UK NEQAS Histocompatibility & Immunogenetics

UK NEQAS H&I

Annual Participant's Meeting 2024-25

@UKNEQAS

Meet The Team!

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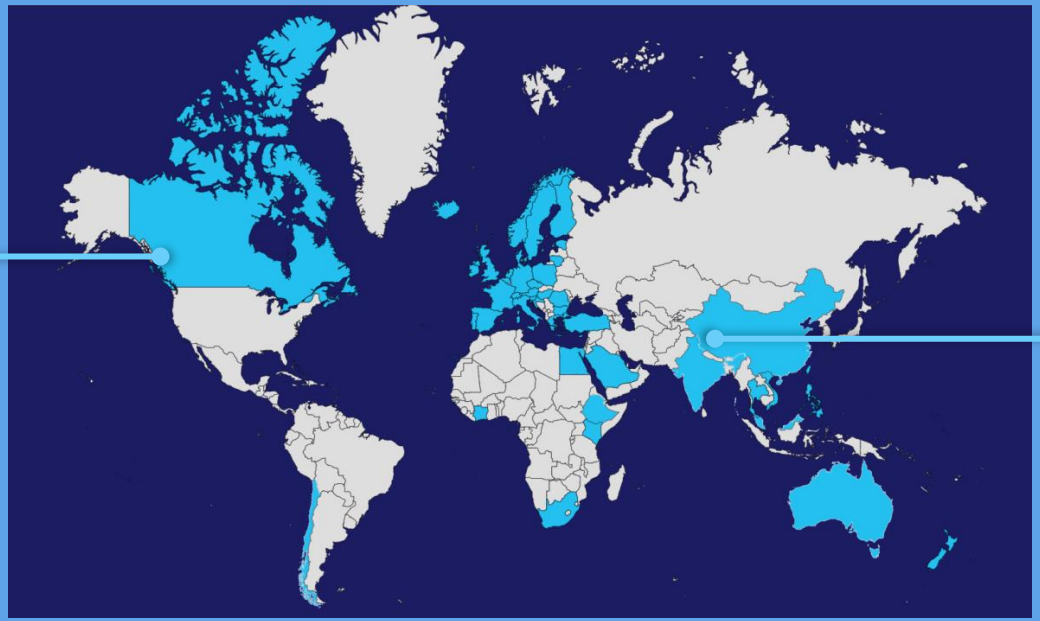
UK NEQAS for H&I Steering Committee 2024-25

Helena Lee (Chair)
Arthi Anand
Katy Derbyshire
Sylvia McConnell
Katherine Mounsey
Anthony Calvert
Sunil Daga (Clinical Representative)
Elizabeth Wroe (BSHI Representative to UK NQAAP)

Rhys Goodhead (Expert Advisor Scheme 5B)
Barbara McNamara (Expert Advisor Scheme 5B)
Tim Clench (Expert Advisor Scheme 5B)

UK NEQAS for H&I: An Overview

>320 participants



>50 countries

UK NEQAS for H&I is 50!

1975
- National Tissue Typing and Reference Laboratory (now OTDT) in Bristol initiated a quality control scheme for HLA typing (1A) and crossmatching (2A)
- Exercises included technical comparisons e.g. comparing batches of complement and the sensitivity of different techniques

1988
- Introduction of HLA antibody specification (Scheme 3)

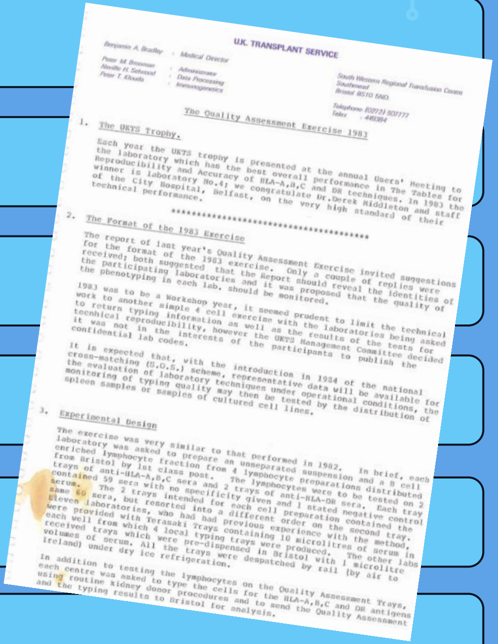
1989
- First Annual Participant Meeting
- Idea for a UK professional society for tissue typers: BSHI formed

1990
- HLA disease association scheme – B27

1992
- HLA genotyping scheme introduced: Class II only (Class I not introduced until 1999)

1994
- First international participants joined

1998
- Founding member of the EFI EPT Committee



U.K. TRANSPLANT SERVICE

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The Quality Assessment Exercise 1983

1. The UKTS Trophy.

Each year the UKTS trophy is presented at the annual Users' Meeting to the laboratory which has the best overall performance in The Tables for Reproducibility and Accuracy of HLA-A,B,C and DR techniques. In 1983 the winner is laboratory No.4; we congratulate Dr.Derek Middleton and staff of the City Hospital, Belfast, on the very high standard of their technical performance.

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2. The Format of the 1983 Exercise

The report of last year's Quality Assessment Exercise invited suggestions for the format of the 1983 exercise. Only a couple of replies were received; both suggested that the Report should reveal the identities of the participating laboratories and it was proposed that the quality of the phenotyping in each lab. should be monitored.

1983 was to be a Workshop year, it seemed prudent to limit the technical work to another simple 4 cell exercise with the laboratories being asked to return typing information as well as the results of the tests for technical reproducibility, however the UKTS Management Committee decided it was not in the interests of the participants to publish the confidential lab codes.

It is expected that, with the introduction in 1984 of the national cross-matching (S.O.S.) scheme, representative data will be available for the evaluation of laboratory techniques under operational conditions, the monitoring of typing quality may then be tested by the distribution of spleen samples or samples of cultured cell lines.

3. Experimental Design

The exercise was very similar to that performed in 1982. In brief, each laboratory was asked to prepare an unseparated suspension and a B cell enriched lymphocyte fraction from 4 lymphocyte preparations distributed from Bristol by 1st class post. The lymphocytes were to be tested on 2 trays of anti-HLA-A,B,C sera and 2 trays of anti-HLA-DR sera. Each tray contained 59 sera with no specificity given and 1 stated negative control serum. The 2 trays intended for each cell preparation contained the same 60 sera, but resorted into a different order on the second tray. Eleven laboratories, who had had previous experience with the method, were provided with Terasaki Trays containing 10 microlitres of serum in each well from which 4 local typing trays were produced. The other labs received trays which were pre-dispensed in Bristol with 1 microlitre volumes of serum. All the trays were despatched by rail (by air to Ireland) under dry ice refrigeration.

In addition to testing the lymphocytes on the Quality Assessment Trays, each centre was asked to type the cells for the HLA-A,B,C and DR antigens using routine kidney donor procedures and to send the Quality Assessment and the typing results to Bristol for analysis.

UK NEQAS for H&I is 50!

2000
- UK NEQAS for H&I relocated to the Welsh Blood Service
- New HFE (5) and antibody detection (6) schemes introduced
- First educational schemes for HLA typing

2008
- Drug hypersensitivities introduced for Abacavir (7)

2011
- 2nd Field HLA Genotyping (4A2) developed
- HLA disease association (8) and KIR genotyping (9) introduced

2015
- ISO 17043 accreditation
- HPA genotyping pilot (10)

2016
- HPA Antibody pilot (11)

2018
- 3rd Field HLA Genotyping

2025
- HNA genotyping (12) and HNA antibody detection (13)

De'Ath A, Rees MT, Pritchard D. The history and evolution of HLA typing external proficiency testing schemes in UK NEQAS for H&I. Front Genet. 2023 Sep 18;14:1272618. doi: 10.3389/fgene.2023.1272618. PMID: 37790700; PMCID: PMC10544324.

Things To Note...

Presentation Focus...

Performance, key trends, discussion points and 2025 changes

Further Details...

The presentation will be available to view on our website.

Lab Locations...

Generally:
1-100 = UK & Ireland.
101+ = Rest of the world

Scheme Assessments

- 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 plus educational schemes where required:

  - *e.g. Scheme 8: HLA Genotyping for Coeliac and Other HLA Associated Diseases*

- 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.

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.

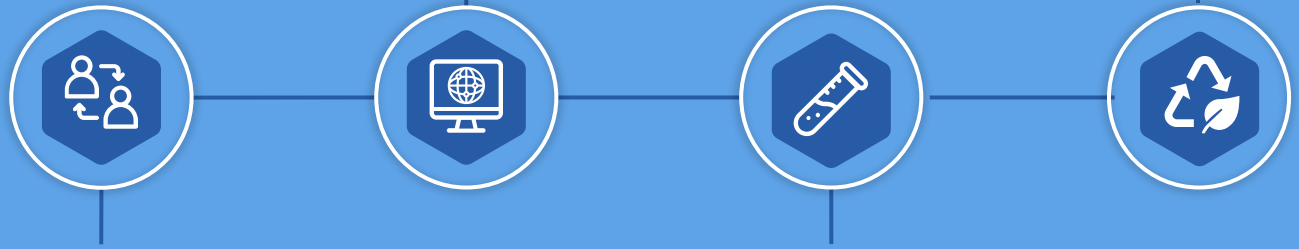
Changes for 2025-26

Pilot Schemes

Scheme 12 – HNA Genotyping
Scheme 13 – HNA Antibody Detection

Sustainability

Paperless: no distribution slips
Packaging: reduce plastic



Courier

Reduction in costs
Used for domestic and international

Scheme Changes

Scheme 7 – HLA-related Pharmacogenetics
Scheme 8 – now only HLA Associated Diseases

Pilot Schemes

12 HNA Genotyping

- Assess participants ability to correctly determine HNA polymorphisms
- 4 blood samples in two distributions
- Pilot Schemes are free of charge and not formally assessed

13 HNA Antibody Detection/Specification

- Assess participants ability to correctly detect the presence and specificity of HNA antibodies
- 4 serum/plasma samples in two distributions
- Pilot Schemes are free of charge and not formally assessed

Scheme 2A

Cytotoxic Crossmatching

Scheme 2A – Cytotoxic Crossmatch

Purpose

Assess participants ability to determine cell/serum cytotoxicity crossmatch status

Consensus

At least 75% agreement on pos/neg result

Satisfactory Performance

85% of reports agree with consensus in distribution year for each cell/DTT type

10 blood samples, 40 serum samples over 5 distributions

Scheme 2A: Performance

All cells with and without DTT	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	71 (18)	71 (22)	66 (16)	63 (15)	59 (15)	47 (10)	47 (8)
Number with Unsatisfactory Performance (< 85%) (UK&I)	16 (7)	5 (1)	7 (0)	4 (0)	6 (3)	2 (2)	5 (0)
% Unsatisfactory Performance (UK&I)	22.5% (38.8%)	7.0% (4.5%)	10.6% (0)	6.3% (0)	10.2% (20%)	4.2% (20%)	10.8% (0%)

2024: 5 Unsatisfactory Performers (0 UK & Ireland)

Scheme 2A: Performance by category

	PBL	PBL +DTT	T Cell	T Cell +DTT	B Cell	B Cell +DTT
Crossmatches assessed (n=40) (UK&I)	31 (31)	33 (33)	36 (39)	34 (36)	25 (33)	30 (36)
NT – Assessed samples only	17.1%	14.2%	37.8%	33.5%	56.9%	53.6%
% incorrect assignments	4.1%	3.0%	9.3%	7.1%	20.4%	11.3%
False Positive	3.2%	1.5%	5.5%	5.3%	11.2%	5.0%
False Negative	0.9%	1.5%	3.8%	1.8%	9.2%	6.3%

Scheme 2A: Unacceptable Performers 2024

Lab ID	PBL -DTT	T -DTT	B -DTT	PBL + DTT	T + DTT	B + DTT	Lab Identified Error
133		80%					No response
189	81.3%			82.4%			Procedural error
226			84.4%				Interpretation criteria (pos cut off)
232						83.3%	Sample quality (delivery delays)
1412	75%	74.4%					Poor cell prep / reagent issues

Scheme 2A: 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

Scheme 2B

Crossmatching by Flow Cytometry

Scheme 2B: Crossmatching by Flow Cytometry

Purpose

Assess participants ability to determine cell/serum flow crossmatch status

Consensus

At least 75% agreement on pos/neg or equivocal result

Satisfactory Performance

85% reports agree with consensus in distribution year for each cell type

10 blood samples, 40 serum samples over 5 distributions

Scheme 2B: Performance

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	83 (22)	84 (23)	80 (21)	80 (22)	84 (19)	83 (21)	79 (20)
Number with Unsatisfactory Performance (< 85%) (UK&I)	15 (2)	12 (1)	11 (0)	5 (0)	6 (2)	10 (0)	4 (0)
% Unsatisfactory Performance (UK&I)	18.1% (9.1%)	14.2% (4.3%)	13.8% (0)	6.3% (0)	7.1% (10.5%)	12% (0)	5% (0)

2024: 4 Unsatisfactory Performers (0 UK & Ireland)

Scheme 2B: Performance by Category

	T Cells			B Cells		
	UK&I	RoW PC	RoW WB	UK&I	RoW PC	RoW WB
Number of participants	20	28	26	20	28	24
Number of XM assessed (>75% consensus)	35/40 (87.5%)	31/40 (77.5%)	36/40 (90%)	36/40 (90%)	36/40 (90%)	36/40 (90%)
Number of Positive XM	24 (69%)	20 (65%)	22 (61%)	32 (89%)	29 (81%)	28 (78%)
Number of Negative XM	11 (31%)	11 (35%)	14 (39%)	4 (11%)	7 (19%)	8 (22%)
Number of incorrect assignments	20	37	21	18	41	36
Number of False Pos	10	12	13	6	14	12
Number of False Neg	10	25	8	12	27	24
Number of equivocal assignments	0	6	0	1	9	1
Number of samples NT	25	162	58	56	111	64

UK&I and RoW receive different blood samples

Scheme 2B: Unacceptable Performers 2024

Lab	T Cell	No. of results submitted	B Cell	No. of results submitted	Issue
118	90%	24/40	77%	24/40	Sample quality (delivery delay)
139	87%	26/40	78%	20/40	No response
189	42%	32/40	41%	32/40	Technical issue (cytometer)
191	97%	40/40	83%	40/40	Sensitivity issue (delivery delays/poor cell prep)

4 labs with UP (<85%)

Scheme 6

HLA Antibody Detection

Scheme 6: HLA Antibody Detection

Purpose

Assess participants ability to determine **presence or absence** of HLA antibodies

Consensus

At least 75% agreement on presence/absence of HLA antibodies

Satisfactory Performance

80% reports agree with consensus in distribution year

12 serum samples over 3 distributions

Scheme 6: Performance

3 Unsatisfactory Performers (1 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	88 (25)	82 (25)	74 (25)	71 (23)	68 (23)	68 (23)	67 (24)
Number with Unsatisfactory Performance (< 80%) (UK&I)	5 (0)	8 (0)	2 (0)	0 (0)	4 (0)	3 (0)	3 (1)
% Unsatisfactory Performance	5.7% (0%)	9.7% (0%)	2.7% (0%)	0% (0%)	5% (0%)	4.4% (0)	4.4% (4.1%)

38% negative

58% positive

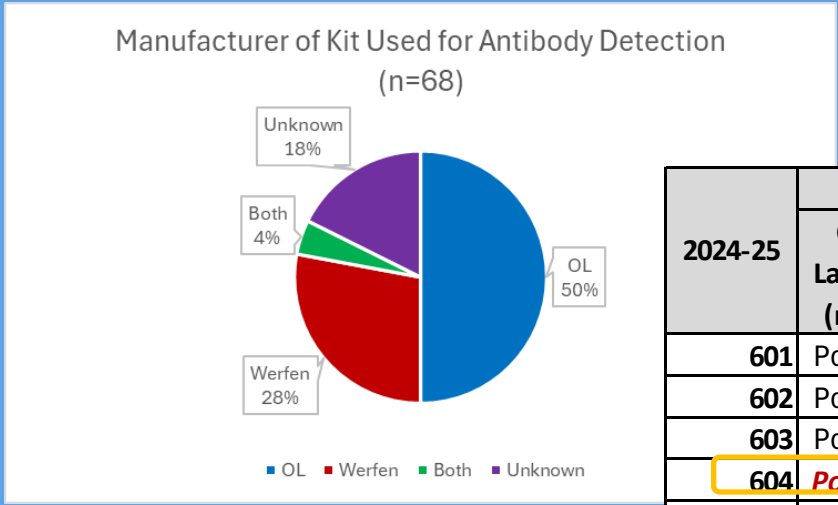
4% samples not assessed

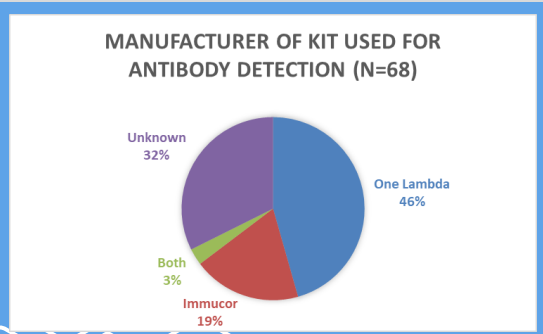
Scheme 6: Unacceptable Performers 2024

Lab	Performance (<80%)	Issue
11	75.0%	Interpretation (pos cut off)
128	75.0%	Interpretation / kit issue
1418	58.3%	Interpretation / kit issue

3 labs with UP (<85%)

Scheme 6: Kit Use and Performance





2024-25	Class I				Class II			
	One Lambda (n=34)	%	Werfen (n=19)	%	One Lambda (n=34)	%	Werfen (n=19)	%
601	Positive	100	Positive	100	Positive	100	Positive	100
602	Positive	100	Positive	100	Negative	84	Negative	100
603	Positive	100	Positive	100	Positive	100	Positive	100
604	***Positive***	**67**	**Negative**	**80**	Negative	100	Negative	87
605	Positive	100	Positive	100	Positive	100	Positive	100
606	Positive	100	Positive	94	Positive	100	Positive	100
607	Negative	94	Negative	100	Negative	94	Negative	94
608	Negative	84	Negative	100	Negative	77	Negative	94
609	Positive	100	Positive	94	Positive	100	Positive	100
610	***Negative***	**66**	**Negative**	**100**	Positive	100	Positive	100
611	Positive	100	Positive	100	Positive	97	Positive	100
612	Negative	97	Negative	94	Negative	97	Negative	100

Scheme 3

HLA Antibody Specificity Analysis

Scheme 3: HLA Antibody Specificity Analysis

Purpose

Assess participants ability to determine **specificity** of HLA antibodies

Satisfactory Performance

75% reports agree with consensus in distribution year

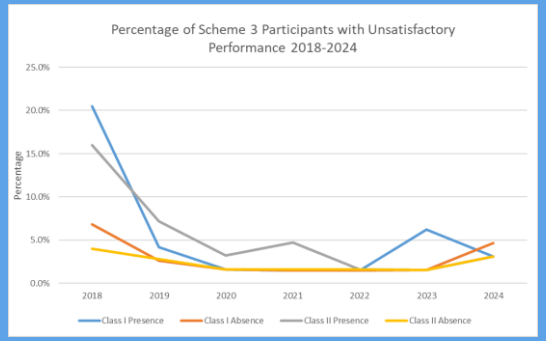
Consensus

At least 75% agreement on presence of HLA antibodies, 95% agreement on absense.

10 serum samples over 3 distributions

Scheme 3: Performance

Class I		2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)		73 (25)	70 (25)	64 (24)	65 (24)	65 (24)	64 (24)	63 (23)
Number with Unsatisfactory Performance (UK&I)	Presence	15 (1)	3 (0)	1 (0)	1 (0)	1 (0)	4 (0)	2 (0)
	Absence	5 (0)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)	3 (0)
% Unsatisfactory Performance	Presence	20.5%	4.2%	1.6%	1.5%	1.5%	6.3%	3.2%
	Absence	6.8%	2.6%	1.6%	1.5%	1.5%	1.5%	4.8%



Overall 3 labs with UP (0 UK&I)

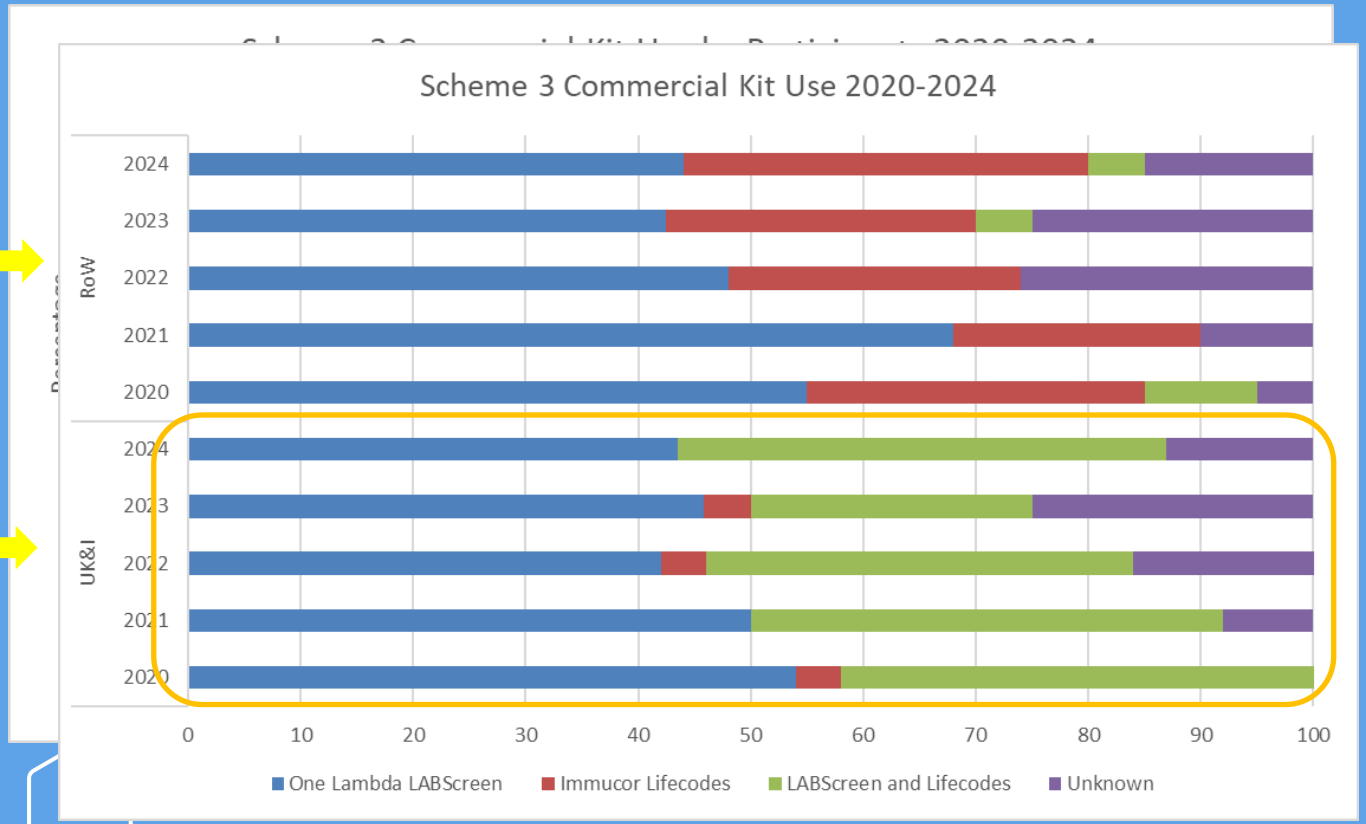
Class II		2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)		75 (25)	69 (25)	63 (24)	64 (24)	64 (24)	64 (24)	63 (23)
Number with Unsatisfactory Performance (UK&I)	Presence	12 (0)	5 (0)	2 (0)	3 (0)	1 (0)	1 (0)	2 (0)
	Absence	3 (0)	2 (0)	1 (0)	1 (0)	1 (0)	1 (0)	2 (0)
% Unsatisfactory Performance	Presence	16.0%	7.2%	3.2%	4.7%	1.6%	1.6%	3.2%
	Absence	4.0 %	2.8%	1.6%	1.6%	1.6%	1.6%	3.2%

Scheme 3: Unacceptable Performers 2024

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

	Class I		Class II		CAPA	Kit
Lab	Presence	Absence	Presence	Absence		
302	62%	53%	57%	72%	No reply	Werfen
1312	74%	55%	48%	52%	No reply	One Lambda
1412		58%			Interpretation issue (pos cut off)	Werfen

Scheme 3: Kit Use 2020-2024

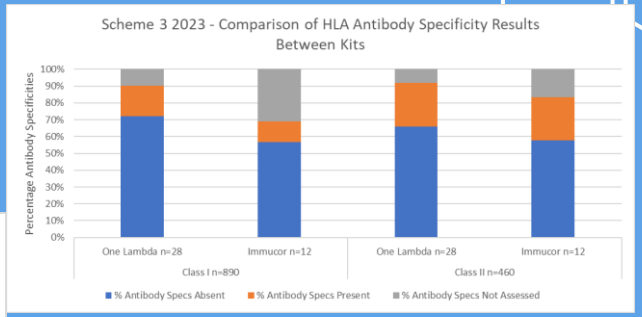


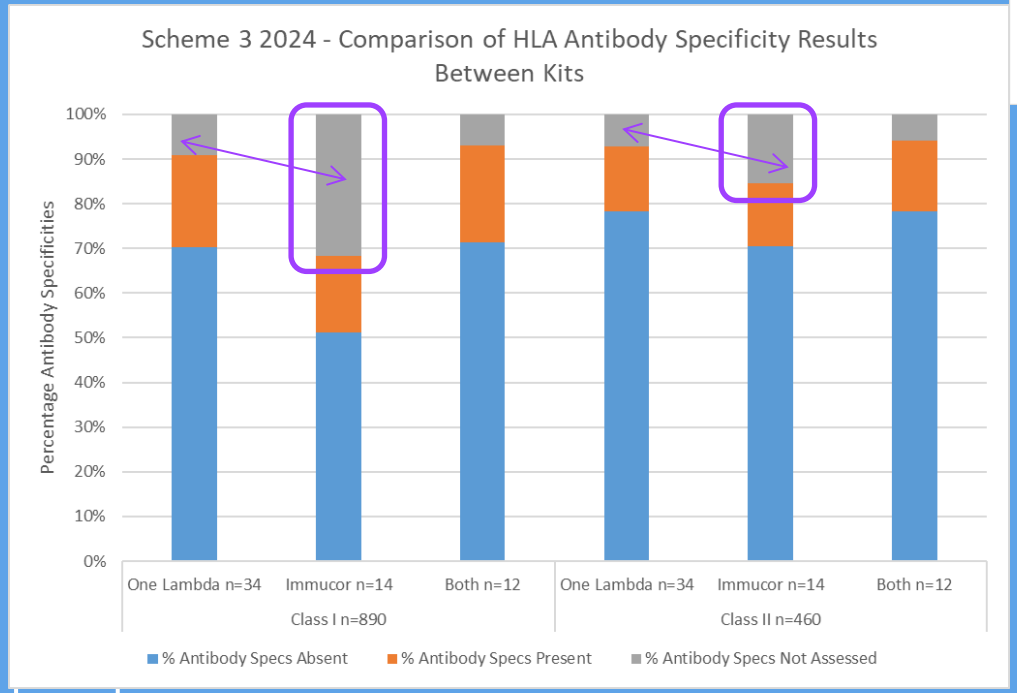
Overall OL kits are the most widely used

UK&I labs are more likely to use a combination of kits

Werfen only kit use more prevalent in RoW labs

Scheme 3: Results by Kit Use





Similar percentage of antibodies reach consensus present (orange) in both kits

Less concordance in 'absent' antibodies

Greater percentage of Class I antibodies classed as not assessed in Werfen group

Scheme 3: Kit Use and Performance

Average overall satisfactory performance for detecting the 'presence' and 'absence' of antibodies was marginally higher for users of both kits.

2024-25

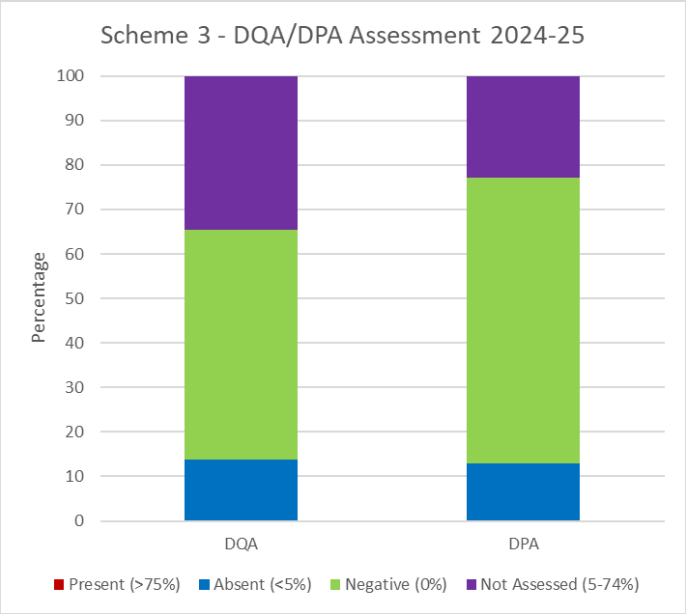
Average Performance	Class I			Class II		
	One Lambda (n=34)	Werfen (n=14)	Both (n=12)	One Lambda (n=34)	Werfen (n=14)	Both (n=12)
Presence	94.1%	86.5%	97.2% ↑	94.5%	89.7%	97.8% ↑
Absence	97.5%	94.2%	99.5% ↑	97.4%	95.3%	99.5% ↑

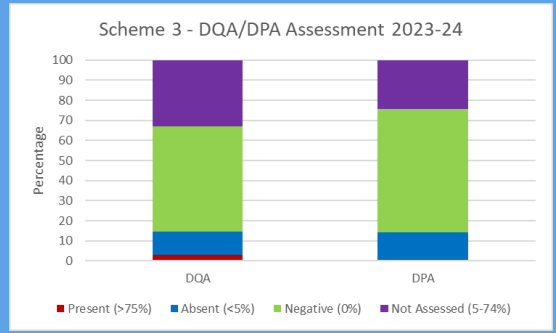
Scheme 3: DQA/DPA Antibody Reporting

Reporting of antibodies to HLA-DQA and –DPA is optional and not assessed.

Overall 42/63 (67%) report DQA, 38/63 (60%) report DPA

Previously 58% and 50%





An analysis of the data submitted for DQA and DPA antibodies in 2024-25 and 2023-24 was performed.

Large proportion of samples are negative or consensus absent.

No antibodies deemed positives.

Approx 25-30% not assessed.

Scheme 11

HPA Antibody Detection/Specification

Scheme 11: HPA Antibody Detection/Specification

Purpose

Assess participants ability to correctly determine pesence and specificty of HPA antibodies.

Satisfactory Performance

At least 75% of specificities in agreement with the consensus result in a distribution year.

Consensus

Presence of specificity determined by at least 75% agreement and absence determined by at least 95% agreement.

8 serum/plasma samples over 2 distributions

Scheme 11: Performance

- 1 Unsatisfactory Performers (0 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	35 (4)	39 (5)	42 (4)	43 (4)	43 (4)	43 (4)	44 (4)
Number with Unsatisfactory Performance (< 75%) (UK&I)	1 (0)	1 (0)	3 (0)	6 (0)	2 (0)	9 (0)	1 (0)
% Unsatisfactory Performance	2.9%	2.6%	7.1%	13.9%	4.5%	20.9%	2.3%

Scheme 11: HPA Antibody Detection/Specification

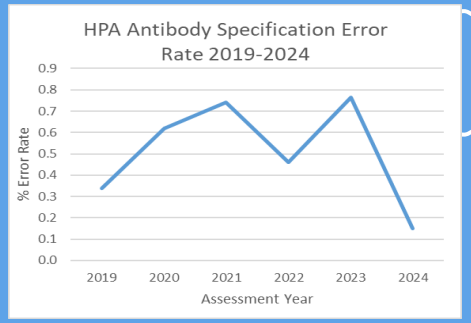
2024 Sample	HPA Detection	HLA Detection	Expected Result	HPA Antibody Consensus	
				Presence	Absence
1	97.6% Pos	86.5% Pos	HPA-5b	HPA 5b 97.6%	HPA GP1a/11a 97.2%%
2	100% Neg	94.4% Neg	HPA neg, HLA neg	N/A	N/A
3	100% Pos	100% Neg	HPA-5b, HLA neg	HPA 5b 100%	HPA GP1a/11a 97.2%
4	97.5% Pos	91.4% Neg	HPA-1a	HPA-1a 97.5%	HPA-3a 92.3%, 4b 90.9%, GPIIb/IIIa 91.7%
5	100% Neg	94.3% Neg	HPA neg, HLA neg	N/A	N/A
6	60% Neg	100% Pos	HPA-15b	N/A	HPA 15b 60% GP11b/111a 97.3%
7	97.2% Neg	94.3% Neg	HPA neg, HLA neg	N/A	HPA 2b 97.2%
8	97.1% Neg	94.3% Neg	HPA neg, HLA neg	N/A	HPA GP1b 97.1%

Scheme 11: Unacceptable Performers 2024

Lab	HPA Presence	HPA Absence	Samples reported	Method	Error
1378	50%	100%	8/8	Immucor/Werfen PakLx	No response

1 lab with UP (<75%)

Scheme 11: Analysis of Errors 2024



- Error rate extremely low (overall 0.15%) but errors often at clinically relevant polymorphisms.

- Errors found at HPA-1a (n=1, error rate 0.3%), 2b (n=1, error rate 0.3%), 5b (n=1, error rate 0.3%) and some glycoproteins.

Errors 2024	HPA-1a	HPA-1b	HPA-2a	HPA-2b	HPA-3a	HPA-3b	HPA-4a	HPA-4b	HPA-5a	HPA-5b	HPA-6a	HPA-6b	HPA-15a	HPA-15b	GP IIb/IIIa	GP Ia/IIa	GP Ib	GP Iv	CD109	Total
False Pos	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	2	1	0	0	5
False Neg	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	2
Total Errors	1	0	0	1	0	0	0	0	0	1	0	0	0	0	1	2	1	0	0	7
% Error Rate	0.3	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.3	0.0	0.0	0.0	0.0	0.3	0.7	0.4	0.0	0.0	0.15
Total Tested	320	304	288	288	312	312	284	268	320	328	108	108	120	120	292	292	280	264	120	4728

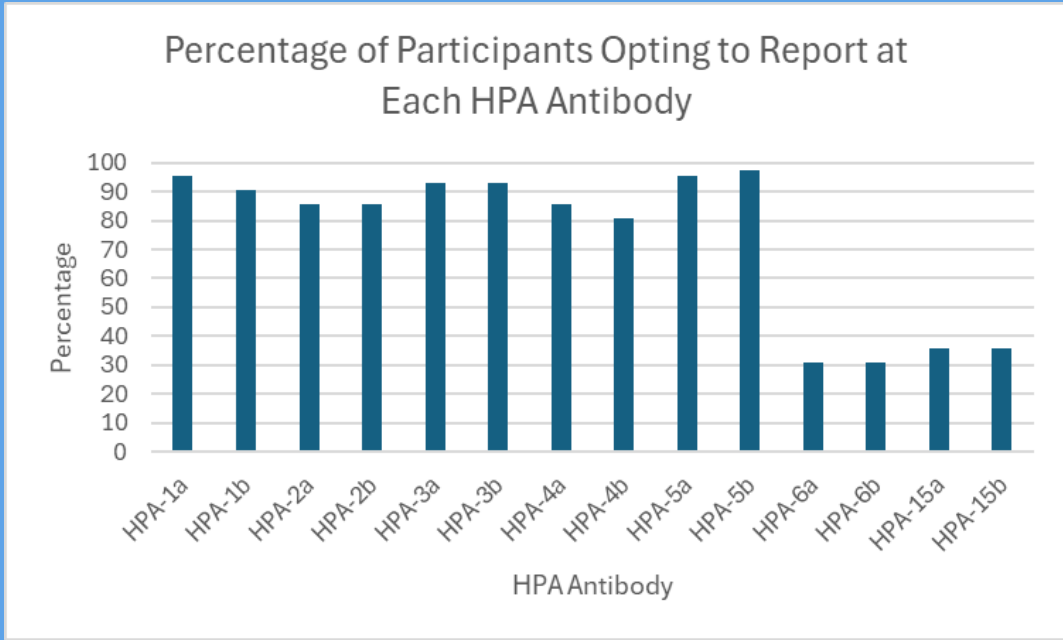
- False positive (n=5) more common than false negative (n=2) errors.

- Most labs had only 1 or 2 errors

Number of Errors	Number of Labs
1	3
2	2

Scheme 11: Selection of HPA Antibodies for Assessment

- Introduced in 2024-25
- Labs can select any/all HPA antibodies for assessment based on their clinical strategy



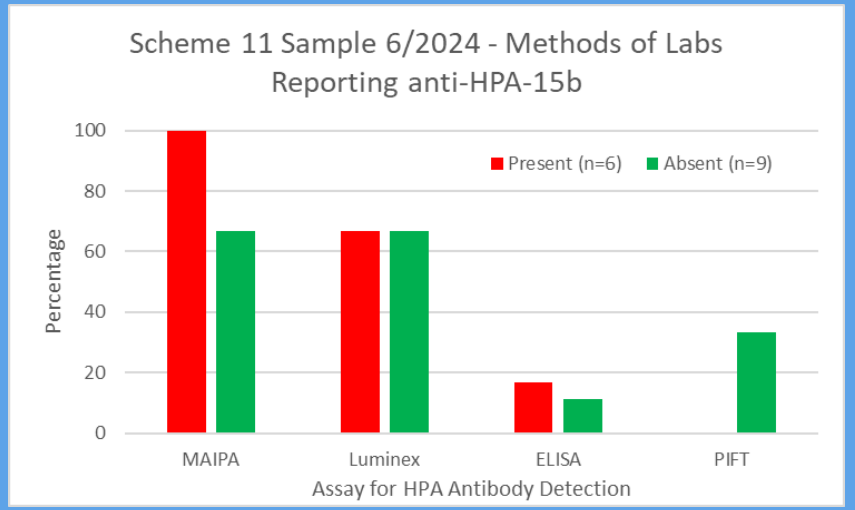
Scheme 11: HPA-15 Detection

- 36% (15/42) of labs selected to be assessed for HPA-15 antibody detection
- We sent NIBSC Standard HPA-15b
- Sample 6/2024:

  60% (9/15) reported HPA-15b absent

  40% (6/15) reported HPA-15b present

  100% reported HLA ab present



Key Data from the Schemes

Deborah Pritchard
UK NEQAS for H&I Director

Scheme 1A

HLA Phenotyping

Scheme 1A: HLA Phenotyping

Purpose

Assess participants ability to use serological and supplementary methods to correctly identify HLA phenotype

Satisfactory Performance

9 or more complete HLA phenotypes in agreement with consensus per distribution year.

Consensus

At least 75% agreement on each specificity.

10 blood samples over 5 distributions

Scheme 1A: Performance

- 0 labs with unsatisfactory performance

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	38 (6)	38 (5)	34 (4)	33 (2)	28 (1)	23 (0)	19 (0)
Number with Unsatisfactory Performance (< 90%) (UK&I)	6 (1)	8 (1)	3 (1)	2 (0)	2 (0)	2 (0)	0 (0)
% Unsatisfactory Performance	15.8%	21.1%	8.8%	6.1%	7.1%	8.7%	0%

Scheme 1A: 2024 Incorrect Assignments

3/190 (1.6%) incorrect HLA types in 2024 reported by 3 labs:

- 2 reports that contained broad not split specificity (e.g. B40 v B60)
- 1 clerical/typo error

0 labs with unsatisfactory performance

Scheme 1A: 2024 Incorrect Assignments (not resulting in UPs)

Sample	ID	Consensus	Report
1A 03	268	A1, A26; B38, B57	A1, A26; B68, B57
1A 05	147 + 159	A3, A23; B49, B65	A3, A23; B49, B14

Scheme 4A1

HLA Typing at 1st Field Resolution

Scheme 4A1: HLA Typing at 1st Field Resolution

Purpose

Assess participants ability to correctly determine HLA genotypes at the 1st field resolution.

Satisfactory Performance

9 or more full HLA types in agreement with consensus/reference result in a distribution year.

Consensus

At least 75% agreement on each allele. When consensus is not met, a reference result is used. Reference result is always used for DPB1 assessment

10 blood samples over 3 distributions

Scheme 4A1: Performance

- 6 labs with unsatisfactory performance (2 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	105 (28)	100 (28)	88 (26)	82 (25)	81 (25)	81 (25)	84 (24)
Number with Unsatisfactory Performance (< 90%) (UK&I)	15 (1)	4 (1)	8 (0)	6 (1)	7 (0)	11 (1)	6 (2)
% Unsatisfactory Performance	14.3% (3.6%)	4% (3.6%)	9.1% (0%)	7.3% (4%)	8.4% (0%)	13.6% (4%)	7.1% (8.3%)

Scheme 4A1: 2024-25 Incorrect Assignments

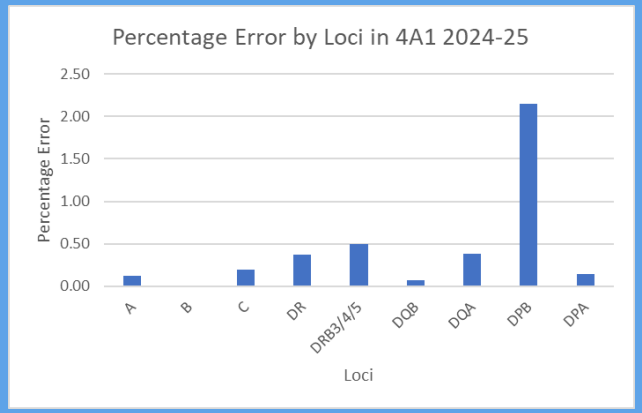
39/11493 (0.34%) errors reported by 20 different labs (3 UK&I) – last year 0.26%

29 samples contained an error:

- 21 samples with incorrect assignments *e.g. C*13 rather than C*07*
- 3 samples with nomenclature issue
- 3 missed assignment (reported homozygous when heterozygous)
- 2 samples with DRB3/4/5 presence/absence reported incorrectly

24 (83%) HLA types with one error
5 (17%) HLA types with multiple errors

14 (70%) labs made 1 error
3 (15%) labs made 2 errors
3 (15%) lab made 3 errors



Scheme 4A1: Unacceptable Performers 2024

Lab	Sample	Error	CAPA Response
41	01+02+03	Multiple issues	Transcription error / interpretation error
6	03+04+07	Incorrect DPB1* assignments	Limitations of kit
172	03+06+08	A* and DQB1* missed / assignment errors	Procedural error (new method)
1412	05+10	DQA1* and DPA1* and DPB1* missed assignments	Procedural error (reagent issue)
1418	07+09	Reporting errors	Transcription errors (staffing levels)
1443	09+10	Multiple reporting errors	EQA specific result entry errors

Scheme 4A1i

Interpretive HLA Genotype

Scheme 4A1: Interpretive HLA Genotype

Purpose

Assess participants ability to correctly interpret their 4A1 genotype result to the 'split' specificity level.

Satisfactory Performance

9 or more full HLA types in agreement with consensus/reference result in a distribution year.

Consensus

At least 75% agreement on each specificity. When consensus is not met, a reference result is used.

10 HLA genotypes from Scheme 4A1

Scheme 4A1i: Performance

- 5 lab with unsatisfactory performance (0 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	40 (21)	44 (22)	44 (22)	42 (21)	40 (21)	40 (21)	41 (20)
Number with Unsatisfactory Performance (< 90%) (UK&I)	6 (0)	8 (1)	6 (2)	5 (1)	2 (0)	1 (0)	5 (0)
% Unsatisfactory Performance	15.0%	18.1%	13.6%	11.9%	5.0%	2.5%	12.2%

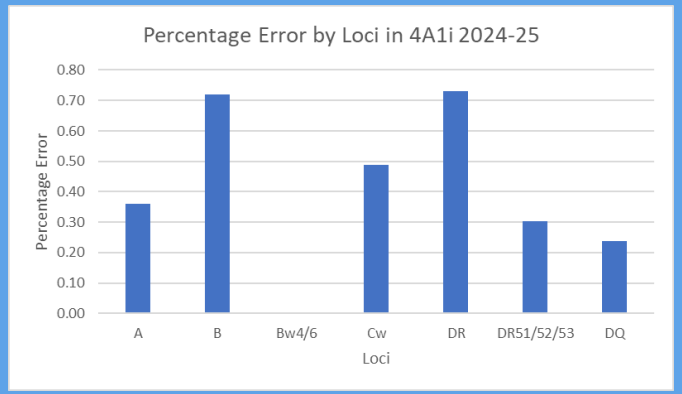
Scheme 4A1i: 2024-25 Incorrect Assignments

- 24/5778 (0.42%) incorrect results reported by 7 different labs (0 UK&I) – last year 0.35%

2 (29%) labs made 1 error
5 (71%) labs made 2-4 errors

- 17 samples contained an error:
  - 5 reporting at broad not split specificity level
  - 3 samples with incorrect assignments
  - 3 samples with missing assignment (reported homozygous when heterozygous)
  - 3 sample with incorrect uses of nomenclature
  - 3 samples with errors at presence/absence of DR51/52/53

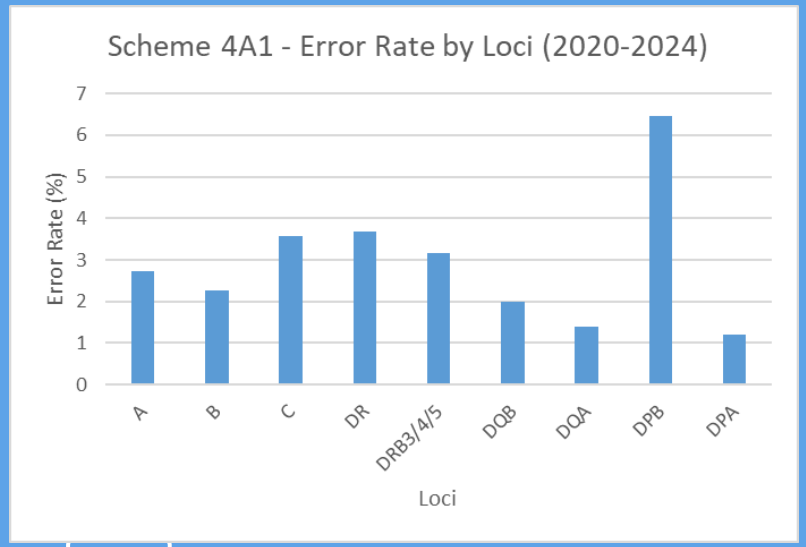
12 (71%) HLA types with single errors
5 (29%) HLA type with multiple errors

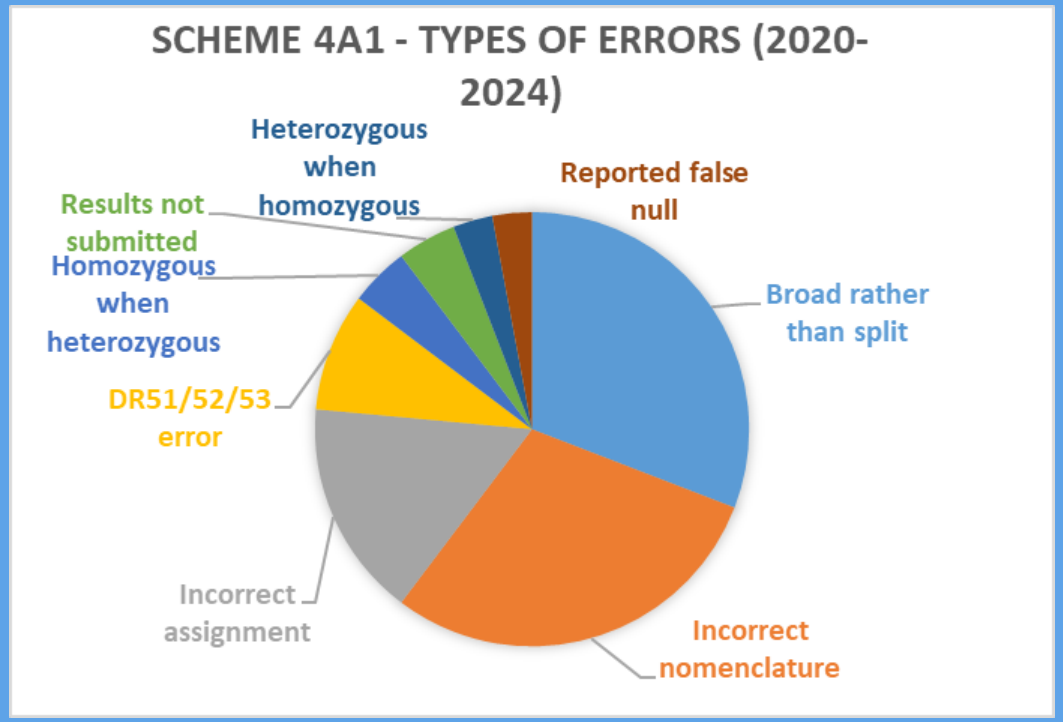


Scheme 4A1i: Unacceptable Performers 2024

Lab	Sample	Error	CAPA Response
1418	01-03 + 07	Broads instead of splits/multiple reporting errors	Staff training / interpretation
111	02+03+05	Incorrect nomenclature	EQA specific reporting errors (new participant)
1412	02+05	Multiple errors	Transcription errors
1372	02+06	Multiple errors	No response
1433	05+07	Multiple errors	Staff training / interpretation

Scheme 4A1: Types of Errors Over 5 Years



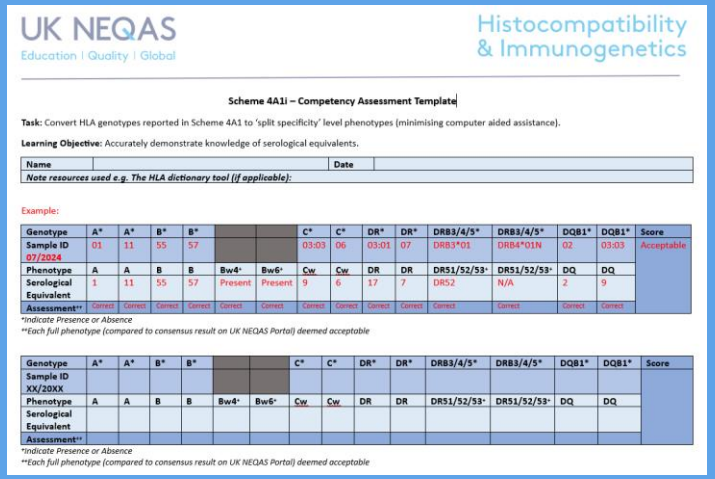


Scheme 4A1i: Serological Equivalents

- 4A1i Interpretative HLA Genotyping, which allows participants to translate genotypes to phenotypes
- Participants are expected to report to the ‘split’ specificity level using serological nomenclature, e.g. HLA-DQB1*03:01 should be reported as DQ7 (DQ3)
- Knowledge and exposure of phenotyping and converting between genotypes and phenotypes may no longer be so commonplace

  Reliance on LIMS/analysis software

  No longer perform phenotyping
- Errors common due to reporting issues (broad rather split or using incorrect nomenclature)
- CAPA repeatedly cite issues due to staff training and knowledge
- Encourage utilisation of 4A1i for competency assessment



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Scheme 4A1i – Competency Assessment Template

Task: Convert HLA genotypes reported in Scheme 4A1 to ‘split specificity’ level phenotypes (minimising computer aided assistance).

Learning Objective: Accurately demonstrate knowledge of serological equivalents.

Name		Date	
Note resources used e.g. The HLA dictionary tool (if applicable):			

Example:

Genotype	A*	A*	B*	B*			C*	C*	DR*	DR*	DRB3/4/5*	DRB3/4/5*	DQB1*	DQB1*	Score
Sample ID 07/2024	01	11	55	57			03:03	06	03:01	07	DRB3*01	DRB4*01N	02	03:03	Acceptable
Phenotype	A	A	B	B	Bw4*	Bw6*	Cw	Cw	DR	DR	DR51/52/53*	DR51/52/53*	DQ	DQ	
Serological Equivalent	1	11	55	57	Present	Present	9	6	17	7	DR52	N/A	2	9	
Assessment**	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	Correct	

*Indicate Presence or Absence
**Each full phenotype (compared to consensus result on UK NEQAS Portal) deemed acceptable

Genotype	A*	A*	B*	B*			C*	C*	DR*	DR*	DRB3/4/5*	DRB3/4/5*	DQB1*	DQB1*	Score
Sample ID XX/20XX															
Phenotype	A	A	B	B	Bw4*	Bw6*	Cw	Cw	DR	DR	DR51/52/53*	DR51/52/53*	DQ	DQ	
Serological Equivalent															
Assessment**															

*Indicate Presence or Absence
**Each full phenotype (compared to consensus result on UK NEQAS Portal) deemed acceptable

UK NEQAS have developed a template:
https://ukneqashandi.org.uk/app/uploads/2025/03/Scheme-4A1i-Template.docx

Scheme 4A2

HLA Typing to 2nd or 3rd Field Resolution

Scheme 4A2: HLA Typing to 2nd or 3rd Field Resolution

Purpose

Assess participants ability to correctly determine HLA type to 2nd or 3rd field.

Consensus

At least 75% agreement on each allele. If consensus is not met, a reference result is used.

Satisfactory Performance

9 or more full HLA types in agreement with consensus/reference genotype in a distribution year.

10 blood samples over 3 distributions

Scheme 4A2: Performance

- 46/67 participants registered for 2nd field
- 22/67 participants registered for 3rd field

- 8 labs with unsatisfactory performance (1 UK&I)

7/8 labs with unsatisfactory performance completed CAPA

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	63 (20)	62 (20)	64 (20)	63 (22)	61 (23)	65 (23)	67 (23)
Number with Unsatisfactory Performance (< 90%) (UK&I)	9 (2)	9 (1)	7 (0)	6 (0)	4 (0)	9 (2)	8 (1)
% Unsatisfactory Performance	14.3%	14.5%	11.0%	11.1%	6.5%	13.8% (8.7%)	11.9% (4.3%)

Scheme 4A2: Incorrect Assignments: 2nd Field

33/8846 (0.37%) incorrect HLA alleles reported by 12 labs (0 UK&I) – last year (0.55%)

- 14 reports of errors at the 2nd field

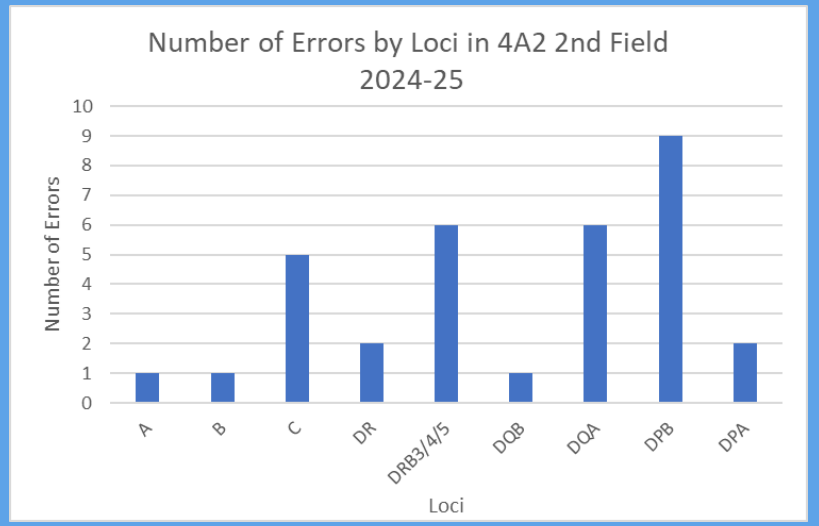
*e.g. DQA1*03:02 rather than DQA1*03:03*

- 3 samples with alleles in a string that should have been resolved
- 3 reports of the wrong HLA type
- 3 reports of incorrect nomenclature

e.g. the use of P / G groups

7 (58%) labs made 1 error
5 (42%) labs made 3-4 errors

17 (74%) HLA types with a single error
6 (26%) HLA types with multiple errors



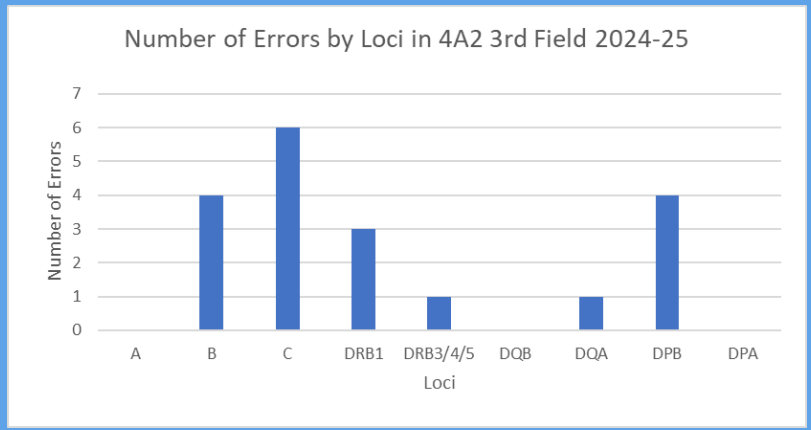
Scheme 4A2: Incorrect Assignments: 3rd Field

19/3560 (0.53%) incorrect HLA alleles reported by 7 labs (1 UK&I) – last year (0.81%)

- 5 errors at 2nd field e.g. C*03:03:01 rather than 03:321:XX
- 5 incorrect assignments e.g. C*04:01:01 rather than C*05:01:01
- 3 errors at 3rd field e.g. DPB1*03:01:03 rather than DPB1*03:01:01
- 1 report of unresolved ambiguities e.g. reporting G groups

4 (57%) labs made 1 error
2 (29%) labs made 2 errors
1 (14%) labs made 3+ errors

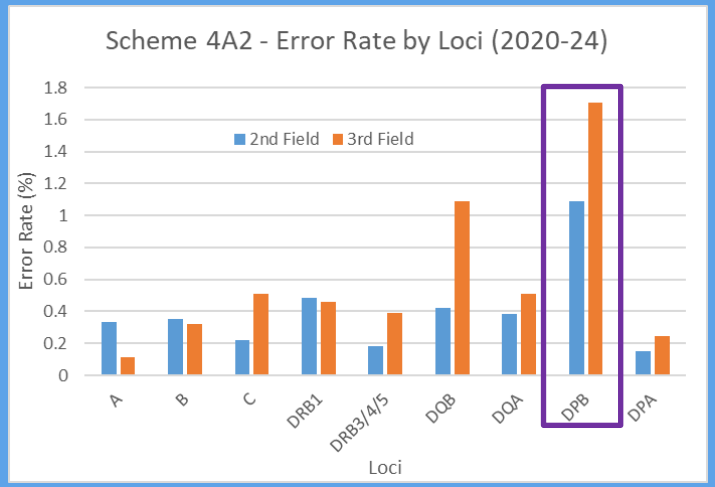
4 (29%) HLA types with multiple errors
10 (71%) HLA types with a single error

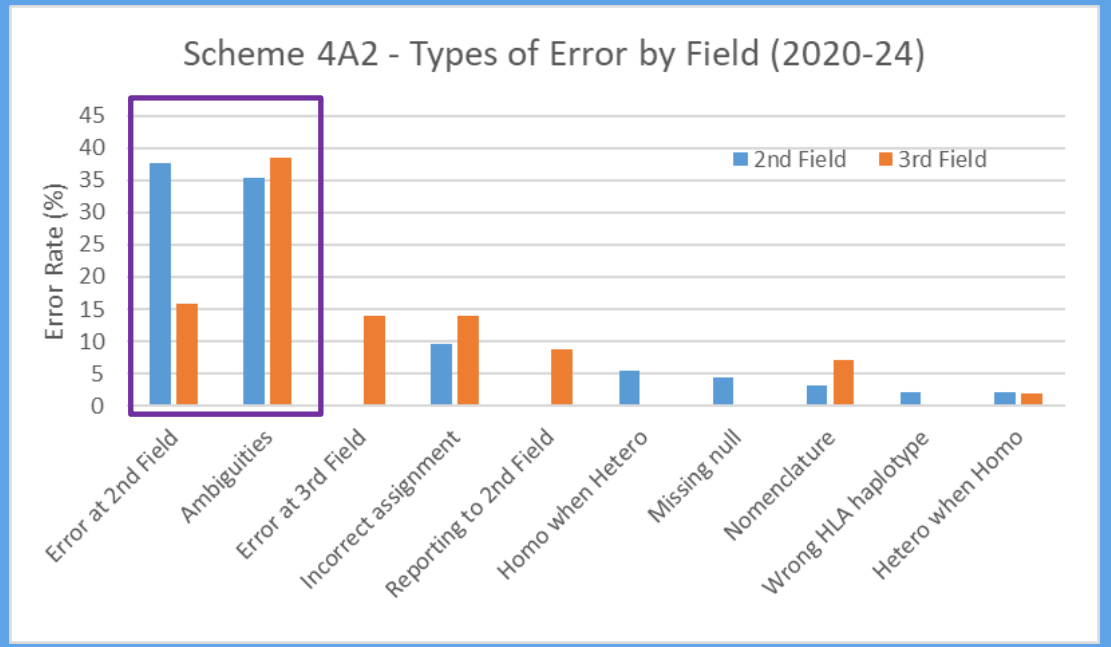


Scheme 4A2: Unacceptable Performers 2024

Lab	Sample	Error	Field	CAPA Response
284	01-03	Reported G groups	2nd	EQA Specific Reporting issue
29	04+05	3rd Field: 4A2 04/2024: Reported B*40:01:01 homozygous, consensus B*40:01:02 homozygous 4A2 05/2024: Reported DPB1*03:01:03, consensus DPB1*03:01:01	3rd	Transcription error
112	02+05+08+10	2nd Field: 4A2 02/2024: Reported A*01:01, 01:03, consensus A*01:01 homozygous 4A2 05/2024: Reported C*03:03, consensus C*03:321 4A2 08/2024: Reported DQA1*03:02, consensus DQA1*03:03 4A2 10/2024: Reported DQA1*04:01, consensus DQA1*04:02	2nd	Kit resolution issue
134	02+07+08+09	3rd Field: 4A2 02/2024: Reported DPB1*02:01:01, consensus DPB1*02:01:02 4A2 07/2024: Reported C*04:01:01, consensus C*05:01:01 4A2 08/2024: Reported DPB1*01:03:01, 02:01:02, consensus DPB1*01:01:01, 04:01:01 4A2 09/2024: Reported incomplete allele (C*07:02:0), consensus C*07:02:01, reported G groups for DRB1*	3rd	No reply
309	03+07+08+09	3rd Field: 4A2 03/2024: Reported DRB3*01:01:02 homozygous, consensus DRB3*01:01:02, 03:01:01 4A2 07/2024: Reported B*15:01:01, consensus B*35:01:01 4A2 08/2024: Reported DRB1*01:01:01 and DQA1*03:01:01, consensus DRB1*03:01:01 and DQA1*03:03:01 4A2 09/2024: Reported B*07:01:01, consensus B*07:02:01	3rd	Transcription error
1433	05+06+09	2nd Field: 4A2 05/2024: Reported C*03:03, consensus C*03:321 4A2 06/2024: Reported B*42:02, consensus B*44:02 4A2 09/2024: Reported DRB1*11:04, consensus DRB1*11:01	2nd	Transcription error / Kit resolution issue
185	08-10	2nd Field: 4A2 08/2024: Reported Unacceptable ambiguities DPB1*677:01/875:01N/1086:01 4A2 09/2024: Reported Unacceptable ambiguities DPB1*677:01/875:01N/1086:01 4A2 10/2024: Reported Unacceptable ambiguities DPB1*727:01/1285:01N, 677:01/875:01N/1086:01	2nd	Unacceptable ambiguities / Kit resolution issue
223	07+09+10	2nd Field: 4A2 07/2024: Reported DRB1*15:02, consensus DRB1*15:01 4A2 09/2024: Reported DQA1*04:01, consensus DQA1*04:05 4A2 10/2024: Reported DQA1*04:01, consensus DQA1*04:02	2nd	Kit resolution issue

Scheme 4A2: Types of Errors Over 5 Years





Scheme 9

KIR Genotyping

Scheme 9: KIR Genotyping

Purpose

Assess participants ability to correctly determine the presence or absence of specific KIR genes.

Satisfactory Performance

9 or more full KIR genotypes in agreement with consensus/reference genotype in a distribution year.

Consensus

At least 75% agreement on the presence/abesence of each gene. Reference type used where consensus is not met

10 blood samples over 2 distributions

Scheme 9: 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

Scheme 9: Performance

- 1 lab with unsatisfactory performance

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	9 (1)	12 (1)	12 (1)	15 (1)	15 (1)	15 (1)	13 (1)
Number with Unsatisfactory Performance (UK&I)	1 (0)	3 (0)	0 (0)	1 (0)	0 (0)	1 (0)	1 (0)
% Unsatisfactory Performance	11.1%	25%	0%	6.7%	0%	6.7%	7.7%

Scheme 9: Unacceptable Performers 2024

Lab	Polymorphism	Error	CAPA Response
332	3DS1 & 2DS5 2DP1	False Pos False Neg	Interpretation issues (staff training)

Scheme 10

HPA Genotyping

Scheme 10: HPA Genotyping

Purpose

Assess participants ability to correctly determine HPA polymorphisms.

Satisfactory Performance

9 or more full HPA types in agreement with consensus/reference genotype in a distribution year.

Consensus

At least 75% agreement on the presence/abesence of each allele. Reference type used where consensus is not met

10 blood samples over 2 distributions

Scheme 10: HPA Genotyping

- Participants able to report any of the following: *HPA-1, HPA-2, HPA-3, HPA-4, HPA-5, HPA-6, HPA-15*
  - 35/38 reported HPA-1, 2 , 3, 4, 5 and 15
  - 30/38 labs reported HPA-6
- Also able to report any other HPA polymorphisms detected, *for information*

Scheme 10: HPA Genotyping

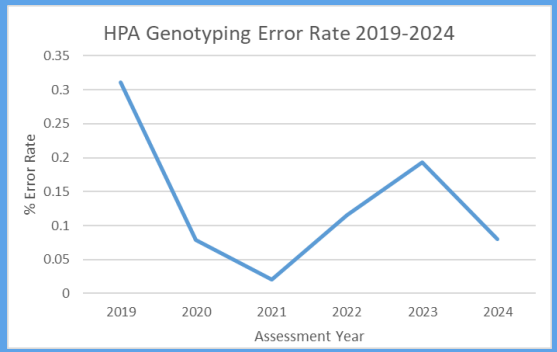
- 0 lab with unsatisfactory performance

	2017	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	15 (5)	37 (6)	38 (6)	40 (0)	38 (6)	39 (6)	39 (6)	38 (6)
Number with Unsatisfactory Performance (< 100%) (UK&I)	1 (0)	1 (0)	3 (0)	0 (0)	0 (0)	1 (0)	1 (0)	0 (0)
% Unsatisfactory Performance	6.7%	2.7%	7.9%	0%	0%	2.6%	2.6%	0%

Scheme 10: Errors in HPA Genotypes 2024

- 3 labs made 1 error
- Error rate extremely low 0.08% but errors at some clinically relevant polymorphisms.
- Errors found at HPA-3b (n=2), HPA-1b (n=1), HPA-4b (n=1)

Errors 2024	HPA-1 a	HPA-1 b	HPA-2 a	HPA-2 b	HPA-3 a	HPA-3 b	HPA-4 a	HPA-4 b	HPA-5 a	HPA-5 b	HPA-6 a	HPA-6 b	HPA-15 a	HPA-15 b	Total
False Neg	0	1	0	0	0	0	0	1	0	0	0	0	0	0	2
False Pos	0	0	0	0	0	2	0	0	0	0	0	0	0	0	2
Total Error	0	1	0	0	0	2	0	1	0	0	0	0	0	0	4
% Error	0.0	0.3	0.0	0.0	0.0	0.5	0.0	0.3	0.0	0.0	0.0	0.0	0.0	0.0	0.08
Total Tested	375	375	375	375	375	375	345	345	375	375	295	295	375	375	5030



- Even split of false positive (n=2) and false negative (n=2) errors.

Scheme 1B

HLA-B27 Testing

Scheme 1B: HLA-B27 Testing

Purpose

Assess participants ability to correctly determine HLA-B27/2708/B*27 status.

Satisfactory Performance

Making 10/10 reports that are in agreement with consensus in a distribution year.

Consensus

At least 75% agreement on B27 status. Reference type used where consensus is not met

10 blood samples sent over 5 distributions

Scheme 1B: Performance

- 16 labs with unsatisfactory performance (3 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	133 (54)	133 (53)	141 (52)	141 (50)	139 (49)	134 (50)	131 (49)
Number with Unsatisfactory Performance (< 100%) (UK&I)	10 (3)	4 (1)	12 (2)	3 (0)	8 (0)	11 (3)	16 (3)
% Unsatisfactory Performance (UK&I)	7.5% (5.5%)	3.0% (1.9%)	8.5% (3.8%)	2.1% (0%)	5.7% (0%)	8.2% (6%)	12.2% (6%)

- 5/10 samples distributed were HLA-B27 positive

Scheme 1B: 2024 Incorrect Assignments

Sample	Result	Lab Number	Technique	HLA Type	Lab Identified Caus
1B 02	False neg	1392 1435	Molecular Serological	B27 B44	No reply No reply
1B 03	False neg	40	Serological	B27 B40	Procedural/processing errors
1B 05 & 06	No results	1441	Serological	B27 B40 B27 B40	No reply
1B 06	False neg	1435 31 225 357	Serological Serological Molecular Serological	B27 B40	No reply Technical/testing issue Kit/interpretation/reagent issue No reply
1B 07 & 08	False pos/false neg	32	Molecular	B*27:08 B35 B7 B40	Sample mix up
1B 07	False neg	1431 106 324 409 1308 1312	Molecular Serological Serological Serological Serological Serological	B*27:08 B35	Reporting error Interpretation/reagent issue Interpretation/cut off values Interpretation issues No reply No reply
1B 09	False pos	324	Serological	B7 B35	Interpretation/cut off values
1B 09 & 10	No results	1402	Unknown	B7 B35 B7 B15	No reply

- 88% false negative, 12% false positive
- 70.5% errors involved serological techniques
- Overall 73% use molecular methods, 27% use serological methods

7/11 labs with unsatisfactory performance completed CAPA

Scheme

5A

HFE Typing

Scheme 5A: HFE Testing

Purpose

Assess participants ability to correctly determine HFE mutations.

3 mutations assessed:

- Codon 63: Histidine63Aspartic acid (H63D)
- Codon 282: cysteine282tyrosine (C282Y)
- Codon 65: Serine63Cysteine (S65C)

Satisfactory Performance

10 reports in agreement with consensus/reference result in a distribution year.

Consensus

At least 75% agreement on each HFE mutation. Reference type used where consensus is not met

10 donor samples sent over 3 distributions

Scheme 5A: Performance

- 3 labs with unsatisfactory performance (1 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	58 (44)	51 (38)	49 (36)	45 (32)	37 (27)	38 (26)	37 (25)
Number with Unsatisfactory Performance (< 100%) (UK&I)	0 (0)	2 (1)	1 (1)	1 (1)	4 (3)	1 (1)	3 (1)
% Unsatisfactory Performance	0%	3.9% (2.6%)	2.0% (2.8%)	2.2% (3.1%)	10.8% (11.1%)	2.6% (3.8%)	8.1% (4%)

CAPA responses (n=2/3)

- Sample mix up – 33.3%
- Transcription error – 33.3%
- No reply – 33.3%

Scheme 7

HLA-B*57:01 Typing for Drug Hypersensitivity

Scheme 7: HLA-B*57:01 Typing for Drug Hypersensitivity

Purpose

Assess participants ability to correctly determine HLA-B*57:01 status

Satisfactory Performance

Making 10 sample reports in agreement with the consensus/reference result in a distribution year.

Consensus

At least 75% agreement on the status of HLA-B*57:01. Reference result used when consensus not met.

10 blood samples over 3 distributions

Scheme 7: Performance

- 1 lab with unacceptable performance

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	67 (27)	67 (27)	67 (27)	64 (25)	52 (18)	50 (18)	46 (18)
Number with Unacceptable Performance (< 100%) (UK&I)	2 (0)	0 (0)	2 (0)	1 (1)	3 (0)	2 (0)	1 (0)
% Unsatisfactory Performance	3.0%	0.0%	3.1%	1.6%	5.8%	4.0%	2.2%

- 5/10 samples distributed were HLA-B*57:01 positive

Scheme 7: Unacceptable Performers 2024

Lab	Sample	Error	CAPA Response
308	03	False neg	No reply

New for 2025-26

Scheme 7: UPDATE

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

HLA-related Pharmacogenetics

NEW ASSESSMENT OPTIONS

(NO ADDITIONAL CHARGES)

Abacavir Hypersensitivity - **B*57:01**
Allopurinol Hypersensitivity - **B*58:01**
Carbamazepine Hypersensitivity - **A*31:01, B*15:02**
Oxcarbazepine Hypersensitivity - **B*15:02**
Lamotrigine Hypersensitivity - **B*15:02**
Flucloxacillin Hypersensitivity - **B*57:01**
Phenytoin Hypersensitivity - **B*15:02**
Tebentafusp Suitability - **A*02:01**

All scheme 7 material will now be previously frozen whole blood

Scheme 8

HLA Genotyping for Coeliac and other HLA Associated Disease

Scheme 8: HLA Genotyping for Coeliac and other HLA Associated Disease.

Purpose

Assess participants ability to correctly determine HLA type associated with various diseases e.g. coeliac disease, narcolepsy.

Satisfactory Performance

Making 10 sample reports in agreement with the reference genotype in a distribution year.

Assessment

Lab results reported in format identical to clinical report. Reference HLA result used for assesment.

10 blood samples over 3 distributions

Scheme 8: Performance

- 10 Unsatisfactory Performers (1 UK&I)

	2018	2019	2020	2021	2022	2023	2024
Number of Participants (UK&I)	52 (10)	50 (11)	55 (12)	55 (10)	54 (11)	57 (11)	55 (11)
Number with Unsatisfactory Performance (< 100%) (UK&I)	14 (4)	13 (2)	17 (5)	12 (2)	25 (5)	18 (2)	10 (1)
% Unsatisfactory Performance	27% (40%)	26% (18%)	31% (42%)	22% (20%)	46.3% (45%)	31.6% (18%)	18.2% (9.1%)

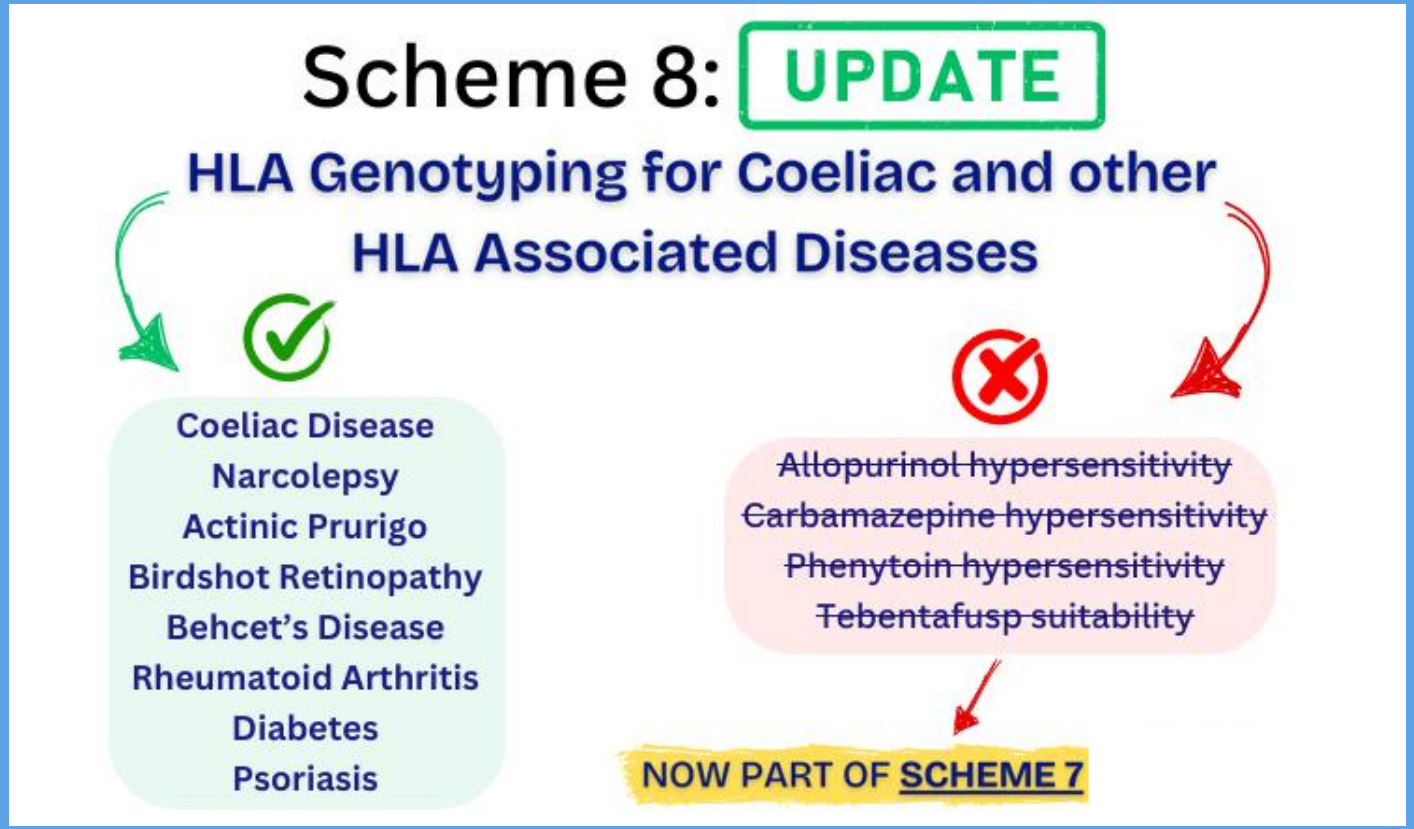
CAPA responses (n=8/10)

- Transcription errors – 46%
- Kit interpretation error – 17%
- Reporting error – 7%
- Procedural error – 7%
- Unknown – 23%

Scheme 8: Unacceptable Performance by Disease

Disease	HLA Association	Number of Participants	No. of Participants with Unacceptable Performance
Coeliac	DQ2.5, DQ8, DQ2.2	51	9 (18%)
Narcolepsy	DQB1*06:02	24	0
Actinic Prurigo	DRB1*04:07	5	0
Birdshot Retinopathy	A*29	14	0
Behçet's	B*51	21	0
Rheumatoid Arthritis	DRB1*04	6	0
Diabetes	DR3, DR4	7	1 (14%)
Psoriasis	C*06	6	0
Allopurinol Hypersensitivity	B*58	8	0
Carbamazepine	A*31:01	9	0
Phenytoin	B*15:02	3	0
Tebentafusp	A*02:01	3	0

New for 2025-26



Scheme 8: Interpretative Comments

- Interpretation of the genotype in terms of predisposition to CD not currently assessed

iv. DQ2.5 heterozygous (cis or trans)

HLA genotype result:
HLA-DQA1*05, DQB1*02
HLA-DQA1*X, DQB1*X
OR
HLA-DQA1*05, DQB1*X
HLA-DQA1*X, DQB1*02

HLA CD heterodimer result:
HLA-DQB1*02, DQA1*05 (DQ2.5) positive
HLA-DQB1*02, DQA1*02 (DQ2.2) negative
HLA-DQB1*03:02 (DQ8) negative

Genotype comment: Positive for DQ2.5 (heterozygous)

Interpretative comment <1>: This individual has a genotype which is associated with coeliac disease

Interpretative comment <2>: This presence of DQA1*05, DQB1*02 (HLA-DQ2.5) has a strong association with coeliac disease in patients where laboratory tests or symptoms or endoscopic features suggest coeliac disease.

Pritchard D, Anand A, De'Ath A, Lee H, Rees MT. UK NEQAS and BSHI guideline: Laboratory testing and clinical interpretation of HLA genotyping results supporting the diagnosis of coeliac disease. Int J Immunogenet. 2024 Jan;51 Suppl 1:3-20. doi: 10.1111/iji.12649. Epub 2023 Dec 28. PMID: 38153308.

Scheme 8: Assessment of Interpretative Comments

- Pilot assessment based on points:

Coeliac Disease	Outcome	Improvement Point	Assessment
HLA Genotype	HLA genotype aligned to reference type	N/A	Acceptable
	Result not reported	N/A	Unacceptable
	HLA genotype not aligned to reference type	N/A	Unacceptable
Interpretation (>1 improvement point = unacceptable)	*HLA Comments / Correct Nomenclature Used	0	Acceptable
	*Incorrect HLA Comments / Incorrect Nomenclature Used	1	Unacceptable
	Risk of CD Present/Absent Correctly Identified	0	Acceptable
	Risk of CD Present/Absent Incorrectly Identified	1	Unacceptable
	*Stratification of Risk Identified	0	Acceptable
	*Stratification of Risk Incorrectly Identified	1	Unacceptable
	Diagnostic Disclaimer Applied Correctly	0	Acceptable
	Diagnostic Disclaimer Not Applied or Incorrect	0.5	Acceptable

Pritchard D, Anand A, De'Ath A, Lee H, Rees MT. UK NEQAS and BSHI guideline: Laboratory testing and clinical interpretation of HLA genotyping results supporting the diagnosis of coeliac disease. Int J Immunogenet. 2024 Jan;51 Suppl 1:3-20. doi: 10.1111/iji.12649. Epub 2023 Dec 28. PMID: 38153308.

Scheme 8: Coeliac Disease – examples

DRB1*07:01, 15:01; DQB1*02:02, 06:02; DQA1*01:02, 02:01
(DQ2.2, DQ6.1)

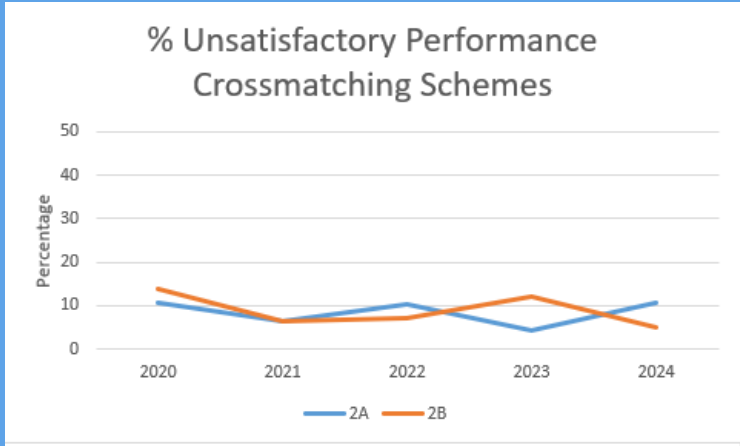
ID	Example of Interpretative Comment	Assessment
1	Positive for DQ2.2. This individual carries HLA-DQA1*02, DQB1*02:02 (DQ2.2) that has a weak association with coeliac disease in patients where laboratory test or symptoms or endoscopic features suggest coeliac disease.	✓ / ✗
2	90-95% of coeliac patients are HLA DQ2 and DQ8 positive.	✓ / ✗
3	The presence of HLA-DQ2 is associated with, but not diagnostic for, coeliac disease. HLA-DQ2 is present in about 21% of Caucasians in the normal population.	✓ / ✗
4	Positive	✓ / ✗

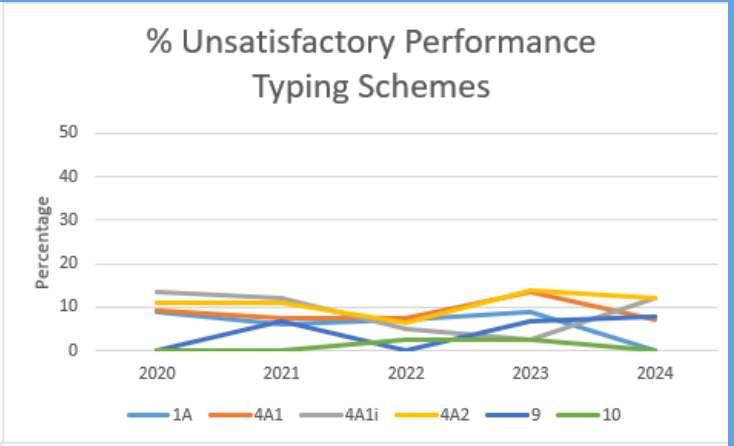
Patient genotype associated with coeliac disease.
Weak association with coeliac disease.
In patients where laboratory tests or symptoms or endoscopic features suggest coeliac disease.
The presence of an associated HLA genotype does not confer a diagnosis of coeliac disease and has a low positive predictive value for coeliac disease.

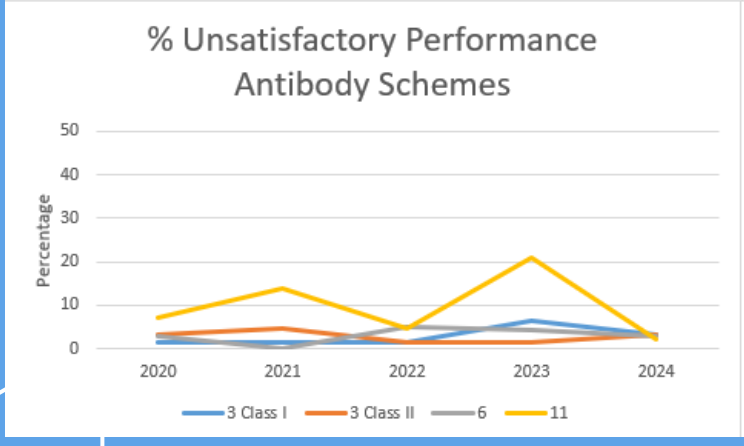
Scheme Summary

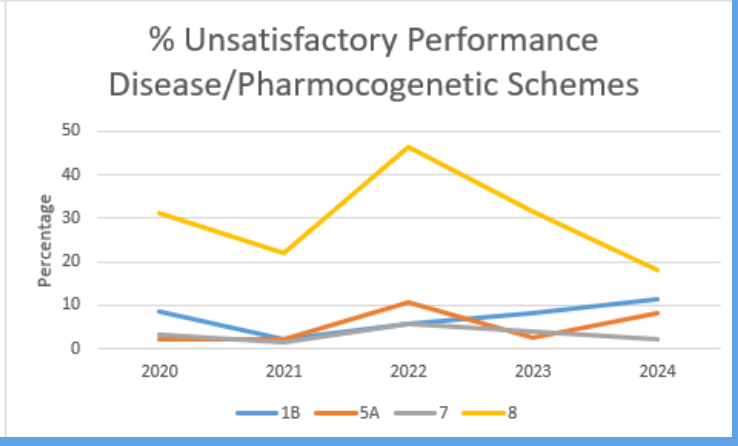
Performance Summary for all Schemes

5 Year Trends in Unsatisfactory Performance









UK NEQAS for H&I
Educational Crossmatch Scenario (EDXM)

Amy De'Ath
UK NEQAS for H&I Manager

UK NEQAS
Histocompatibility
& Immunogenetics

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

Whole Process ‘EQA’

Assessed Schemes

- 1A, 4A1, 4A2 – HLA Typing
- 6 – HLA Antibody Detection
- 3 – HLA Antibody Specification
- 2A, 2B – Crossmatching

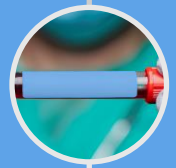
Educational Schemes

- Interpretative Educational Scenarios
- Educational Crossmatch Scheme
  - 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 (repertoires, cut-offs)

Educational Scheme Distribution

Educational Scheme Distribution

‘Donor’ Sample

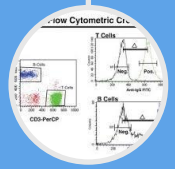


‘Patient’ Samples

3 x Serum Samples

HLA Typing

(Schemes 4A1 & 4A2)



Crossmatching

(Schemes 2A & 2B)

Antibody Detection / Specification

(Schemes 3 & 6)

Clinical Interpretation
Transplant Risk Stratification

2024 Submissions

- 33 participants submitted results
- Not all labs reported results for all tests

- HLA genotype:

Consensus HLA Type	A*	B*	C*	DRB1*	DRB4*	DQA1*	DQB1*	DPA1*	DPB1*
	02:01	40:01	03:04	04:04	01:03	03:01	03:02	01:03	04:02
	32:01	51:01	15:02	09:01		03:02	03:03	02:01	11:01
Number of reports	32	32	32	32	24	29	32	21	29
% Labs in consensus	100%	100%	100%	100%	100%	100%	100%	100%	100%

01 Serum 1

Results

Serum 1 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	No Consensus	58% (19/33)	
HLA Class II Antibodies	Negative	76% (25/33)	
DSA	None	100% (31/31)	
CDC XM	PBL Negative T cell Negative *B cell No Consensus*	100% (4/4) 100% (10/10) *71% (5/7 Neg)*	CDC Negative – B cell XM with DTT 100% negative, without DTT 71% (5/7) negative FCXM Negative
FCXM T Cell	Negative	96% (27/28)	
FCXM B Cell	Negative	96% (25/26)	
Transplant Risk	Low/Standard Intermediate	97% (29/30) 3% (1/30)	
Immunological Advice	Suitable for direct transplantation. Low level HLA antibodies present but not donor specific.		
Recommendations	Proceed to transplant.		

02 Serum 2

Results

Serum 2 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	100% (33/33)	Multiple A, B and Cw ab >10,000
HLA Class II Antibodies	Negative	85% (28/33)	
DSA	Present	100% (31/31)	100% B antibody reported at 6-20,000 39% Cw antibody 600-1,750
CDC XM	PBL Negative T cell Negative B cell Negative	75% (3/4) 100% (10/10) 86% (6/7)	CDCXM Negative FCXM Positive
FCXM T Cell	Positive	89% (25/28)	
FCXM B Cell	Positive	81% (21/26)	
Transplant Risk	Intermediate High/Contraindication	16% (5/31) 84% (26/31)	
Immunological Advice	Not suitable for direct transplantation. High risk of AMR. If transplant proceeds use enhanced immunosuppression and post-transplant monitoring. Test for non-HLA and autologous antibodies.		
Recommendations	Seek alternative donor. Consider de-sensitisation. Monitor antibodies over time to consider de-listing. Discuss risk with patient.		

03 Serum 3

Results

Serum 3 Results

	Result	% Consensus	Comments
HLA Class I Antibodies	Positive	100% (33/33)	B and Cw antibodies 2,000 - >10,000 MFI
HLA Class II Antibodies	Positive	100% (33/33)	DQ and DP antibodies 2,000 - >10,000 MFI
DSA	Present	100% (31/31)	Multiple DSA to CI and CII ranging from 600-33,000
CDC XM	PBL No consensus T cell Negative B cell Positive	50% (2/4 Pos) 78% (7/9) 86% (6/7)	CDCXM T cell Negative, B cell Positive FCXM Positive
FCXM T Cell	Positive	100% (28/28)	
FCXM B Cell	Positive	92% (24/26)	
Transplant Risk	High/Contraindication	100% (31/31)	
Immunological Advice	Not suitable for direct transplantation. Risk of AMR. Consider de-sensitisation. If transplant proceeds use enhanced immunosuppression and post-transplant monitoring. Test for non-HLA and autologous antibodies.		
Recommendations	Seek alternative donor. Consider de-sensitisation. Monitor antibodies over time to consider de-listing. Discuss risk with patient.		

Summary of Crossmatch and DSA Detection Results

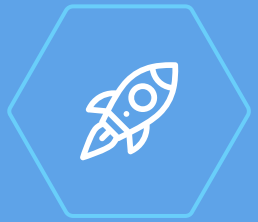
2024 Results		Serum 1		Serum 2		Serum 3	
DSA Defined by Luminex		Class I	Class II	Class I	Class II	Class I	Class II
MFI >10,000		N/A	N/A	B60 (100%)	N/A	B51 (100%) Cw10 (97%)	DR4 (100%)
MFI 5,001-9,999		N/A	N/A	N/A	N/A	Cw15 (84%)	DQ8 (97%) DQ9 (97%)
MFI 2,501-5,000		N/A	N/A	N/A	N/A	N/A	DR9 (45%) DQA1*03:02 (3%)
MFI <2,500		N/A	N/A	Cw10 (39%) Cw3 (3%)	N/A	N/A	DR53 (10%)
CDCXM B CELL	No DTT	Negative		Negative		Positive	
	DTT	Negative		Negative		Positive	
FCXM	T Cell	Negative		Positive		Positive	
	B Cell	Negative		Positive		Positive	
Risk		Low (97%) Intermediate (3%)		High (84%) Intermediate (16%)		High (100%)	

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

Benefits

Benchmarking

Monitor performance of multiple techniques
Make clinical interpretations on own results
Compare local policies for clinical assessment



Education

Monitor concordances
Review variations
Staff training

Competency

Laboratory staff
Clinical staff

Future Considerations

Formal Assessment

Basis of future scheme design

Complexity

How to assess the correct clinical interpretation

Workload

Participants
NEQAS team

Competency

Individual competency assessment

Any ideas?

Do you have any questions?

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