03**
1A 01	315	DQ5	**DQ1**
1A 01&02	139		**Sample mix-up**
1A 01&02	289		**No results returned / suspended**
1A 02	41	A1, A68; B8, B37; Cw6, Cw7; DR8, DR17; DQ2, DQ4	**A01**, A68; **B08**, B37; **Cw06**, **Cw07**; **DR08**, **DR03:01**; **DQ02**, **DQ04**
1A 02	159	DR8, DR17; DQ2, DQ4	**DR08**, **DR03**; **DQ02**, **DQ04**
1A 03	315	DQ8	**DQ3**
1A 03	147 & 163	DR4, DR17; DQ2, DQ8	**DR04**, DR17; **DQ02**, **DQ08**
1A 04	147 & 163	DR4, DR11; DQ7,-	**DR04**, DR11; **DQ07**, -
1A 05& 06	209	A1 DQ8 & DQ6 respectively	**A1/36 DQ8/9** & **DQ1**
1A08	209 & 315	A3, A32; B55, B65	A2, A32; B55, **B14**

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2019 Incorrect Assignments resulting in UPs

Sample	Lab Number	Consensus	Report
1A07	401	A3,-; B7,-; DR4, DR15; DQ6, DQ8	**A02**, **A03**; **B07**, **B40**; **DR04**, DR15; **DQ03**, **DQ06**
1A08	401	A3, A32; B55, B65; DR13, DR14; DQ5, DQ6	**A02**, A32; B55, **B14**; DR13, DR14; **DQ05**, **DQ06**
1A09	209	DQ8	**DQ3**
1A09	401	A24, A68; B39, B51; Cw2, Cw7; DR4, DR11; DQ7, DQ8	**A24, A31; B35, -; Cw1, Cw4; DR4, -; DQ3,-**
1A10	209	A2, A24; B7, B57; DR7, DR15; DQ6, DQ9	**A1**, A24; B7, B57; DR7, DR15; **DQ1**, **DQ3**
1A10	401		No results returned

19/380 (5.0%) incorrect HLA types in 2019 reported by 10 labs;
- 13 reports of incorrect broad/split specificity
- 13 reports of molecular based nomenclature
- 7 reports of sample mix-up/incorrect type
- 3 reports not returned with results

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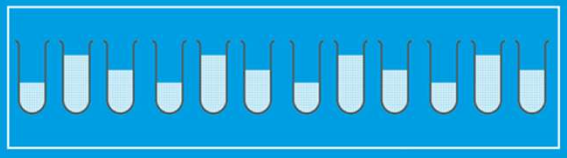
Scheme 4A1

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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4A1 Performance 2019

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

	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	96 (30)	96 (30)	100 (29)	102 (28)	106 (28)	105 (28)	100 (28)
Number with Unsatisfactory Performance (< 90%) (UK&I)	5 (0)	9 (0)	7 (1)	21 (4)	11 (1)	15 (1)	4 (1)
% Unsatisfactory Performance	5.2%	9.4%	7.0%	20.6%	10.4%	14.3%	4%

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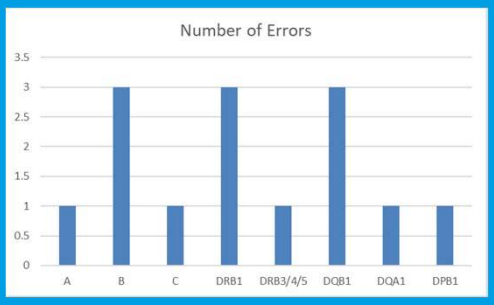
Incorrect Assignments

- 14/1010 (1.4%) incorrect HLA types reported by labs 8 (3 UK&I)
  - 6 incorrect assignments (e.g.. B*44 instead of B*40, DPB1*02:01 instead of DPB1*01:01) (1 UK&I)
  - 2 missed assignments (e.g.. reported homozygous/blank when hetero)
  - 6 other errors e.g.. missed loci, DRB3/4/5 presence/absence errors, nomenclature and/or reporting errors/broad not split (2 UK&I)



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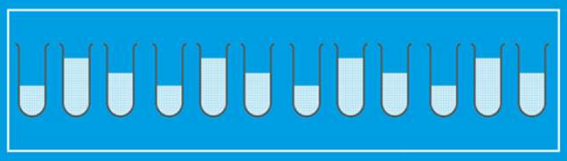
Scheme 4A1i

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 sourced from 4A1
- ***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 2019

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

	2017	2018	2019
Number of Participants (UK&I)	36 (20)	40 (21)	44 (22)
Number with Unsatisfactory Performance (< 90%) (UK&I)	6 (1)	6 (0)	8 (1)
% Unsatisfactory Performance	16.7%	15.0%	18.1%

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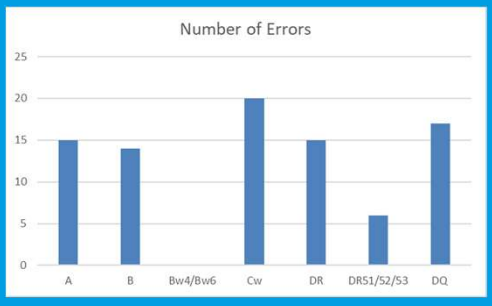
Interpreted DNA Results

- 34/440 (7.7%) incorrect HLA types reported by 15 labs (5 UK&I)
  - 1 report with multiple errors in HLA type
  - 1 report of incorrect split specificity (e.g.. B60 instead of B61) (1 UK&I)
  - 4 missed assignments (e.g.. reported homozygous/blank/null instead of hetero)
  - 6 DR51/52/53 presence/absence error (2 UK&I)
  - 22 incorrect nomenclature used (e.g.. 05 rather than Cw5) (1 UK&I)



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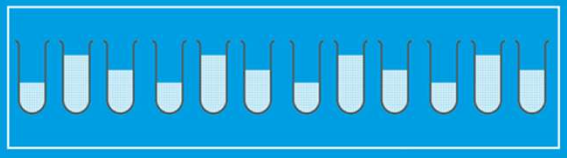
Scheme 4A2

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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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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4A2 Performance 2019

- 9 Unsatisfactory Performers (1 UK & Ireland)

	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	59 (21)	59 (20)	63 (21)	66 (21)	63 (20)	62 (20)
Number with Unsatisfactory Performance (< 90%) (UK&I)	5 (1)	7(1)	8 (2)	4 (0)	9 (2)	9 (1)
% Unsatisfactory Performance	8.5%	11.9%	12.7%	6.1%	14.3%	14.5%

- 42/66 participants registered for 2nd field
- 24/66 participants registered for 3rd field

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2019 Incorrect Assignments: 2nd Field

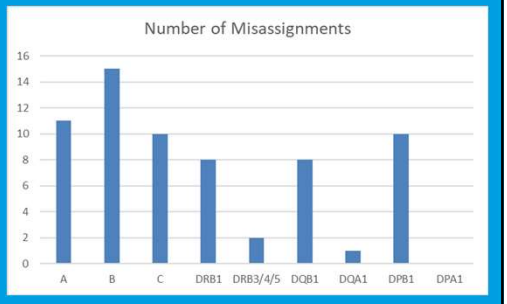
- 65/585 (11%) incorrect HLA types reported by 9 labs (2 UK&I)

– 13 reports of alleles in a string that differ from the consensus allele (e.g.. A*01:01/09) (1 UK&I)

– 3 reports of incorrect allele (e.g.. C*17:01 not C*17:03) (1 UK&I)

– 1 report of incorrect antigen (e.g.. B*27:01 instead of B*57:01)

– 48 reports of an incorrect type due to sample mix up by one lab



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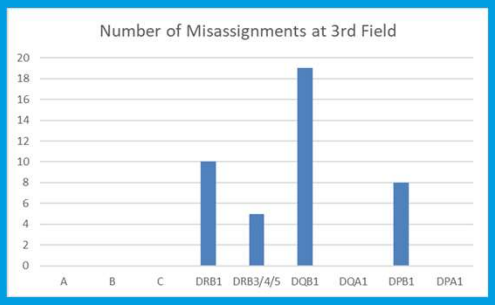
2019 Incorrect Assignments: 3rd Field

- 42/364 (11.5%) incorrect assignments reported by 11 labs (2 UK&I)
  - 1 report of 1st field rather than 3rd field resolution
  - 13 reports at 2nd field only
  - 2 reports of incorrect allele (e.g.. DRB4*01:01:01 rather than 01:03:02)
  - 3 reports with an error at 3rd field (1 UK&I)
  - 3 reports of a wrong type
  - 20 reports with unresolved ambiguities (1 UK&I)



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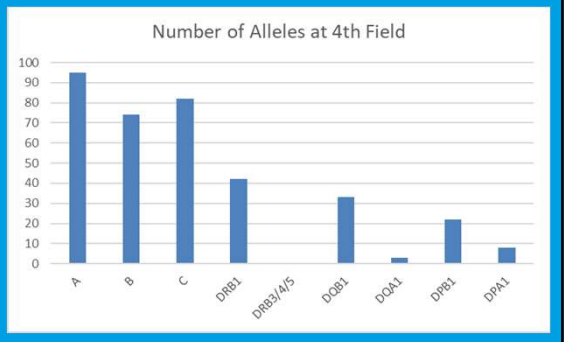
4th Field Results

- 8 labs reported results at 4th field resolution

359 out of a possible of 11880 (3%) alleles had unambiguous results at 4th field resolution (e.g.. B*07:02:01:01)

There were a further 2 reports of alleles that contained 4th field ambiguities (e.g.. A*02:01:01:01/16/31/50)



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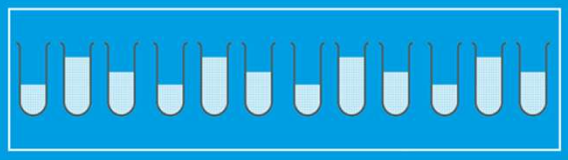
Schemes 9, 10 and 11

KIR and HPA



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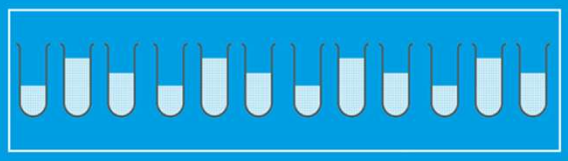
Scheme 9

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 2019

- 8 Errors
- 3 Unsatisfactory Performers

	2015 Pilot	2016 Pilot	2017	2018	2019
Number of Participants (UK&I)	7 (1)	11 (2)	8 (3)	9 (1)	12 (1)
Number with Unsatisfactory Performance (UK&I)	N/A	N/A	0 (0)	1 (0)	3 (0)
% Unsatisfactory Performance (UK&I)	N/A	N/A	0%	11.1%	25%

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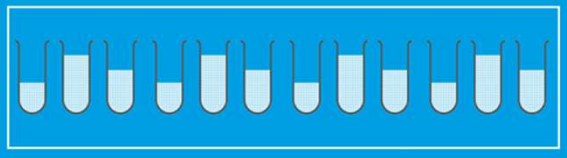
Scheme 10

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
  - 30/38 reported HPA-1, 2 , 3, 4, 5 and 15
  - 30/38 labs reported HPA-4
  - 24/38 labs reported HPA-6
- Also able to report any other HPA polymorphisms detected, for information

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Performance 2019

- 15 Errors (RoW only)
- 3 Unsatisfactory Performers

	2015 Pilot	2016 Pilot	2017	2018	2019
Number of Participants (UK&I)	14 (3)	12 (4)	15 (5)	37 (6)	38 (6)
Number with Unsatisfactory Performance (< 100%) (UK&I)	N/A	N/A	1 (0)	1 (0)	3 (0)
% Unsatisfactory Performance (UK&I)	N/A	N/A	6.7%	2.7%	7.9%

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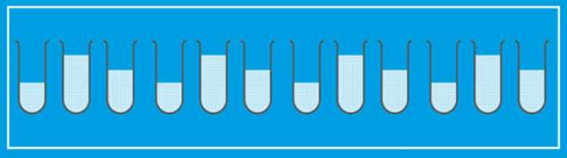
Scheme 11

HPA Antibody Detection/Specification



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Scheme 11

- *NIBSC no longer offering platelet genotyping or antibody schemes, participants offered to transfer to NEQAS*
- ***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 2019

- 1 Unsatisfactory Performer (0 UK & Ireland)

	2017 Pilot	2018	2019
Number of Participants (UK&I)	13 (3)	35 (4)	39 (5)
Number with Unsatisfactory Performance (< 75%) (UK&I)	N/A	1 (0)	1 (0)
% Unsatisfactory Performance (UK&I)	N/A	2.9%	2.6%

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HPA Antibody Detection/Specification

- All samples could be assessed for HPA detection

2019 Sample	HPA Detection	HLA Detection	HPA Antibody ID	
			Presence	Absence
1	100% Neg	100% Neg	100% Neg	
2	100% Pos	100% Pos	HPA-5b 100%	2.6% GPIIb/IIIa
3	97.4% Neg	93.8% Pos	2.6% GP1b	
4	94.7% Neg	100% Pos	2.6% GP1b	
5	97.4% Pos	100% Pos	HPA-5b 97.4%	2.6% HPA-15b
6	87.2% Pos	100% Pos	HPA-5b 87.2%	
7	94.9% Pos	93.3% Neg	HPA-1a 94.9%	2.6% HPA-4a GP1b
8	92.1% Pos	100% Pos	HPA-5b 92.1%	2.6% HPA-4a GP1v CD109

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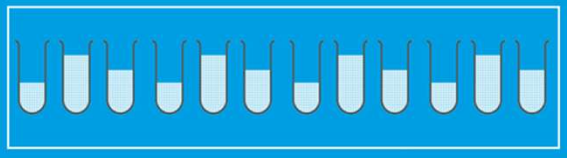
Schemes 1B, 5A, 5B, 7 and 8

Disease Association/Pharmacogenetics



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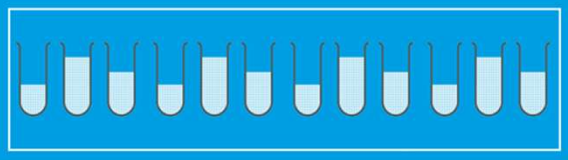
Scheme 1B

HLA-B27 Testing



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HLA-B27 Testing

- ***Purpose:*** To assess ability to correctly determine HLA-B27/2808/B*27 status
- 10 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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Performance 2019

- 4 Unsatisfactory Performers (1 UK & Ireland)

	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	96 (47)	107 (51)	115 (54)	123 (54)	127 (52)	133 (54)	133 (53)
Number with Unsatisfactory Performance (< 100%) (UK&I)	4 (1)	4 (2)	8 (4)	15 (6)	7 (2)	10 (3)	4 (1)
% 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%)	3.0% (1.9%)

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2019 Incorrect Assignments

Sample	Result	Lab Number	Technique	HLA Type	Lab Identified Cause
1B04	False Pos	236, 409	Serological	B7, B35	No reply
1B05	False Pos	409	Serological	B7, B8	Low cell viability/transport delay

6/10 samples distributed were HLA-B27 positive
3 errors: 3 False Pos
2 labs did not return results

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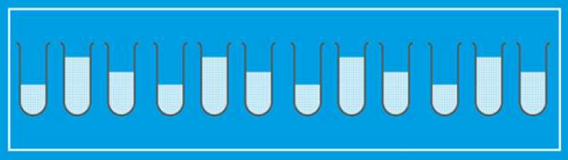
Scheme 5A

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 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

- 2 Unsatisfactory Performers (1 UK&I)

	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	58 (10)	59 (50)	60 (49)	58 (49)	56 (42)	58 (44)	51 (38)
Number with Unsatisfactory Performance (< 100%) (UK&I)	2 (2)	2 (2)	0 (0)	3 (2)	3 (2)	0 (0)	2 (1)
% Unsatisfactory Performance	3.4%	3.4%	0%	5.2%	5.3%	0%	3.9%

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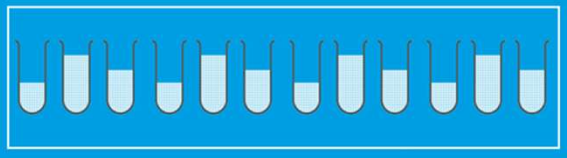
Scheme 5B

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

2019 – all 4 scenarios

6 penalty points per scenario, 24 in total

4	labs got	0 penalty points
6	labs got	1 penalty point
4	labs got	2 penalty points
1	lab got	3 penalty points
2	labs got	4 penalty points
2	labs got	5 penalty points
1	lab got	10 penalty points
1	lab got	11 penalty points

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Scheme 5B Performance

- 3 Unsatisfactory Performers (1 UK&I)

	2012	2013	2014	2015	2016	2017	2018	2019
Number of Participants	21	19	20	18	19	20	21 (18)	21 (17)
Number with Unsatisfactory Performance	3	3	5	0	0	0	1 (1)	3 (1)
% Unsatisfactory Performance	14.3 %	15.8 %	25.0 %	0%	0%	0%	4.8%	14%

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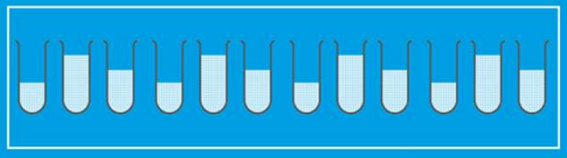
Scheme 7

*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

- 6/10 samples distributed were HLA-B*57:01 positive
- No lab with unacceptable performance

	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	47 (23)	56 (24)	62 (26)	62 (25)	64 (26)	67 (27)	67 (27)
Number with Unacceptable Performance (< 100%) (UK&I)	0 (0)	1 (0)	0 (0)	1 (1)	4 (1)	2 (0)	0 (0)
% Unsatisfactory Performance	0.0%	1.8%	0.0%	1.6%	6.3%	3.0%	0.0%

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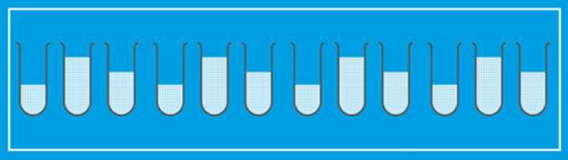
Scheme 8

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 donor 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

- 13 Unsatisfactory Performers (2 UK & Ireland)

	2013	2014	2015	2016	2017	2018	2019
Number of Participants (UK&I)	19 (8)	21 (9)	30 (8)	39 (8)	45 (9)	52 (10)	50 (11)
Number with Unsatisfactory Performance (< 100%) (UK&I)	2 (1)	3 (2)	8 (0)	8 (3)	15 (2)	14 (4)	13 (2)
% Unsatisfactory Performance	10.5% (12.5%)	14.3% (22.2%)	26.7% (0%)	20.5% (37.5%)	33.3% (22.2%)	26.9% (40%)	26% (18.2%)

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2019 Unacceptable Performance by Disease

Disease	HLA Association	Number of Participants	No. of Participants with Unacceptable Performance
Coeliac	DQ2, DQ8, DQA	50	12
Narcolepsy	DQB1*06:02	21	2
Actinic Prurigo	DRB1*04:07	3	0
Birdshot Retinopathy	A*29	7	0
Behçet's	B*51	12	0
Rheumatoid Arthritis	DRB1*04	2	0
Diabetes	DR3, DR4	5	2

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2019 Incorrect Assignments

Sample	Lab	Result	HLA Type	Error
801	17	Negative for DQ2 and DQ8	DRB1*07:01, DRB1*08:01; DQB1*02:02, DQB1*04:02; DQA1*02:01, DQA1*04:01	Interpretation issue
	176	DQA1*05 Pos		Interpretation error
	317	DQA1x02, DQA1x02/x0301, DQB1x02, DQB1x02/x0302		Nomenclature/reporting issue
	319	Negative for DQ2 and DQ8		No response
	331	DQB1*02:01, DQB1*03:02		Interpretation issue
802	317	DQA1x03, DQA1x02/x0301, DQA1x05, DQB1x02/x0302	DRB1*04:04, DRB1*11:01; DQB1*03:01, DQB1*03:02; DQA1*03:01, DQA1*05:05	Nomenclature/reporting issue
	331	DQB1*03:01/03:13, DQB1*03:04		Transcription error
803	126	Negative for DQ2	DRB1*03:01, DRB1*04:07; DQB1*02:01, DQB1*03:01; DQA1*03:03, DQA1*05:01	Sample mix up
	150	DQA1*03:02		Transcription error
	317	DQA1x03, DQA1x0302/03, DQA1x05, DQB1x02, DQB1x02/x0302		Nomenclature/reporting issues

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2019 Incorrect Assignments

Sample	Lab Number	Result	HLA Type	Error
804	150	DQA1*03:02, DQA1*05:01	DRB1*04:01, DRB1*11:01; DQB1*03:01,-; DQA1*03:03, DQA1*05:05	Interpretation issue
	278	Positive for DQ8		Interpretation issue
806	24	Incorrect DQA1*03:01	DQA1*01:02, DQA1*03:03	Interpretation issue
808	24	Reported DQA1*03:01 only	DRB1*04:04, DRB1*04:07; DQB1*03:01, DQB1*03:02; DQA1*03:01, DQA1*03:03	Interpretation issue
	129	DRB1*04:03		Interpretation issue
	307	Incorrect DQA1		Interpretation issue
	331	Incorrect DQB1 & DRB1* typo error		
809	129	No DQ8 reported in phenotype	DRB1*03:01, DRB1*04:04; DQB1*03:01; DQB1*03:02; DQA1*03:01, DQA1*05:01	Interpretation issue
	269	Incorrect DQB1*03 negative		Interpretation issue

- 20 incorrect assignments in 2019 (3 UK&I), 17/20 in Coeliac Disease

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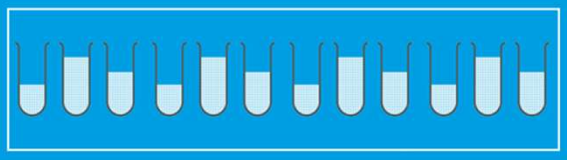
EDXM Scheme

Incorporating Crossmatching, HLA Typing and Antibody Detection/Specification



Tracey Rees

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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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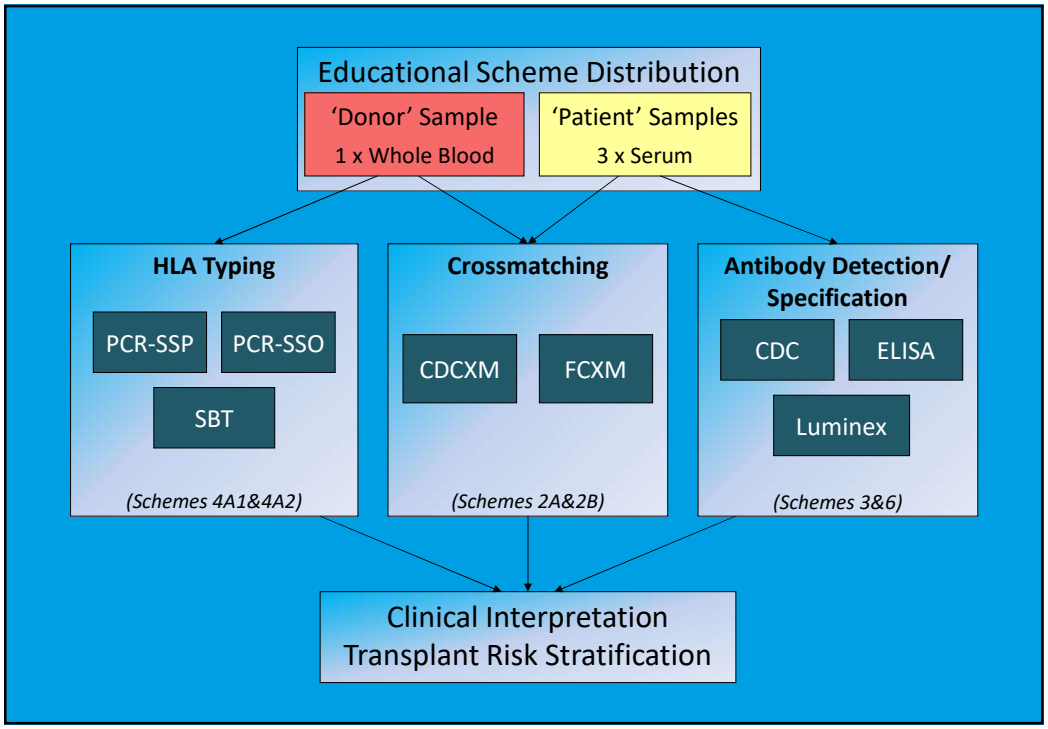

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2019 Results

- 34 participants (14 UK&I)
  - not all labs reported results for all tests
- 100% agreement on HLA type except DPB1
  - Some labs reported DPB1*02:01, DPB1*04:01

	A*	B*	C*	DRB1*	DRB4*	DRB5*	DQA1*	DQB1*	DPA1*	DPB1*
	3	**7**	**05**	**09**	**01**	**01**	**01**	**06**	**01**	**02:01**
	32	**15**	**07**	**15**	**-**	**-**	**03**	**03**	**-**	**126**
Number of reports	34	34	33	34	23	23	29	34	19	20
% Labs in consensus	100%	100%	100%	100%	100%	100%	100%	100%	100%	65%

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Serum 1 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	100%	
HLA Class II Antibodies	Positive	100%	
DSA	Yes	100%	Huge range in MFI reported e.g.. B7 8,792-23,377
CDC XM	PBL Positive T cell Positive B cell Positive	83% (5/6) 100% (18/18) 90% (18/20)	
FCXM T Cell	Positive	100%	
FCXM B Cell	Positive	100%	
Transplant Risk	Contraindication /High	94% (32/34)	2 respondents (6%) reported medium risk

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Serum 2 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	74% (25/34)	
HLA Class II Antibodies	Positive	100%	
DSA	Yes	97% (33/34)	Huge range in MFI reported e.g.. DQ9 6,088-21,575
CDC XM	PBL Negative T cell Positive B cell Negative	100% (6/6) 100% (18/18) 95% (19/20)	
FCXM T Cell	Negative	96% (25/26)	
FCXM B Cell	Not Assessed	42% (11/26)	
Transplant Risk	Contraindication /High	61% (20/33)	13 respondents (39%) reported low/medium risk

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Serum 3 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Negative	100%	
HLA Class II Antibodies	Negative	100%	
DSA	None	100%	
CDC XM	Negative	100%	
FCXM T Cell	Negative	96% (25/26)	
FCXM B Cell	Negative	96% (23/24)	
Transplant Risk	Low Risk	100%	

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Summary of Crossmatch and DSA Detection Results

2019 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		A33 (94%) B7 (100%)			DQ7 (9%) DQ8 (9%) DQ9 (97%)		
MFI 5,000-9,999		A32 (100%)					
MFI 3,000-4,999			DR9 (94%) DR15 (100%)				
MFI 1,500-2,999				A33 (3%)			
MFI <1,499			DQ6 (9%) DQ9 (21%)	A3 (3%) B7 (15%)			
CDCXM	No DTT	Positive		Negative		Negative	
CDCXM	DTT	Positive		Negative		Negative	
FCXM	T Cell	Positive		Negative		Negative	
FCXM	B Cell	Positive		Negative		Negative	
Risk		Contraindication/High (94%)		Contraindication/High (61%)		Low (100%)	

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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Thank you

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