

HLA Typing to the 3rd and 4th Field Resolution: Results from the UK NEQAS for H&I Pilot External Quality Assessment Scheme

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Introduction

UK NEQAS for H&I offers 19 external quality assessment (EQA) schemes to over 350 participants worldwide. This includes HLA typing schemes for phenotyping (1A), 1st field resolution (4A1) and 2nd field resolution (4A2).

The introduction of 'next generation' sequencing technology has enabled laboratories to routinely HLA type samples at a higher resolution, for which no EQA scheme exists. Therefore, in 2017 we introduced a pilot scheme to monitor 3rd and 4th field HLA typing results.

Pilot Scheme

Participants were invited to HLA type 10 scheme 4A2 blood samples to the 3rd or 4th field resolution. Participants could report any combination of 3rd/4th field results for any combination of HLA-A, B, C, DRB1, DRB3/4/5, DQA1, DQB1, DPA1, DPB1. Results were not assessed, but summarised to allow comparison of results between laboratories.

Results

17 labs tested between 5-10 samples, resulting in 1763 alleles reported at the 3rd or 4th field resolution. The highest number of 3rd/4th field results were reported for HLA-B, followed by HLA-C, A, DRB1, DQB1, DPB1, DRB3/4/5, DQA1, then DPA1 (Figure 1).

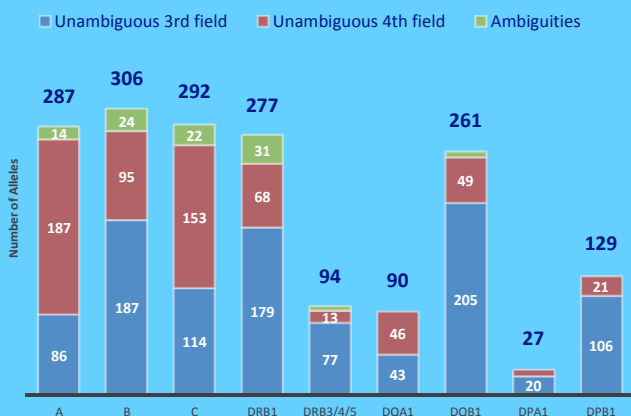


Figure 1: Number of alleles typed to 3rd or 4th field resolution

- 1017 alleles (57.7%) were reported as an unambiguous 3rd field result (e.g. B*07:02:01)
- 639 (36.2%) were reported as unambiguous 4th field result (e.g. B*07:02:01:01)
- 102 (5.8%) contained reports of multiple alleles with ambiguities at the 3rd or 4th field (e.g. B*07:02:01:01/03)

The highest proportion of unambiguous 4th field results were reported for HLA-A (65.2% of A results) and the least for DPB1 (16.3%). The highest proportion of 3rd/4th field ambiguities were reported for HLA-DRB1 (11.2% of DRB1 results), while none were reported for DQA1, DPA1 or DPB1 (Figure 1).

Discordant Results

There were 6 alleles from 4 samples where the 3rd or 4th field results from participants were not all in agreement.

- Sample 4A02/2017: a HLA-C allele was reported as C*04:01:01, *04:01:79, *04:01:01:06 and *04:01:NEW (Table 1)

Table 1: Sample 4A2 02/2017 3rd /4th field results

Reported Allele	No. of results
C*04:01:01	3
C*04:01:79	7
C*04:01:01:06	1
C*04:01:NEW	2

- Sample 4A03/2017: a DRB1 allele was reported as DRB1*04:01:01, *04:01:01:01 and *04:01:01:02. A DPB1 allele was also reported as DPB1*04:01:01, *04:01:01:01, 04:01:01:02 and 04:01:01:NEW (Table 2)

Table 2: Sample 4A2 06/2017 3rd /4th field results

Reported Allele	No. of results	Reported Allele	No. of results
DRB1*04:01:01	11	DPB1*04:01:01	7
DRB1*04:01:01:01	2	DPB1*04:01:01:01	1
DRB1*04:01:01:02	3	DPB1*04:01:01:02	1
		DPB1*04:01:01:NEW	1

- Sample 4A2 06/2017: a DRB1 allele was reported as DRB1*15:01:01, 15:01:01:01, 15:01:01:02. The DPB1 type was also reported as DPB1*04:01:01 homozygous, 04:01:01:01 homozygous and 04:01:01:01, 04:01:01:06 (Table 3).

Table 3: Sample 4A2 06/2017 3rd /4th field results

Reported Allele	No. of results	Reported Type	No. of results
DRB1*15:01:01	8	DPB1*04:01:01, -	4
DRB1*15:01:01:01	1	DPB1*04:01:01:01, -	1
DRB1*15:01:01:02	1	DPB1*04:01:01:01, 04:01:01:06	1

- Sample 4A2 07/2017: A HLA-C allele was reported as C*14:02:01, 14:02:01:01 and 14:02:01:04 (Table 4)

Table 4: Sample 4A2 07/2017 3rd /4th field results

Reported Allele	No. of results
C*14:02:01	6
C*14:02:01:01	5
C*14:02:01:04	3

Comment

It is currently unknown if the finding of discrepant 3rd/4th field HLA types is due to technical, interpretation, reporting or other issues, but demonstrates that an EQA scheme is required to monitor the accuracy of test results reported at this resolution.

Accordingly, UK NEQAS for H&I will formally assess results reported at the 3rd field from 2018 and continue to monitor results at the 4th field as part of Scheme 4A2.