UK NEQAS
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Histocompatibility & Immunogenetics

# Differences in UK Unacceptable HLA Antigen Listing for Deceased Donor Kidney Transplantation

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## Introduction

Educational clinical scenarios are distributed annually to UK Histocompatibility and immunogenetics (H&I) laboratories as part of the UK NEQAS for H&I external quality assessment service. These patient scenarios provide relevant test results and require result interpretation and clinical decisions/advice reflective of clinical practice.

Two clinical scenarios since 2013 have required labs to define unacceptable antigens for patients requiring kidney transplantation. Responses to these scenarios were used to investigate the consistency of unacceptable HLA antigen mismatch listing between H&I laboratories.

## Scenario 1 Results

This case from 2014 was based on a multiparous female patient requiring registration on the deceased donor kidney transplant waiting list. H&I laboratories were asked to detail the HLA specificities they would list as unacceptable antigens, based on results from two Luminex Single Antigen Bead (SAB) tests.

All 19 laboratories that responded listed some specificities as unacceptable antigens. There was good agreement on HLA-A and -B specificities with an MFI over 2,500, however lower MFI and HLA-C antibodies were more varied (Table 1). Listing of unacceptable antigens was generally based on MFI values above a locally defined threshold.

**Table 1: Number of laboratories reporting specificities as unacceptable antigens**

| Specificity | Luminex MFI | Number of Labs (n=19) | Specificity | Luminex MFI | Number of Labs (n=19) |
|---|---|---|---|---|---|
| A2 | 5497-7879 | **19** | B18 | 1627-1859 | 13 |
| B57 | 2595-6341 | **19** | Cw2 | 1454-1643 | 13 |
| B58 | 2987-4621 | **19** | DQ2 | 423-1187 | 10 |
| A69 | 2710-2676 | **19** | DR9 | 342-1255 | 6 |
| B35 | 2872-3006 | **19** | DR7 | 881-921 | 1 |
| Cw4 | 3489-3768 | 17 | A68 | 0-475 | 1 |

MFI range is the lowest and highest MFI values recorded over several samples

The number of unacceptable antigens listed by each laboratory varied from 5-10 (median 8), resulting in 10 different unacceptable antigen profiles for this scenario (Table 2). The variation in unacceptable antigen listing would result in the patient being listed with a calculated reaction frequency (cRF) of between 62-88% depending on the centre.

**Table 2: Unacceptable antigen profiles and corresponding calculated reaction frequency**

| Unacceptable Antigen Profile | | | | | | | | | No. of labs | cRF |
|---|---|---|---|---|---|---|---|---|---|---|
| A2 | | A69 | B35 | B18 | B57 | B58 | Cw2 | Cw4 | 4 | 71% |
| A2 | | A69 | B35 | | B57 | B58 | | Cw4 | 3 | 65% |
| A2 | | A69 | B35 | B18 | B57 | B58 | Cw2 | Cw4 DQ2 | 3 | 87% |
| A2 | | A69 | B35 | B18 | B57 | B58 | Cw2 | Cw4 DR9 DQ2 | 3 | 87% |
| A2 | | A69 | B35 | | B57 | B58 | | | 1 | 62% |
| A2 | | A69 | B35 | B18 | B57 | B58 | | Cw4 | 1 | 69% |
| A2 | | A69 | B35 | | B57 | B58 | | Cw4 DQ2 | 1 | 84% |
| A2 | | A69 | B35 | B18 | B57 | B58 | | Cw4 DR9 DQ2 | 1 | 86% |
| A2 | | A69 | B35 | B18 | B57 | B58 | Cw2 | Cw4 DR9 | 1 | 71% |
| A2 | A68 | A69 | B35 | B18 | B57 | B58 | | DR7 DR9 DQ2 | 1 | 88% |

## Scenario 2 Results

This 2019 case was based on a multi transfused male, with a functioning heart transplant (mismatch grade 112) and failed live donor kidney graft (mismatch grade 010), requiring registration on the kidney transplant waiting list. H&I laboratories were given results of four Luminex SAB tests, which consisted of a complex Class II profile with self-reacting beads i.e. beads displaying self alleles were positive in the test. There were responses from 22 H&I laboratories.

**Table 3: Number of laboratories reporting specificities as 'unacceptable antigens'**

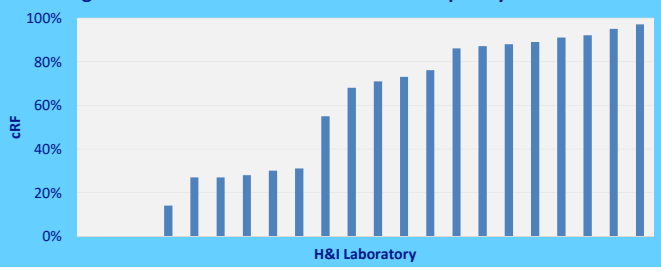
| Specificity | Luminex MFI | Number of Labs (n=22) | Specificity | Luminex MFI | Number of Labs (n=22) |
|---|---|---|---|---|---|
| None | - | 3 | **B8** [a,b] | - | 6 |
| DR7 | 1238-3520 | 18 | **A30** [b] | - | 6 |
| DR9 | 1557-4242 | 17 | DR52 | 3154 | 4 |
| DR103 | 1125-3669 | 13 | DR14 | 1001-2575 | 4 |
| DR10 | 704-2229 | 12 | **DQ2** [a] | - | 4 |
| **DR17** [a] | 930-2527 | 12 | **Cw3** [b] | - | 4 |
| **DR15** [a] | 1102-1749 | 11 | **DQ9** [b] | - | 4 |
| DR8 | 1053-3234 | 8 | **A1** [a] | - | 3 |
| DR51 | 912-2991 | 8 | **DQ6** [a] | - | 3 |
| DR13 | 1069-2716 | 7 | DR1 | 838-2597 | 1 |
| DR12 | 601-2481 | 6 | | | |

[a] Functioning heart transplant mismatch, [b] Failed live kidney transplant mismatch
MFI range is the lowest and highest MFI values recorded over several samples

The number of unacceptable antigens listed varied from 0-21 (median 5). Three laboratories listed no unacceptable antigens due to the SAB self reactivity. The remaining labs had limited agreement on the unacceptable antigen profile for this challenging scenario (Table 3), with 18 different unacceptable antigen profiles.

In addition to MFI, reasons for unacceptable antigen listing included MFI consistency, historic/current detection and variation in dealing with SAB self-reactivity. Differences in management of previous graft mismatches were apparent; some labs did not list any, others listed if antibody present, while others considered all previous graft mismatches as unacceptable antigens regardless of antibody detection. This contributed to the large variation in cRF for this scenario 0-97% (Figure 1).

**Figure 1: Scenario 2 calculated reaction frequency variation**




## Comment

Unacceptable antigen definition can be extremely complex. These educational scenarios highlight important differences in unacceptable antigen listing practices, especially for low MFI antibodies and previous graft mismatches. This variation is likely to be due to different centre policies, risk appetite and experience. The differences could have equity of access implications for patients awaiting transplantation.

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