Bi-ennial Report

2009 - 2011

UK NATIONAL EXTERNAL QUALITY ASSESSMENT SCHEME

for Blood Transfusion Laboratory Practice

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Issued May 2012

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1. INTRODUCTION

The Blood Group Serology Scheme was first recognised in 1979 when it was based at the BGRL in Oxford. The first exercises distributed covered crossmatching only. Over the next few years the Scheme expanded to include ABO and D grouping, antibody screening and antibody identification.

The Scheme completed a move from NIBSC at Potters Bar to Watford General Hospital in Watford in September 1995 to be sited alongside UK NEQAS for General Haematology. This coincided with a change in management and staff, although the Scheme Organiser remained the same. A change of name from Blood Group Serology to Blood Transfusion Laboratory Practice was made in April 1999 to encompass the non-serological aspects of transfusion practice that are assessed, particularly through non-scoring exercises and questionnaires. Red cell phenotyping was introduced in 2007.

The Scheme is advised by the Steering Committee (see Appendix I for composition) for Blood Transfusion Laboratory Practice, which meets three times a year. The meetings include discussion of past and future exercises; aims and objectives for the year; the organisation of the annual educational meeting; comments and complaints from participants; overall levels of performance.

In April 2001, the Scheme's UK activity was integrated fully into West Hertfordshire Hospitals NHS Trust reporting to the CEO through the Pathology Board. At the same time, the administrative aspects of the non-UK activity have been dealt with by a new company, Educational and Quality Laboratory Services (Blood Transfusion) Ltd. [EQUALS (BT) Ltd], through a contract for services with the Trust.

Historically, this report has covered the financial year, i.e. April to March; however, in order to align with other reporting years, it will in future cover calendar years. This report presents data for the period April 2009 to December 2011.

2. STAFF

Chair of the Steering Committee – Dr Ann Benton
Scheme Director - Dr Megan Rowley
Scheme Manager and Deputy Director - Mrs Clare Milkins
Deputy Scheme Manager - Ms Jenny White
EQA Scientist – Mrs Dalila Benkhaled (left March 2011); Arnold Mavurayi (started May 2011)
Executive Assistant – Ms Isabella De-Rosa

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3. PARTICIPANTS

The number of participants registered at December 2011 is shown in table 1. Overseas participation by country is shown in table 2.

Table 1 - Participation December 2011

Type of Participant	Number Registered
UK clinical (including Ireland, BFPO and Channel Islands)	410
Overseas clinical	265
Diagnostic companies	8

Table 2 - Overseas Participation by Country (excluding BFPO; including non-clinical)

Country	No. Participants	Country	No. Participants
Australia	1	Macau	1
Bahrain	1	Malawi	1
Belgium	2	Malta	3
Bolivia	1	Mexico	1
Chile	2	Netherlands	4
China	1	New Zealand	1
Croatia	2	Norway	4
Cyprus	7	Oman	2
Denmark	33	Poland	1
Egypt	1	Portugal	48
Estonia	2	Romania	1
Faroe Islands	1	Saudi Arabia	1
Finland	4	Serbia	2
France	1	Slovenia	1
Germany	2	Spain	2
Gibraltar	1	Sweden	3
Greece	15	Switzerland	3
Greenland	1	Sri Lanka	1
Hong Kong	1	Turkey	33
Iceland	1	Uganda	1
Israel	19	United Arab Emirates	3
Italy	51	USA	1
Jamaica	1		

4. SUMMARY OF EXERCISES DISTRIBUTED (TABLE 3)

Exercise Code	Date Distributed	Contents	Main aim: (Q indicates that a questionnaire was included)
09R4	20 April 09	ABO/D, AS, ABID, XM, PH	Detection of 3 incompatibilities (Fy^a); Rh phenotyping.
09E5	18 May 09	AS, ABID	Identification of an antibody mixture and detection of a weak antibody.
09E6	15 June 09	AS, ABID	Reporting of anti-S in combination with an enzyme non-specific antibody; identification of an antibody mixture.
09R7	20 July 09	ABO/D, AS, ABID, XM, PH	Assessment of ABO/D grouping of samples with 2 different strengths of positive DAT; detection of incompatibilities (S).
09E8	21 Sept 09	AS, ABID	Detection and identification of weak antibodies.
09R9	22 Oct 07	ABO/D, AS, XM	Detection of IgG antibody (S) in a serological crossmatch (urgent scenario); Q
09E10	19 Nov 07	AS, ABID	Identification of 2 antibody mixtures.
10R1	18 Jan 10	ABO/D, AS, ABID, XM, PH	Detection of 2 ABO and 2 IgG (Fy^a) incompatibilities; Phenotyping for Jk^a/Jk^b
10E2	15 Feb 10	AS, ABID	Detection of the UK NEQAS 'standard' weak anti-D; Identification of an antibody mixture
10E3	15 March 10	AS, ABID	Identification of 2 antibody mixtures.
10R4	19 April 10	ABO/D, AS, ABID, XM, PH	ABO/D typing of 2 DAT positive samples; detection of 5 IgG incompatibilities (S,s); phenotyping for Fy^a/Fy^b.
10E5	17 May 10	AS, ABID	Identification of an antibody mixture and detection of a weak antibody.
10E6	21 June 10	AS, ABID	Detection of 2 weak antibodies.
10R7	12 July 10	ABO/D, AS, ABID, XM, PH	Detection of MF reactions in 3 ABO/D groups; detection of 3 IgG incompatibilities (K, Fy^a); phenotyping for S/s; Q
10E8	20 Sept 10	AS, ABID	Identification of 2 antibody mixtures.
10R9	18 Oct 10	ABO/D, AS, ABID	Assessment of provision of blood in an emergency situation; Q.
10E10	15 Nov 10	AS, ABID	Detection of a weak antibody and identification of antibody mixture.
11R1	19 Jan 11	ABO/D, AS, ABID, XM, PH	Detection of ABO and IgG antibodies in the crossmatch; Rh phenotyping; D typing of r'r; Q
11E2	14 Feb 11	AS, ABID	Identification of an antibody mixture; Detection of a weak antibody.
11E3	21 March 11	AS, ABID	Detection of weak antibodies; EDTA trial.
11R4	18 April 2011	ABO/D, AS, ABID, XM, PH	Detection of ABO and IgG antibodies in the crossmatch, and identification of an antibody mixture.
11E5	23 May 2011	AS, ABID	Detection of weak antibodies and trial of material for new UK NEQAS anti-D 'standard'.
11E6	20 June 2011	AS, ABID	Identification of antibody mixtures.
11R7	18 July 2011	ABO/D, AS, ABID, XM, PH	Consistency in detecting a weak IgG antibody in the crossmatch, and D typing rr DAT positive sample.
11E8	19 Sept 2011	AS, ABID and optional titration	Identification of an antibody mixture including an antibody to a low frequency antigen. Titration of a single IgG antibody. Q.
11R9	17 Oct 2011	ABO/D, AS, ABID	Provision of blood in an urgent situation, to assess the serological crossmatch.
11E10	14 Nov 2011	AS, ABID	Identification of a single antibody and an antibody mixture.

AS - Antibody Screen   ABID - Antibody Identification
XM - Crossmatch   PH – Red Cell Phenotyping   Q - Questionnaire

5. DETAILS OF EXERCISE MATERIAL AND RESULTS

5.1. General Information

- Data is split between two categories, namely, UK laboratories and non-UK laboratories, with the following definitions:
    i. UK laboratories – clinical laboratories within the UK (NHS and private) and Ireland.
    ii. Non-UK laboratories – overseas clinical laboratories (including BFPO) and commercial companies (UK and overseas).

- Antibody titres quoted are those obtained in the UK NEQAS laboratory on the closing date, by LISS spin tube, against red cells bearing heterozygous expression of the relevant antigen, unless otherwise stated.

- Numbers of errors reported includes late results, and any amendments to scores made following appeals.

- Numbers of participants include those who returned late results, which would not have been included in the exercise specific reports distributed at the time.

- Each 'Patient' whole blood sample comprises a pool of four or five donations, which may be diluted with ABO compatible FFP and Modified Alsever's solution.

- Each 'Patient' plasma sample comprises a pool of ABO compatible plasma, some of which may contain red cell antibodies.

- Each 'donor' sample comprises a single red cell donation, diluted in modified Alsever's solution to make approximately 2 litres in total, giving a red cell concentration of 7-10%.

5.2. 09R4

Material

‘Patient’ 1: O D neg, anti-Fy^a+S (>32 and 2)	‘Donor’ W: O D neg, r’r, Fy(a+b+), ss
‘Patient’ 2: B D pos, inert	‘Donor’ Y: O D pos, R_2R_2, Fy(a+b+), ss
‘Patient’ 3: A D pos, inert	‘Donor’ Z: O D pos, R_1r, Fy(a+b+), Ss

Performance monitoring

Patient 1 (anti-Fy^a+S) was withdrawn from scoring for antibody identification, due to deterioration of the anti-S throughout the course of the exercise. The anti-S was no longer detectable with all S+ positive cells by the closing date, but was still showing dosage by some technologies.

Table 4 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
ABO Grouping	**All Samples**	**2/439**	**4** [1]	**1/214**	**1**
D Grouping	**All Samples**	**2/439**	**2** [1]	**0/214**	**0**
Antibody Screening	**All Samples** - P1 - anti-Fy^a+S - P3 - inert	**0/434**	**0**	**3/207**	**3** 2 **1** 1
Antibody Identification	**All Samples** - P1 - anti-Fy^a+S	***23/387*** ***(not scored)***	***23***	**18/161**	**18**
Incompatibilities	**All Samples** - P1DW (Fy^a) - P1DY (Fy^a) - P1DZ (S)	**3/423**	**6** [1] 2 2 2	**9/191**	**14** 7 4 3
Compatibilities	**All Samples**	**3/423**	**5** [2]	**1/191**	**6**
Phenotyping (Rh)	**All Samples** - False pos - False neg	**9/261**	**10** ***5*** [4] **5** [4]	**5/88**	**5** 4 1

[1] All due to transcription or sample transposition error
[2] Four due to transcription or sample transposition error
[3] One due to transcription or sample transposition error
[4] One due to testing of wrong exercise material

UK Errors (excluding transcription, result transposition and web data-entry errors)

ABO/D grouping

- One laboratory transposed samples 2 and 3 whilst attaching accession number labels; however, this error was not detected because the routine validation step was not carried out.

Crossmatching

- Three laboratories made crossmatching errors:
  - One tested the ‘donor’ samples from 09R2 instead of 09R4
  - One missed both incompatibilities, possibly using plasma from Patient 2 or Patient 3 in error.
  - One deselected Donor Z – reason unknown.

Phenotyping

- Nine laboratories recorded five false positive and five false negative Rh phenotyping results, including one testing samples from 09R2 instead of 09R4.
  - Some of these recorded the correct probable genotype based on incorrect reaction grades, suggesting possible transcription error.

Exercise Comments

The labelling error in this exercise highlights that labelling of samples with accession numbers is a critical point in the pre-transfusion process, requiring a validation step. The same error also demonstrates the importance of treating EQA samples, wherever possible, in the same way as clinical samples. This will ensure that EQA tests that the system is working as intended, and any errors made will provide opportunities for effective CAPA.

The anti-S was only detectable with SS cells by some technologies by the closing date and (and was negative with some SS cells by some technologies). Sixteen laboratories did not mention the potential presence of anti-S, and this serves to highlight the importance of basing exclusion on a negative reaction with homozygous cells where possible.

5.3. 09E5

Material

'Patient' 1: Inert 'Patient' 2: Anti-c+K (titre 16 and 8 respectively) 'Patient' 3: Inert 'Patient' 4: Anti-Jk^a (titre 1)

Performance Monitoring

Patient 4 was withdrawn from scoring for antibody identification due to significant deterioration of the anti-Jk^a throughout the course of the exercise. A negative reaction was obtained with some Jk(a+b+) cells during in-house testing on the closing date.

Table 5 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**3/425**	**3**	**9/92**	**9**
	- P4 - anti-Jk^a		**1**		**9**
Antibody ID	**All Samples**	**53/381**	**54**	**10/87**	**10**
	- P2 - anti-c+K		54[1]		10

[1] One due to sample transposition error

UK Errors (excluding transposition errors)

Antibody screening

- Three laboratories missed the anti-Jk^a in the screen:
  - One used a manual DiaMed technique, and was still unable to detect the antibody on repeat, but did detect it with some of the ID panel cells.
  - One used a manual BioVue 'addition' technique and could not detect it on repeat.
  - One used an automated CAT technique, and on re-examination of the image found that a weak reaction had been interpreted as negative, requiring resetting of the camera threshold and retesting of clinical samples.

Antibody identification

- 53 (14%) laboratories reported incorrect or incomplete results for Patient 2:
  - Six made UI submissions with which the Scheme disagreed
  - Three overlooked anti-c entirely (2 possibly due to transcription errors)
  - 14 overlooked anti-K entirely.

Exercise Comments

The anti-K was probably masked by the anti-c in many of the panels of cells in use. The 14 participants who overlooked the presence of anti-K, would not have done so had they gone through a systematic process to exclude further antibodies of likely clinical significance. This is an essential part of the antibody identification process.

5.4. 09E6

Material

‘Patient’ 1: Anti-S + enzyme non-specific antibody (titre >32) * ‘Patient’ 2: Inert ‘Patient’ 3: Inert ‘Patient’ 4: Anti-D+Jk^b (titre >32 and 8, respectively)

**Anti-S and anti-S+ENS were both acceptable results. Anti-S+UI did not incur a penalty.*

Table 6 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**0/428**	**0**	**0/102**	**0**
Antibody ID	**All Samples** - P1 - anti-S - P4 - anti-D+Jk^b	**9/385**	**9** 2[1] 7[2]	**4/92**	**4** 0 4

[1] – One due to transcription error

[2] – Three due to transcription error

UK Errors (excluding transcription errors)

Antibody Identification

- Seven laboratories made antibody identification errors:
  - One reported anti-K+S due to misinterpretation of results
  - One reported anti-Jk^b alone, indicating that they were unable to exclude anti-D or anti-C; further examination of their results showed that they could have identified anti-D.
  - Three reported a third specificity not actually present.

Exercise Comments

Reporting of the enzyme non-specific reactions

- 50% of participants reported anti-S+ENS
- 48% reported anti-S alone
- 64% of those using an enzyme panel reported the ENS antibody (cf. 55% in 08E6)

The 113 using an enzyme panel for ‘Patient’ 1 but not reporting ENS, may have chosen not to do so, possibly due to a difference in the way EQA samples are reported. It is also possible that the ENS was not detected by all of those using an enzyme panel, since the Scheme has no data regarding the enzyme method used (two stage enzyme, enzyme IAT, papain/ficin etc.) or its influence on the results obtained.

5.5. 09R7

Material

'Patient' 1: A D neg, DAT pos, anti-S (2)	'Donor' W: O D neg, Fy(a+b-), Ss, kk
'Patient' 2: B D pos, inert	'Donor' Y: O D neg, Fy(a-b+), ss, Kk
'Patient' 3: O D neg, DAT pos, anti-Fy[a] (titre 4)	'Donor' Z: O D neg, Fy(a-b+), SS, Kk

Table 7 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
ABO Grouping	**All Samples**	**2/434**	**3**[1]	**2/231**	**3**
D Grouping	**All Samples** - False pos	**12/434**	**17** 17[2]	**11/231**	**18** 18
Antibody Screening	**All Samples** - P3 - anti-Fy[a] - P1 - anti-S	**3/429**	**3** 3 0	**8/215**	**10** 6 4
Antibody Identification	**All Samples** - P1 - anti-S - P3 - anti-Fy[a]	**3/383**	**4**[3] 1 2	**4/167**	**4** 2 2
Incompatibilities	**All Samples** - P1DW (S) - P1DZ (S) - P3DW (Fy[a])	**10/417**	**13**[4] 3 5 5	**27/200**	**50** 21 21 8
Compatibilities	**All Samples**	**9/417**	**16**[4]	**13/200**	**24**
Phenotyping (Kk)	**All Samples** - False pos - False neg	**4/253**	**10** 3[1] 7[5]	**7/95**	**11** 1 10

[1] All due to transcription or transposition error
[2] One due to transcription error
[3] Two due to result transposition error
[4] Seven due to transcription or transposition error
[5] Four due to transcription or transposition error

UK Errors (excluding transcription/transposition errors):

ABO/D grouping

- Six laboratories reported a false positive D type for 'Patient' 1.
- Ten laboratories reported a false positive D type for 'Patient' 3.

Antibody screening

- Three laboratories missed the anti-Fy[a] in the screen:
  - One tested whole blood samples in error.
  - Two laboratories used CRRS in the Gallileo:
    - One had manually edited a weak pos reaction (brought forward for review) and proceeded to 'issue' Fy(a+) unit by EI
    - One obtained positive reactions with new screening cells

Antibody Identification

- Two laboratories reported additional specificities not present.

Crossmatching

- Four laboratories recorded five false negative results with no clear cause.
- Six false positive results were based on false positive reactions.
- Four laboratories deselected 'Donor' Y for 'Patient' 1 and 'Donors' Y and Z for 'Patient 3.

Phenotyping

- One laboratory reported all 3 'donors' as k negative.

Exercise Comments
This exercise demonstrates the risk of performing electronic issue based on results that, although obtained on automated systems, have been subject to manual edit.

D typing of DAT positive samples: Full supplementary report in Appendix 2

5.6. 09E8

Material

'Patient' 1: Inert
'Patient' 2: Anti-c (titre 8)
'Patient' 3: Anti-K (titre 1)
'Patient' 4: Inert

Table 8 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples** - P3 - anti-K - P4 - inert	**7/423**	**7** 4 3[1]	**7/99**	**7** 6 1
Antibody ID	**All Samples** - P2 - anti-c - P3 - anti-K	**1/379**	**1[1]** 1	**3/88**	**4** 3 1

[1] – All due to transcription or transposition error

UK Errors (excluding transcription/transposition errors):

Antibody screening

- Four laboratories reported a negative screen for 'Patient' 3 (anti-K):
  - All used automated Capture:
    - Two obtained negative reactions on the Gallileo, even on repeat
    - One obtained an initial equivocal reaction on the Gallileo, but a negative reaction on repeat
    - One obtained an initial negative reaction on the Gallileo, but a clear positive reaction using a 3-cell screen on the Echo; this was followed by a series of negative and equivocal results on the Gallileo with a 4-cell screen.
  - All reported a negative screen because they would have done so with a patient sample, which would not have undergone the additional testing.

Exercise Comments

Additional in-house testing using CRRS

In-house manual testing on screen cells submitted by one of the four laboratories above (both 3 and 4 cell screens) all gave clear positive reactions after the closing date. Further examination of participants' results showed that there was no difference in the detection rate between those testing at the beginning and those testing at the end of the exercise.

5.7. 09R9

Material

'Patient' 1: O D pos, anti-c+S (8 and 32)	'Donor' W: O D pos, R_1r, ss
'Patient' 2: A D pos, inert	'Donor' Y: O D pos, R_1R_1, Ss
'Patient' 3: B D pos, inert	'Donor' Z: O D pos, R_1R_1, Ss

The aim of this exercise was to assess serological crossmatching for all participants, and the scenario given was an urgent situation where there is insufficient time to undertake antibody identification or phenotyping.

Table 9 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
ABO Grouping	**All Samples**	**2/432**	**2**	**0/232**	**0**
D Grouping	**All Samples**	**0/432**	**0**	**1/232**	**1**
Antibody Screening	**All Samples**	**3/432**	**4**	**4/215**	**4**
	- P1 - anti-c+S		3[1,2]		2
	- P2 - inert		0		1
	- P3 - inert		1[1]		1
Incompatibilities	**All Samples**	**2/418**	**6**[3]	**8/203**	**20**
	- P1DW (c)		2		7
	- P1DY (S)		2		7
	- P1DZ (S)		2		6
Compatibilities	**All Samples**	**2**	**2**	**2/203**	**3**

[1] – One error due to sample transposition
[2] – Two errors due to use of the whole blood sample instead of the plasma sample
[3] – Three errors due to use of the whole blood sample instead of the plasma sample

UK Errors (excluding transcription/transposition errors):

ABO/D grouping

- One laboratory reported a result of group AB for P3 instead of group B. Clear positive reactions were obtained with anti-A, anti-B and A cells, and this was flagged as an anomaly by the automation. The laboratory interpreted this as A_2B with anti-A_1 without further confirmatory testing. The analyser was new and not yet validated for use with patient samples.
- One laboratory used the plasma sample for reverse grouping instead of the whole blood sample and reported UI for Patient 2, due to the anti-c affecting the reverse group in a BioVue cassette.

Exercise Comments

Where ABO grouping is performed using automation, a degree of security is implied; however, where liquid reagents are dispensed (even in automated systems), there is an increased risk of error.

Any anomalous ABO groups should be investigated and resolved prior to reporting a blood group, with no assumptions made as to the cause of the anomaly.

The purpose of EQA is to assess the routine process and EQA samples should therefore be handled and tested in the same way as patients samples within the limitations of the material provided.

5.8. 09E10

Material

‘Patient’ 1: Anti-D+M*(titre >32 and 8 respectively)
‘Patient’ 2: Anti-E+Jk^b (both titre 4)
‘Patient’ 3: Inert
‘Patient’ 4: Inert

**The anti-M was reactive at 37°C and therefore considered to be clinically significant*

Table 10 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**1/423**	**2**[1]	**2/98**	**3**
	- P1 - anti-D+M				1
	- P2- anti-E+Jk^b				2
Antibody ID	**All Samples**	**20/379**	**21**	**10/88**	**12**
	- P1 - anti-D+M		4		3
	- P2- anti-E+Jk^b		17[1,2]		9

1 – One participant tested the wrong exercise material
2 – Two due to transcription error

UK Errors (excluding transcription/transposition errors):

Antibody screening

- One laboratory tested exercise 09E8 in error, resulting in one false positive and one false negative antibody screen.

Antibody identification

- Eighteen laboratories made 19 antibody identification errors:
  - Two reported anti-M only, due to misinterpretation where positive reactions with D+, M- cells were overlooked.
  - One missed the anti-M.
  - Seven reported additional specificities not actually present.
  - One reported anti-D+Jka based on false negative reactions by IAT in the identification panel.
  - Three overlooked the anti-E due to masking, though its presence should have been suspected by differential reactivity, and clearly could not be excluded.
  - Five were aware of the potential presence of all specificities actually present, but were unable to complete the identification and did not make a UI submission.

Exercise Comments

When interpreting antibody identification results all available information should be taken into account, including patient phenotype, differential reaction by technique, and results of all cells tested (including the screening panel). It is vital that the presence of an additional clinically significant antibody(ies) is excluded before a final interpretation is made.

5.9. 10R1

Material

'Patient' 1: B D pos, anti-Fy^a (4)	'Donor' W: O D neg, Fy(a+b+), Jk(a+b-),
'Patient' 2: O D UI, (80:20 D pos:DVI)[1], inert	'Donor' Y: B D pos, Fy(a-b+), Jk(a-b+),
'Patient' 3: A D neg, inert	'Donor' Z: O D neg, Fy(a+b-), Jk(a+b-)

[1] – One unit in pool was unintentionally DVI positive.

Table 11 – Summary of results for 10R1

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**2/433**	**2[1]**	**1/229**	**1**
D Grouping	**All Samples**	**3/433**	**3[1]**	**2/229**	**2**
Antibody Screening	**All Samples**	**0/427**	**0**	**4/209**	**5**
	- P1- anti-Fy^a				4
	- P2 - inert				1
Antibody Identification	**All Samples**	**2/383**	**2**	**7/174**	**7**
Incompatibilities	**All Samples**	**4/418**	**9**	**12/198**	**19**
	- P1DW (Fy^a)		3[2]		10
	- P1DZ (Fy^a)		4[2,3]		8
	- P2DY(ABO)		1[3]		0
	- P3DY(ABO)		1[3]		1
Compatibilities	**All Samples**	**5/418**	**7[4]**	**8/198**	**8**
Phenotyping (Jk^a/Jk^b)	**All Samples**	**5/243**	**10**	**4/94**	**6**
	- False pos		4[5]		2
	- False neg		6[5]		4

[1] – All due to transcription error
[2] – One used whole blood instead of plasma samples
[3] – One due to donor sample transposition
[4] – Three due to donor sample transposition
[5] – Three due to transposition of results

UK Errors (excluding transcription/transposition errors):

Antibody Identification

- Six laboratories made errors, and one made a UI submission which was agreed:
  - One reported anti-Fy^a + UI, but did not make a UI submission
  - Four reported anti-Fya + a specificity not actually present (-Cw x3; Lua x1)
  - One reported anti-Fya + enzyme non-specific.

Crossmatching

- One did not follow their own procedure to phenotype the donors, and selected the units based on ABO only, without a serological crossmatch
- One, using manual DiaMed, obtained strong reactions on repeat testing; cause of error is unknown, but testing was undertaken but a BMS not yet signed off as competent
- Three labs reported a further three missed compatibilities.

Phenotyping (Jk^a/Jk^b)

- Four laboratories reported one false positive and three false negative results.

Exercise Comments

Where automated grouping interfaced to the LIMS is available, it should be used at all times to maximize security of data transfer. Any manual intervention in an automated process introduces an increased risk of error.

Nineteen laboratories (4%) recorded a mixed field reaction with an anti-D reagent for 'Patient' 2, and six of these made a D typing interpretation based on this result (the remainder reporting UI). A mixed field D typing reaction in a patient with no historical group might be due to a D negative patient being transfused D positive blood, and no interpretation should be made until the cause of the anomaly can be confirmed.

Once all reactions in the identification and screening panel have been accounted for by the presence of antibodies already identified, there is no need to exclude antibodies of low clinical significance or those directed against low frequency antigens.

5.10. 10E2

Material

'Patient' 1: Anti-D (UK NEQAS standard)
'Patient' 2: Inert
'Patient' 3: Inert
'Patient' 4: Anti-E+Fy^a (titre 8 and >32, respectively)

Problems with material

The standard anti-D deteriorated during the course of the exercise and was undetectable against a range of D positive red cells; it was therefore withdrawn from scoring.

Table 12 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**1/417**	**1**[1]	**2/92**	**3**
	- P2 – inert				1
	- P3 - inert				1
	- P4 - anti-E+Fy^a				1
Antibody ID	**All Samples**	**6/375**	**6**	**3/89**	**3**
	- P4 - anti-E+Fy^a		6[2]		3

[1] - Excluded from performance monitoring
[2] - Four due to transcription or result transposition error

UK Errors (excluding transcription/transposition errors):

Antibody screening

- One laboratory missed the anti-D in the screen using automation; a weak reaction was detected on repeat with the R_2R_2 cell only; the company was called in and adjustments made to the volume of red cells dispensed.

Antibody identification

- Two laboratories made antibody identification errors:
  - One reported anti-E, and did not follow up additional positive reactions
  - One reported anti-Fy^a with anti-E as 'not excluded', but did not make a UI submission.

Exercise comments

This exercise highlights the importance of accounting for all reactions obtained in antibody identification, to avoid misinterpretation and missing additional specificities present.

5.11. 10E3

Material

'Patient' 1: Anti-D+K (titre >32 and 16, respectively) 'Patient' 2: Inert 'Patient' 3: Anti-E+Jk^b (titre 8 - both) 'Patient' 4: Inert

Table 13 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples** - P4 - inert	**1/418**	**1** 1	**2/93**	**2** 2
Antibody ID	**All Samples** - P1 - anti-D+K - P3 - anti-E+Jk^a	**19/377**	**19** 0 19	**14/92**	**15** 2 13

UK Errors

Antibody screening

- One laboratory reported one false positive result, probably due to data entry error.

Antibody identification

- One laboratory reported anti-Kp^a in addition to anti-E+Jk^b.
- 16 laboratories reported anti-Jk^b only:
  - Six recorded anti-E as 'not excluded' but did not make a UI submission.
  - Ten overlooked the presence of anti-E:
    - Eight did not have any E+ Jk(b-) cells
    - Two recorded a positive reaction with an E+ Jk(b-) cell:
      - One overlooked this during the interpretation
      - One excluded anti-E based on negative reactions in a 1 stage enzyme test, and disregarded the positive reaction by IAT.
- Four laboratories made UI submissions (Jk^b+UI), two of which were agreed.

Exercise Comments

A systematic approach to antibody identification is required, whereby all clinically significant specificities are excluded before a conclusion is reached.

The presence of Rh antibodies can be excluded based on negative reactions with enzyme treated cells, but only where a sensitive validated enzyme technique is used**.**

5.12. 10R4

Material

'Patient' 1: B D neg, inert	'Donor' W: O D neg, SS, Fy(a+b+)
'Patient' 2: O D neg, DAT pos, anti-S (titre 4)	'Donor' Y: O D neg, Ss, Fy(a-b+)
'Patient' 3: A D neg, DAT pos, anti-s (titre 1)	'Donor' Z: O D neg, Ss, Fy(a+b-)

Problems with material

Airspace was closed due to volcanic ash cloud, so non-UK labs were not sent material until 7 days after the planned distribution date.

'Donor' Y was haemolysed due to an infected batch of modified Alsever's. Repeat samples were sent to labs reporting that haemolysis would prevent analysis of the samples. In-house testing on the closing date using a grossly haemolysed sample, gave the expected reactions, and the decision was taken to score the exercise as usual.

Table 14 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**0/423**	**0**	**0/231**	**0**
D Grouping	**All Samples**	**4/423**	**4**[1]	**11/231**	**17**
Antibody Screening	**All Samples**	**0/419**	**0**	**0/214**	**0**
Antibody ID	**All Samples**	**13/379**	**13**	**11/172**	**12**
	- Anti-S		2		5
	- Anti-s		11		7
Incompatibilities	**All Samples**	**24/409**	**50** [1]	**33/202**	**84**
	- P2DW (S)		1		5
	- P2DY (S)		14		16
	- P2DZ (S)		13		24
	- P3DY (s)		8		18
	- P3DZ (s)		14		21
Compatibilities	**All Samples**	**12/409**	**13**	**14/202**	**22**
Phenotyping (Fy^a/Fy^b)	**All Samples**	**5/241**	**8**	**8/103**	**23**
	- False pos		2[2]		6
	- False neg		6[2]		17

[1] - One due to transcription error [2] - Two due to transposition of samples or results

UK Errors (excluding transcription and transposition errors)

D Typing

- Three laboratories made D typing errors:
  - Two reported P2 as D positive, based on positive reactions with anti-D and the reagent control in BioVue cassettes: in 1 case (manual) the reagent control gave a weaker reaction; in the other case, automated results brought forward for review, were manually edited to D positive.
  - One reported P3 as D positive, based on a weak reaction with anti-D and a negative reagent control in BioVue cassettes.

Antibody Identification

- Three laboratories reported incorrect specificities, probably due to misinterpretation of antibody identification panel results.
- Nine laboratories positively 'identified' the antibody present plus an additional clinically significant specificity not present.

Crossmatching
- 23 laboratories missed a total of 49 incompatibilities:
  - One missed all of the incompatibilities, suggesting some sort of procedural error
  - There was no correlation of errors with IAT technology used or with reported haemolysis of the whole blood samples

Phenotyping (Jk^a/Jk^b)
- Four laboratories reported false negative results

Exercise Comments
An interpretation of D positive should not be made on the basis of a weak positive result with a single anti-D reagent. (BCSH guidelines 2004).

Where a reagent control gives a positive reaction the test is invalidated regardless of the strength of reaction relative to anti-D reagent(s), and no interpretation should be made until the D status has been confirmed using saline reacting monoclonal anti-D reagents.

The specificity of an antibody should only be assigned when it is reactive with at least two examples of reagent red cells carrying the antigen and non-reactive with at least two examples of reagent red cells lacking the antigen (BCSH guidelines 2004). This rule applies independently to each antibody specificity potentially present in an antibody mixture.

5.13. 10E5

Material

‘Patient’ 1: Anti-c+Jk^b (titre 8 and 4 respectively)
‘Patient’ 2: Inert
‘Patient’ 3: Anti-c (titre 4)
‘Patient’ 4: Inert

Table 15 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples** - P2/P4 inert	**1/417**	**2** 2[1]	**1/90**	**1** 1
Antibody ID	**All Samples** - P1 – anti-c+Jk^b - P3 – anti-c	**18/381**	**19** 14 5[2]	**6/89**	**8** 6 2

[1] – Both due to transcription error [2] – One due to transcription error

UK Errors (excluding transcription and transposition errors)

Antibody identification
- 15 laboratories reported incorrect or incomplete results for ‘Patient ‘1:
  - 13 identified anti-c, but did not positively identify anti-Jk^b
    - Ten recorded that they were unable to exclude anti-Jk^b but did not make UI submissions
    - Four did not mention anti-Jk^b (including 1 UI submission):
      - One overlooked a positive reaction
      - One misread the phenotype as Jk(b+)
      - One overlooked the possibility of the antibody, which was masked by anti-c
  - One reported anti-Jk^b+M
  - Five made UI submissions that were agreed
- Three laboratories reported an incorrect identification for ‘Patient’ 3:
  - One reported anti-e probably due to data entry error
  - Two reported an additional specificity

Exercise Comments

When interpreting antibody identification results it is vital that the presence of additional clinically significant antibodies is systematically excluded, and that all positive reactions are accounted for before a final interpretation is made.

Ten laboratories identifying anti-c+/-E and recording anti-Jk^b as not excluded (presumably due to lack of additional panel cells) did not take the opportunity to make a UI submission.

5.14. 10E6

Material

‘Patient’ 1: Anti-E (titre 4)
‘Patient’ 2: Inert
‘Patient’ 3: Anti-Jk^a (titre 1 – weak reaction)
‘Patient’ 4: Inert

Table 16 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples** - P3 – anti-Jk^a	**1/415**	**1** 1	**4/89**	**4** 4
Antibody ID	**All Samples** - P1 - anti-E - P3 - anti-Jk^a	**2/378**	**2** 1[1] 1	**3/87**	**3** 1 2

[1] – Due to probable transcription error

UK Errors (excluding transcription errors)

Antibody screening

- One laboratory reported 1 false negative result using a manual DiaMed technique; the antibody was detected retrospectively, with the cause of the original error unknown

Antibody identification

- One laboratory reported UI for ‘Patient’ 3 but did not make a UI submission

5.15. 10R7

Material

'Patient' 1: A D pos/O D neg (10:90), anti-K+Fy^a (titre 16 & 32)	DW: O D Neg, Kk, Fy(a-b+), Ss
'Patient' 2: A D pos/O D neg (25:75), inert	DY: O D Neg, kk, Fy(a+b+), SS
'Patient' 3: A D pos/O D neg, (50:50), inert	DZ: O D Neg, kk, Fy(a+b+), ss

Problems with material and data

Varying degrees of haemolysis were noted by the majority of participants, and six did not return ABO/D results due to reported unsatisfactory sample quality (SQ). It is possible that the perception of the level of haemolysis was increased because of the mixed field (MF) results obtained.

40% reported using more than one technology for ABO/D typing, either due to the haemolysis, the MF or both. These data had to be excluded from analysis by technique. A short SurveyMonkey survey was distributed retrospectively to try and ascertain what techniques did or did not detect the MF. However, the data was not helpful and has not been included in the final analysis.

Table 17 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**N/A**		**N/A**	
D Grouping	**All Samples**	**N/A**		**N/A**	
Antibody Screening	**All Samples** - P3 - anti-Fy^a	**0/421**	**0**	**0/216**	**0**
Antibody Identification	**All Samples**	**3/381**	**3**	**17/178**	**17**
Incompatibilities	**All Samples** - P1DY (Fy^a) - P1DW (K) - P1DZ (Fy^a)	**2/410**	**4**[1] 2 0 2	**3/203**	**7** 3 2 2
Compatibilities	**All Samples**	**5/410**	**6**	**1/203**	**2**
Phenotyping (S/s)	**All Samples** - False pos - False neg	**4/235**	**8** 5 3	**6/111**	**12** 5 7

1 – All due to transcription error

UK Errors (excluding transcription errors)

Antibody identification

- Three laboratories made identification errors:
  - One reported anti-K+Jk^a
  - One reported anti-Fya only
  - One reported anti-Fya + UI but did not make a UI submission

Crossmatching

- Five laboratories missed a total of six compatibilities, five of which were based on false positive reactions in the IAT crossmatch

Phenotyping

- 39 laboratories had no anti-S and a further 53 no anti-s available
- Four laboratories mistyped five samples, resulting in:
  - Two false negative reactions
  - Five false positives reactions

Exercise Comments

ABO/D grouping

The 'summary of reactions' table below includes laboratories reporting reaction grades vs. both anti-A and anti-D, and shows the percentage recording strong, weak, negative and MF reactions for each of the three 'patient' samples.

Table 18 - Summary of reactions

Sample	Reaction strength vs. anti-A (%)				Reaction strength vs. anti-D (%)			
	Strong	Weak	Neg	MF	Strong	Weak	Neg	MF
Patient 1 (n=412) 10:90	2	7	10 [3]	81 [1]	<1	7	35 [3]	58 [1,2]
Patient 2 (n=412) 25:75	3	7	4	86	1	13 [4]	15	71
Patient 3 (n=414) 50:50	17 [3]	3	<1	79	26 [3]	2	0	72 [2]

[1] Detection rate for MF D was lower than for MF A.
[2] Detection of MF D increased with increasing proportion of D cells
[3] In the 50:50 mix, most of those who did not report MF, recorded a positive reaction, contrasting with the 10:90 mix where the majority (not reporting MF), recorded a negative reaction with the anti-D, and an equal split for anti-A.
[4] A proportion of labs recorded a weak reaction, most marked in P2 against anti-D. This was replicated in-house by BioVue technique.

- 23% of those recording a MF reaction with anti-A made an interpretation of A
- 15% of those recording a MF reaction with anti-D made an interpretation of D pos or D variant.

An extensive supplementary report was distributed and is reproduced in Appendix 3, but the following summarises the questions raised and hypotheses considered:

Questions & hypotheses:

1. **Why are some laboratories not detecting the A cells or D pos cells in the 10:90 mix?** At too low a level and so dispersed through the matrix that they are not being seen by automation or eye. However, some labs recorded a clear MF.

2. **Why is there such a big difference in detection rate of the A cells and D pos cells by BioVue in the 50:50 mix?** The agglutinates are trapping the negative cells; this may be affected by avidity and exacerbated by the higher levels of PEG in the anti-D reagent.

3. **Why is automation generally better than manual (at least for the 25:75 and 50:50 mix)?** The negative cells in the bottom of the column are being overlooked.

4. **Why are some users (particularly BioVue) seeing weak rather than MF reactions?** Depending on the affinity of the antibody, the agglutinates are disrupted by shear forces as they pass through the matrix.

5.16. 10E8

Material

'Patient' 1: Anti-D+C (>32 and 8, respectively)
'Patient' 2: Inert
'Patient' 3: Anti-E+Jk^b (titre 16 and 4 respectively)
'Patient' 4: Inert

Table 19 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**1/414**	**2**	**0/94**	**0**
	- P3 - anti-E+Jk^b		1[1]		
	- P4 – inert		1[1]		
Antibody ID	**All Samples**	**6**	**6**	**12/93**	**14**
	- P3 - E+Jk^b		6[2]		10
	- P1 - D+C				4

[1] – Due to sample transposition during labelling
[2] – One due to transcription error

UK Errors (excluding transcription errors)

Antibody identification

- Six laboratories recorded incorrect antibody identification results for 'Patient' 3:
  - one was unable to exclude anti-E but did not make a UI submission
  - four overlooked the anti-E, which was masked by the anti-Jk^b
    - three do have a formal policy, but this was not followed.

Exercise Comments

Labelling of samples with accession numbers is a critical step, and should be subject to a check prior to the authorisation of results, as recommended in BCSH guidelines (BCSH 2004).

Laboratories should have a process in place for identifying antibodies of potential clinical significance that may be masked by specificities already identified. Regular training and competency assessment in this process is required, even where samples are referred for confirmation of antibody identification.

5.17. 10R9

Material

10R9 Emergency exercise using named patient samples and request forms

'Patient' 1: A D negative, inert – blood in 10-15 mins 'Patient' 2: AB D positive, inert – blood in 10-15 mins 'Patient' 3: O D positive, anti-c – blood in 60-90 mins

Problems with material

Calls were received from two hospital transfusion laboratory managers who said they were not allowed to book fictitious patients into their system.

Table 20 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**1/419**	**2**[1]	**3/244**	**4**
D Grouping	**All Samples** - False pos - False neg - Unable to interpret	**1/419**	**2**[1] 1 1 	**2/244**	**3** 1 2
Antibody Screening	**All Samples**	**0/415**	**0**	**1/228**	**2**
Antibody Identification	**All Samples**	**1/377**	**1**	**4/181**	**4**

[1] – Both due to sample transposition where the samples were not given accession numbers

UK Errors (excluding transposition errors)

Submitted non-emergency results

Antibody Identification

- One laboratory reported an additional specificity – anti-Lu^a
- Three UI submissions were made and all were agreed.

Exercise Comments

The ABO/D grouping errors occurred where EQA samples were not booked into the system in the same way as clinical samples, and essential checks routinely performed on clinical samples were omitted. To obtain the maximum benefit from EQA, it is essential to treat EQA samples in the same way as clinical samples, within the inevitable confines of the exercise format.

A supplementary report on emergency testing can be found in Appendix 4.

The following key points are highlighted:

- In addition to the laboratory which transposed the samples at the start of testing, one recorded an incorrect result of AB D positive for 'Patient' 1, and three recorded incorrect ABO results for 'Patient' 2 within the 15 minutes prior to emergency release of red cells.

- 22 laboratories (8%) selected non group O blood for 'Patient' 2 (AB), following a single forward group only and no immediate spin crossmatch; of these, ten did not include a control.

5.18. 10E10

Material

‘Patient’ 1: Inert
‘Patient’ 2: Anti-K (titre 8)
‘Patient’ 3: Anti-K+S (titre 16 and 2 respectively)
‘Patient’ 4: Inert

Table 21 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**0/413**	**0**	**0/103**	**0**
Antibody ID	**All Samples**	**15/378**	**16**	**7/92**	**7**
	- P2 - anti-K		2[1]		0
	- P3 - anti-K+S		14		7

[1] – One due to sample transposition

UK Errors

Antibody identification

- One laboratory transposed samples from P2 and P3 during labelling, but used a different system from that used to barcode clinical samples. The results attributed to P2 were then misinterpreted as anti-M+S

- Fourteen laboratories made a further 15 antibody identification errors:
  - One reported an additional enzyme non-specific antibody
  - Two reported one of the two specificities present and recorded the other as ‘not excluded’, but did not make UI submissions
  - One reported ant-Fy^b, using an identification panel where the combined reactions for anti-K+S matched exactly those of anti-Fy^b
  - Seven reported anti-Fyb in combination with anti-K or anti-S
  - Four reported anti-M in combination with either anti-K or anti-S.

Exercise Comments

This exercise demonstrates that a systematic process for antibody identification is not always followed in terms of inclusion and/or exclusion of antibody specificities.

By coincidence, the combined reactions of the antibodies present in ‘Patient’ 3 were a ‘perfect’ match on a commonly used antibody identification panel for an antibody that was not present, and ‘Patient’ 3 also lacked the corresponding antigen (Fy^b). This has further highlighted the pitfalls of ‘pattern matching’ alone. Laboratories should have a process in place for identifying antibodies of potential clinical significance that may be masked by specificities already identified.

Regular training and competency assessment in this process is required to ensure the validity of results reported ‘in-house’, and that correct decisions are made regarding referral for confirmation of antibody identification.

5.19. 11R1

Material

'Patient' 1: AB D pos, inert	'Donor' W: AB D Pos, R_1R_1, Jk(a+b-)
'Patient' 2: A D neg, (r'r), inert	'Donor' Y: A D Neg, rr, Jk(a+b+)
'Patient' 3: A D pos, anti-Jk^b (titre 8)	'Donor' Z: A D Pos, R_0, Jk(a-b+)

Performance monitoring

The crossmatch between 'Patient' 2 and 'Donor' Z was withdrawn from scoring since 76 laboratories worldwide (27 UK+Ireland) reported this crossmatch as 'incompatible'. The majority presumably based on de-selection of a D positive donor for a D negative patient.

Table 22 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
ABO Grouping	**All Samples**	**1/418**	**2**[1]	**0/244**	**0**
D Grouping	**All Samples**	**1/418**	**1**[2]	**0/244**	**0**
Antibody Screening	**All Samples** - P3 - anti-Jk^b	**0/414**	**0**	**1/228**	**1** 1
Antibody Identification	**All Samples**	**3/378**	**3**[2]	**5/182**	**5**
Incompatibilities	**All Samples** - P2DW (ABO) - P3DW (ABO) - P3DY (Jk^b) - P3DZ (Jk^b)	**9/406**	**13** 5[3,4] 1 4[3] 3[3]	**12/216**	**14** 4 1 7 2
Compatibilities	**All Samples**	**5/406**	**6**	**53/216**	**67**
Phenotyping (Rh)	**All Samples** - False pos - False neg	**4/263**	**6** 4[5] 2[5]	**2/128**	**3** 2 1

[1] – Both due to sample transposition during manual grouping
[2] – One due to transcription error
[3] – One due to transcription or web data entry error
[4] – One due to donor transposition error
[5] – Two due to probably transcription error

UK Errors (excluding transcription and transposition errors)

Compatibility Testing

- Four laboratories missed a total of five compatibilities due to theoretical de-selection
- Six laboratories missed nine incompatibilities (four due to ABO and five to anti-Jk^b):
  - Two used 'EI' without being able to book the EQA 'donors' into their IT systems - neither would use 'electronic issue' without IT in a clinical situation.
  - One ignored a low red cell level warning on their automation.
  - Three used manual column agglutination techniques:
    - One obtained positive results on repeat after the closing date, and possibly omitted plasma from one column; a liquid level check before incubation was subsequently introduced.
    - One identified badly fitting pipette tips which might have led to sub-optimal levels of reagents being dispensed.
    - One was cause unknown, but no obvious pattern to suggest transposition of samples or results.

Antibody ID

- Two reported an additional specificity not actually present.

Phenotyping (and interpretation of probable Rh genotype)

- Two laboratories each recorded one false positive reactions

- Of those with correct reaction grades
  - 18/262 (7%) reported incorrect interpretations
  - 25 recorded the interpretation for 'Donor 'Z (R_0) as 'Other'

Exercise Comments

In some previous EQA exercises, misinterpretation of reactions with anti-CDE reagents has led to incorrect D typing for r'r and r"r samples, but this was not a problem with Patient 2 (r'r) in this exercise.

This exercise has highlighted the need for careful checking at critical points in manual testing, the risks of overriding warnings from automation, and the potential pitfalls of using 'electronic issue' where all steps are not controlled by computer algorithms.

5.20. 11E2

Material

'Patient' 1: Anti-c+K (titre 4 and >32 respectively) 'Patient' 2: Inert 'Patient' 3: Anti-Fy^a (titre 8) 'Patient' 4: Inert

Table 23 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**0/404**	**0**	**0/94**	**0**
Antibody ID	**All Samples**	**18/371**	**18**	**5/93**	**6**
	- P1 - anti-c+K		17[1]		4
	- P3 - anti-Fy^a		1		2

[1] – One due to transcription error

UK Errors (excluding data entry errors)

Antibody Identification

- Sixteen laboratories reported incorrect antibody identification results for 'Patient' 1
  - One did not positively identify either of the specificities present
  - 15 identified anti-c, but not anti-K:
    - 3 made UI submissions that were not agreed.
    - 11 reported anti-K as not excluded but did not make a UI submission.
    - 1 reported anti-c+S and did not list anti-K as not excluded, due to misinterpretation of panel results, which might have been averted had the results of the screening panel been taken into account.
- One laboratory identified an additional specificity that was not present for 'Patient' 3.

Exercise Comments

When interpreting antibody identification results all available information should be reviewed, including patient phenotype, differential reaction by technique, and results of all cells tested, including the screening panel.

Interpretation and documentation of antibody identification results is an error-prone manual process, and this should be considered when establishing procedures for reporting antibody identification for both clinical and EQA samples.

Twelve laboratories positively identifying anti-c+/-E and recording anti-K as 'not excluded' did not take the opportunity to make a UI submission.

5.21. 11E3

Material

‘Patient’ 1: Anti-K (titre 2)
‘Patient’ 2: Anti-K (titre 2)
‘Patient’ 3: Inert
‘Patient’ 4: Anti-Fy^a (titre 8)

Table 24 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**0/400**	**0**	**0/96**	**0**
Antibody ID	**All Samples**	**0/367**	**0**	**0/94**	**0**

UK Errors

There were no errors made in this exercise.

Exercise Comments

Exercise material trial

Samples for Patients 1 and 2 were prepared from the same pool containing a weak anti-K, with EDTA added to Patient 2 only. The aim was to demonstrate that the addition of EDTA did not affect detection of a weak antibody, so that it can be incorporated into sample production to prevent problems with fibrin developing in EQA samples. There was no statistical difference between the reaction grades recorded by participants for Patients 1 and 2, or in those obtained in house by any of the technologies in common use in the UK. There was no difference in reported sample quality between Patients 1 and 2 (both 100% satisfactory). Given these findings, EDTA will be added to EQA plasma samples in future.

5.22. 11R4

Material

'Patient' 1: O D pos, inert	'Donor' W: O D neg, E-, Ss, Jk(a+b-)
'Patient' 2: A D pos, anti-E+S (titre 8 and 4 respectively)	'Donor' Y: A D pos, E+, ss, Jk(a+b+)
'Patient' 3: B D neg, inert	'Donor' Z: O D neg, E-, Ss, Jk(a-b+)

Performance monitoring

Patient 2 was withdrawn from scoring for antibody identification, as the anti-E component did not react typically with enzyme treated red cells.

Table 25 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**1[1]/411**	**2**	**4/254**	**4**
D Grouping	**All Samples**	**1[1]/410**	**2**	**4/253**	**4**
Antibody Screening	**All Samples**	**1/407**	**1**	**4/240**	**6**
	- P2 - anti-E+S		1[2]		2
	- P1 / P3 - inert				4
Antibody Identification	**All Samples**	**n/a**	**n/a**	**n/a**	**n/a**
Incompatibilities	**All Samples**	**27/400**	**37**	**24/226**	**45**
	- P1 vs. DY		1[1]		4
	- P2 vs. DW		6		12
	- P2 vs. DY		25[3]		17
	- P2 vs. DZ		4		8
	- P3 vs. DY		1		4
Compatibilities	**All Samples**	**2/400**	2[1]	**8/226**	**18**
Phenotyping	**All Samples**	**10/241**	**11**	**7/127**	**14**
	- False pos		2		2
	- False neg		9		12

[1] - One due to result transposition
[2] - Transcription error between automated system and LIMS where no electronic interface was available
[3] - Two due to transcription error

UK Errors (excluding transcription and transposition errors)

Crossmatching)

- 23 laboratories missed 33 IgG incompatibilities
  - Four missed all three incompatibilities – all detectable on repeat after closing
    - one tested directly using donor samples in Alsever's
    - one had problems with a pipette used to dispense plasma
    - one had difficulty in making cell suspensions for automated crossmatching, but this did not result in a low red cell level warning from the automation
    - one was unable to identify source of error
- 19 (all BioVue) missed the incompatibility P2 (anti-E) vs. DY (R_2r) and two of these also missed one of the incompatibilities due to anti-S.
  - 8/9 of those contacted used a BLISS addition method rather than a 0.8% diluent suspension method.
  - one missed a compatibility based on a weak reaction by IAT.

Phenotyping

- Ten laboratories reported two false positive and nine false negative results
- 25 laboratories were unable to test for either Jk^a or Jk^b and a further 13 were unable to test for anti-Jk^b.

Exercise Comments
This exercise highlights the need for robust checks at critical points, including transcription of information, and also the need for regular maintenance and calibration of equipment.

Ortho Clinical Diagnostics provide validated methods for crossmatching by both 'suspension' and 'addition', for both manual and automated testing. However, they advised that the suspension method, using Ortho 0.8% diluent, has a higher sensitivity due to a lower ionic strength in the final reactant mixture, compared to the addition method using 3-5% cells and BLISS.

5.23. 11E5

Material

'Patient' 1: Anti-D (titre 4)
'Patient' 2: Anti-D (titre 2)
'Patient' 3: Anti-D (titre 2)
'Patient' 4: Anti-D+C (titre 16 and 8 respectively)

Table 26 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**0/400**	**0**	**1/95**	**1**
	- P2 - anti-D				1
Antibody ID	**All Samples**	**4[1]/369**	**6**	**3/91**	**3**
	- P1- anti-D		1		0
	- P2- anti-D		0		2
	- P3 -anti-D		1		1
	- P4- anti-D+C		4		0

[1] – All due to transcription or transposition errors

UK Errors (excluding transcription errors)

Antibody Identification

- Two laboratories transposed samples at the labelling stage and did not detect the error later in the process because they did not log the sample onto the LIMS.
- Two laboratories recorded anti-D+UI for Patients 1, 2 and 3 – one was agreed initially and the other on appeal following belated UI submission.

Exercise Comments

It is vital to maintain the continuity of patient and sample identification throughout the transfusion process, and care must be taken at critical steps such as labelling samples in the laboratory.

UK NEQAS Anti-D 'Standard'
The aim of this exercise was to assess the reaction strength and stability of an anti-D at different dilutions, and to determine the optimum dilution for use as a new UK NEQAS anti-D 'standard'. The dilution used as Patient 2 was selected as it was detected by all, gave weak reactions in 85% laboratories and remained stable for the duration of the exercise.

5.24. 11E6

Material

‘Patient’ 1: Inert
‘Patient’ 2: Anti-E+ Fy[a] (both titre 4)
‘Patient’ 3: Inert
‘Patient’ 4: Anti-D+K (both titre 16)

Table 27 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**2/403**	**3**	**0/90**	**0**
	- P1 – inert		2[1,2]		
	- P2 – anti-E+Fy[a]		1[1]		
Antibody ID	**All Samples**	**2/372**	**2**	**5/87**	**5**
	- P2 – anti-E+Fy[a]		2[1]		4
	- P4 – anti-D+K		0		1

[1] One due to transcription error at data entry
[2] One due to transposition of results

UK Errors (excluding transcription errors)

- One laboratory transposed antibody screen and identification results for Patients 1 and 2: panel results for Patient 2 were recorded on panel sheet for Patient 1 and this was used to enter both screen and ID results on the web.
- One laboratory missed the anti-E due to lack of sensitivity in both IAT and enzyme testing.

Exercise Comments

The result transposition error highlights the vulnerability of manual steps in antibody identification and transcription of results. Wherever possible, manual steps should be avoided in antibody screening; however, for antibody identification some manual intervention is inevitable and this should be taken into consideration when establishing procedures for reporting results for both clinical and EQA samples.

5.25. 11R7

Material

'Patient' 1: A D pos, anti-Fy[a] (titre 8)	'Donor' W: O D neg, Fy(a+b+), Jk(a+b+), K-
'Patient' 2: B D pos, inert	'Donor' Y: O D neg, Fy(a+b+), Jk(a+b+), K-
'Patient' 3: O D neg, rr DAT positive, anti-Jk[b] (titre 8)	'Donor' Z: O D neg, Fy(a+b+), Jk(a+b+), K-

Sample details and performance monitoring

The whole blood sample for 'Patient' 3 comprised a pool of group O rr, Jk(b+) donations coated with IgG anti-Jk[b]. D negative or UI (unable to interpret) were considered appropriate results for this sample. All three donor samples were prepared from a single pool of group O D negative Jk(a+b+), Fy(a+b+) donations.

Table 28 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
ABO Grouping	**All Samples**	**3/409**	**6[1]**	**12/257**	**15[2]**
D Grouping	**All Samples**	**5/408**	**5[1]**	**19/256**	**20**
	- P1 / P2		2[1]		2[3]
	- P3 - rr DAT pos		3[1]		18
Antibody Screening	**All Samples**	**2/405**	**2**	**6/247**	**8**
	- P1 – anti-Fy[a]		1		1
	- P2 - inert				4
	- P3 – anti-Jk[b]		1		3
Antibody Identification	**All Samples**	**6/372**	**6**	**6/199**	**6**
	- P1 – anti-Fy[a]		2		0
	- P3 – anti-Jk[b]		4		6
Incompatibilities	**All Samples**	**8/397**	**21**	**10/229**	**44**
	- P1 vs. DW		3		7
	- P1 vs. DY		5		6
	- P1 vs. DZ		3		6
	- P3 vs. DW		4		9
	- P3 vs. DY		3		9
	- P3 vs. DZ		3		7
Compatibilities	**All Samples**	**0/397**	**0**	**3/229**	**9**
Phenotyping	**All Samples**	**2/254**	**4**	**3/132**	**3**
	- False pos		3		3
	- False neg		1		0

[1] All due to transcription / transposition error
[2] Includes eight 'unable to interpret'
[3] includes one 'unable to interpret'

UK Errors (excluding transcription / transposition errors)

Antibody screening

- One laboratory missed the anti-Jk[a] in a manual technique with no cause established.
- One laboratory missed the anti-Fy[a] – the plasma samples were not barcoded suggesting that the whole blood was used in error.

Antibody identification

- Four laboratories reported additional specificities not actually present
- Two laboratories were unable to complete the antibody identification for Patient 3 (reporting anti-Jk^b+UI), but did not make UI submissions.

Crossmatching

- Eight laboratories made crossmatching errors
  - One missed all six incompatibilities using an automated technique; this was not reproducible and it is likely that the cell suspensions were incorrectly prepared.
  - One reported Donors W and Y as compatible with Patient 3 using automated DiaMed, and obtained the same results by automation on repeat after the closing date, but the incompatibilities were detected using manual DiaMed. This appeared to be a problem with a bottle of Diluent 2 – DiaMed suggested a pH change, though internal controls were all working as expected.
  - Four missed a single incompatibility (two each for Patients 1 and 3)
  - Two tested the whole blood sample intended for ABO/D grouping only, resulting in nine missed incompatibilities.

Phenotyping

- One laboratory recorded three false positive K types, and another recorded a false negative K type for Donor Z, reporting the rare phenotype K-k-.

(15 labs were unable to test for anti-K, and a further 170 typed for anti-K only)

Exercise Comments

D typing rr DAT positive sample

There were no D typing errors in the UK due to the positive DAT, and only one positive reaction recorded with either anti-D or the control reagent, which is an improvement on previous similar exercises. A positive DAT was reported by 72/82 (88%) who recorded a result for the DAT.

It is not clear why using anti-Jk^b to coat the rr cells did not cause positive reactions with the control reagent in BioVue technology, in the same way that coating with anti-c has done in previous exercises. It is also unclear whether 10/82 participants have a sensitivity issue with their DATs or whether the DAT positive samples were unstable.

There were 18 errors in the non-UK group: one of these appeared to be due to sample or result transposition with Patient 2; there was no pattern in the use of technology in the remaining 17, with 6 using DiaMed, 6 Grifols, 3 BioVue, one liquid phase microplate and one 'other. Both automated and manual systems were in use and none recorded a positive reaction with the control reagent. Nine recorded a weak positive reaction, 2 a strong positive, and 6 a negative reaction with anti-D.

Reproducibility of crossmatching

The same reaction grade was reported for all 3 (identical) donors vs. both patients by 94% participants. However, 6% recorded variable results, demonstrating the vulnerability of the serological crossmatch, where factors such as preparation of red cell suspensions can affect sensitivity and each reaction cannot be controlled individually.

5.26. 11E8

Material

'Patient' 1: Inert 'Patient' 2: Inert 'Patient' 3: Anti-K+Kp^a (titre 16 and 4 respectively 'Patient' 4: Anti-E (titre 16)

Performance Monitoring

Anti-K+Kp^a and anti-K were accepted as correct antibody identification results for 'Patient' 3, as Kp^a was either 'masked' by K or absent in some panel profiles used, and there is no requirement to detect anti-Kp^a in the antibody screen or to exclude it at identification in either clinical or EQA samples.

Table 29 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	**Total No. of errors**	**Participants with errors**	**Total No. of errors**
Antibody Screening	**All Samples**	**0/400**	**0**	**0/90**	**0**
Antibody ID	**All Samples** - P3 – anti-K+Kp^a - P4 – anti-E	**2/370**	**4**[1] 2[1] 2[1]	**0/87**	**0**

[1] - All due to transposition of results at sample labelling or data entry to web

UK Errors (excluding transcription errors

Exercise Comments

The presence of anti-Kp^a in 'Patient' 3 plasma was reported by 94% participants; the detection and subsequent identification of anti-Kp^a will have been influenced by the antigen profile of the screening and identification panels used. An antibody identification panel from one company did not include a Kp(a+) cell. Reagents from another company included a K- Kp(a+) cell on the screening panel, but on the corresponding identification panel the only Kp(a+) cell was also K+; in this situation, a reaction by IAT with a K- cell on the screening panel would be unaccounted for in the identification panel.

There is no requirement to exclude antibodies of unlikely clinical significance and/or antibody(ies) to low frequency antigens in either clinical or EQA samples, and therefore no need to be concerned that the corresponding antigens might be masked.[1]

Where reactions in the screen and / or panel cannot be attributed to the antibody(ies) already positively identified, it is essential to investigate the potential presence of other antibodies (regardless of probable clinical significance), in order to safely complete the antibody identification process. Accounting for all reactions will cover the possibility of error in the initial identification, ensure that all clinically significant antibodies are identified, and prevent unexpected problems in crossmatching should the patient require transfusion.

Labelling of samples with accession numbers is a critical step, and should be subject to a check prior to the authorisation of results, as recommended in BCSH guidelines[1].

Optional Antibody Titration

Exercise 11E8 included an optional, non-scoring titration (of anti-E in 'Patient' 4), intended for laboratories where titration of IgG antibodies is routinely undertaken as part of antenatal testing. A full analysis of the titration results, and accompanying questionnaire covering the titration methods used and details of local policy regarding the management of antenatal cases with IgG alloantibodies, is included as Appendix 5 and a summary in section 9.

11R9 (Urgent format)

Material

'Patient' 1: AB D neg, anti-D (titre >64)	Donor W: A D neg, SS
'Patient' 2: B D pos, inert	Donor Y: A D neg, Ss
'Patient' 3: A D pos, anti-S (titre 4)	Donor Z: A D neg, ss

Performance monitoring

Patient 2 (group B) was withdrawn from scoring for crossmatching because the reaction strength by IAT vs. Donor Y (group A) deteriorated throughout the course of the exercise and was no longer detectable by all technologies (including tube) on the closing date. Donor Y has been investigated at IBGRL and found to be a weak A_2. Donor Z was withdrawn from scoring for crossmatching as it developed a weak positive DAT.

Table 30 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
ABO Grouping	**All Samples**	**2/407**	**3**[1]	**3/257**	**3**
D Grouping	**All Samples**	**3/405**	**3**[1]	**4/256**	**4**
Antibody Screening	**All Samples**	**6/402**	**9**	**4/246**	**4**
	- P1 – anti-D		2		0
	- P2 – inert		4[2,3]		2
	- P3 – anti-S		3[2]		2
Antibody ID	**All Samples**	**n/a**	**n/a**	**n/a**	**n/a**
Incompatibilities	**All Samples**	**13/396**	**17**	**12/221**	**17**
	- P3 vs. DW		4[2]		8
	- P3 vs. DY		13[4]		9
Compatibilities	**All Samples**	**5/396**	**8**	**7/221**	**13**
Phenotyping	**All Samples**	**n/a**	**n/a**	**n/a**	**n/a**

[1] - All due to error at data entry
[2] - One due to error at data entry
[3] - One due to transcription error
[4] - Four due to transposition error at data entry

UK Errors (excluding transcription / transposition errors)

Antibody screening

- Two laboratories used the whole blood samples intended for ABO/D typing only
- Two laboratories reported false positive screens based on weak positive reactions by IAT

Crossmatching

- Three laboratories missed both incompatibilities due to anti-S, possibly used the whole blood sample intended for ABO/D typing only
- Six laboratories missed the anti-S vs Donor Y (Ss), apparently due to lack of sensitivity in testing, but there was no correlation with technology
- Excluding those for Donor Z (not scored), there were eight missed compatibilities

Exercise Comments

Many of the errors made in this exercise were procedural, and in some cases a directly comparable error would be unlikely to occur in routine clinical practice. However, it is not possible to avoid the need for transcription of information in the transfusion laboratory, especially in situations where IT and automated testing systems are down and blood is required urgently.

The crossmatch between Patient 2 and Donor Y was not scored due to deterioration of the survey material. The density of A antigens on the red cells of group A individuals varies considerably and many patients have low levels of IgM and/or IgG ABO isoagglutinins that may be difficult to detect in a serological crossmatch. Routine laboratory systems have many barriers to prevent issue of ABO incompatible blood to patients, and it is difficult to comment on the clinical significance of the lack of serological reactivity in the unlikely event of these failing.

5.27. 11E10

Material

'Patient' 1: Anti-D+Fy^{a} (titre >32 and 8 respectively) 'Patient' 2: Anti-K (titre 16) 'Patient' 3: Inert 'Patient' 4: Inert

Table 31 – Summary of results

Test category		UK Laboratories		Non-UK Laboratories	
		Participants with errors	Total No. of errors	Participants with errors	Total No. of errors
Antibody Screening	**All Samples**	**0/395**	**0**	**0/96**	**0**
Antibody ID	**All Samples** - P1 – anti-D+Fy^{a} - P2 – anti-K	**3/365**	**3** 3 0	**2/93**	**2** 1 1

UK Errors

Antibody Identification

- Three laboratories reported incorrect or incomplete antibody identification results for Patient 1
  - Two reported anti-D+s without recording the potential presence of anti-Fy^{a}.
  - One reported anti-Fy^{a}+UI but did not make a UI submission.

Exercise Comments

It is important that a systematic process for antibody identification is always followed in terms of inclusion and/or exclusion of antibody specificities.

6. SUMMARY OF ERROR RATES

The error rate is based on the number of opportunities for error by all participants returning results. Figures shown in brackets following the error rate for UK laboratories are the percentages known to be due to transcription or transposition errors (Tx). This information is not available for non-UK laboratories, as these participants are not contacted regarding errors made.

Tables 32 and 33 compare error rates over the last four years for UK and non-UK participants respectively, where n = the number of tests distributed in each category, that were suitable for scoring. It should be noted that the time period has changed from April to March (2007 to 2010), to the calendar year (2011).

***Table 32* – UK error rates** (Tx = transcription or sample transposition, or incorrect sample tested)

Analyte	11R1 – 11E10		09R4 – 10E3		08E4 – 09E3		07E4 – 08E3	
	n	error rate (%Tx)	n	error rate (%Tx)	n	error rate (%Tx)	n	error rate (%Tx)
ABO	12	0.26 (92%)	12	0.17 (78%)	11	0.26 (100%)	12	0.24 (77%)
D	12	0.22 (91%)	12	0.46 (23%) [1]	10	0.67 (43%) [1]	12	0.45 (20%) [1]
False Neg Ab Screen	21	0.11 (89%)	14	0.21 (21%)	16	0.05 (67%)	18	0.09 (71%)
False Pos Ab Screen	15	0.10 (67%)	19	0.07 (83%)	20	0.06 (20%)	18	0.05 (50%)
ABID (single)	12	0.32 (36%)	6	0.4 (44%)	9	0.6 (10%)	9	0.4 (23%)
ABID (dual)	6	1.3 (29%)	7	3.7 (11%)	5	1.1 (36%)	8	1.3 (17.5%)
Missed Incompatibility	17	1.3 (18%)	9	0.62 (62%)	8	0.8 (79%)	16	0.7 (47%)
Missed Compatibility	14	0.32 (33%)	23	0.31 (50%)	13	0.4 (61%)	20	0.4 (56%)
False Pos Phenotyping	11	0.31 (11%)	8	0.59 (58%)	6	1.0 (44%)	6	0.6 (50%)
False Neg Phenotyping	13	0.36 (8%)	16	0.50 (44%)	12	0.7 (22%)	18	0.7 (13%)

[1] - Adjusted figures for the D typing error rate excluding DAT positive sample(s) are:
0.18% (56% tx) for 2007/08;
0.27% (100% tx) for 2008/09;
0.13% (100% tx) for 2009/10

***Table 33* - Non-UK error rates**

Analyte	11R1 – 11E10		09R4 – 10E3		08E4 – 09E3		07E4 – 08E3	
	n	error rate	n	error rate	n	error rate	n	error rate
ABO	12	0.72	12	0.18	11	0.79	12	0.47
D	12	0.93	12	0.77 [1]	10	1.02 [1]	12	0.79 [1]
False Neg Ab Screen	21	0.35	14	1.74	16	1.1	18	1.34
False Pos Ab Screen	15	0.44	19	0.30	20	0.1	18	0.3
ABID (single)	12	1.2	6	1.5	9	1.0	9	0.6
ABID (dual)	6	2.0	7	7.0	5	4.0	8	4.2
Missed Incompatibility	17	3.2	9	4.0	8	3.0	16	3.7
Missed Compatibility	14	3.4	23	0.9	13	1.0	20	1.5
False Pos Phenotyping	11	0.49	8	0.96	6	0.9	6	0.5
False Neg Phenotyping	13	0.78	16	1.0	12	1.4	18	0.2

[1] - Adjusted figures for the D typing error rate excluding DAT positive sample(s) are:
0.26% for 2007/08
0.64% for 2008/09
0.18% for 2009/10
0.06% for 2010/11

7. LEARNING POINTS FROM EXERCISE RESULTS

Table 34

Issue	Exercise(s)	Learning point
ABO/D Grouping		
Discrepancy between the ABO forward and reverse group	09R9	Anomalous ABO groups should be investigated and resolved prior to reporting a blood group, with no assumptions made as to the cause of the anomaly.
Making ABO/D interpretations based on mixed field reactions	10R1 10R7	A mixed field D typing reaction in a patient with no historical group might be due to a D negative patient being transfused D positive blood, and no interpretation should be made until the cause of the anomaly can be confirmed.
Issue of ABO group specific red cells in an emergency situation	10R9	Minimum testing to standards set out in BCSH guidelines for pre-transfusion testing should be undertaken before group compatible blood is issued in an emergency situation.
Interpretation of D type based on a weak reaction with an anti-D reagent	10R4	An interpretation of D positive should not be made on the basis of a weak positive result with a single anti-D reagent.
Interpretation of D type in the presence of a positive reaction with a reagent control	09R7; 10R4	Where a reagent control gives a positive reaction the test is invalidated regardless of the strength of reaction relative to anti-D reagent(s), and no interpretation should be made until the D status has been confirmed using saline reacting monoclonal anti-D reagents.
Antibody Identification		
Selection of cells used for antibody exclusion	09R4	Whilst it is acceptable to exclude an antibody on the basis of a single negative result, wherever possible, the presence of anti-Jk^a, -Jk^b, -S, -s, -Fy^a and –Fy^b, should be excluded with a panel cell bearing homozygous expression of the relevant antigen.
Recognition that an additional specificity may be masked in an antibody mixture	09E5; 09E10 10E3; 10E5 10E10	When interpreting antibody identification results it is vital that the presence of additional clinically significant antibodies is systematically excluded, and that all positive reactions are accounted for before a final interpretation is made.
Use of screening panel results and phenotype when interpreting ID results	11E2	When interpreting antibody identification results all available information should be taken into account, including patient phenotype, differential reaction by technique, and results of all cells tested (including the screening panel).
Positive reactions not accounted for by the specificity already identified.	09E10; 10E2 10E3; 10E8 11E8	Where reactions in the screen and/or panel cannot be attributed to the antibody(ies) already positively identified, it is essential to investigate the potential presence of other antibodies (regardless of clinical significance), in order to safely complete the antibody identification process. Accounting for all reactions will cover the possibility of error in the initial identification, ensure that all clinically significant antibodies are identified, and prevent unexpected problems in crossmatching should the patient require transfusion.
Excluding antibodies using a panel of enzyme treated cells.	10E3	The presence of Rh antibodies can be excluded based on negative reactions with enzyme treated cells, but only where a sensitive validated enzyme technique is used.
Positively identifying antibodies not actually present	10R4 11E10	The specificity of an antibody should only be assigned when it is reactive with at least two examples of reagent red cells carrying the antigen and non-reactive with at least two examples of reagent red cells lacking the antigen. This rule applies independently to each antibody specificity potentially present in an antibody mixture, including those considered of unlikely clinical significance.
Pitfalls of pattern matching	10E10	This follows on from the above point: it might not be possible to distinguish between a single specificity and a mixture (or two or more in a mixture) until the exclusion process has been completed and any necessary additional testing has been undertaken to confirm what is present.
Antibodies of low clinical significance and to low frequency antigens	09E10 10R4 11E8	Once all reactions in the identification and screening panel have been accounted for by the presence of antibodies already identified, there is no need to exclude antibodies of low clinical significance or those directed against low frequency antigens.
Exclusion of antibodies in the presence of enzyme non-specific antibodies	09E6	It is not uncommon to encounter ‘non-specific’ enzyme antibodies in clinical practice. Where an enzyme pan-agglutinin is detected, there is no need to be concerned about additional specificities being ‘masked’ in the enzyme panel, as long as all clinically significant antibodies can either be positively identified and/or excluded by IAT. BCSH compatibility testing guidelines state that ‘the majority of antibodies detectable only by an enzyme technique are unlikely to be of clinical significance’.
Procedure for recording and interpreting ID results	11E2 11E6	Interpretation and documentation of antibody identification results is an error-prone manual process, and this should be considered when establishing procedures for reporting antibody identification for both clinical and EQA samples.

Issue	Exercise(s)	Learning point
Crossmatching and general areas		
Proceeding to 'electronic issue' based on a manually edited automated screen	09R7	Electronic issue should not be performed based on group and screen results that, although obtained on automated systems, have been subject to manual edit.
Sample labelling errors not detected prior to reporting	09R4; 10E8 10E10;11E5	Labelling of samples with accession numbers is a critical step, and should be subject to a check prior to the authorisation of results, as recommended in BCSH guidelines.
Not treating EQA samples in the same way as clinical samples	09R4: 09R9 10R9; 10E10	EQA results should be submitted for assessment based on routine testing; however, spare material may subsequently be used for other purposes, such as training or validation of new equipment.
Risks of manual testing	11R1; 11E6	All stages of manual testing are error prone and secure automation should be used wherever available to reduce the risk.
Manual override of warnings on automation	10R1; 11R1	The security of automated testing is compromised where manual edits are made and/or machine alerts of invalid results do not result in repeat testing to resolve potential anomalies.
Manual transcription of results from automation to LIMS	11R4	Where automated grouping interfaced to the LIMS is available, it should be used at all times to maximize security of data transfer. Any manual intervention in an automated process introduces an increased risk of error.
Equipment maintenance	11R4	Laboratory equipment should be regularly calibrated and maintained, to avoid suboptimal testing (in this case inaccurate measurement of reactants by a faulty pipette leading to reduced sensitivity of the IAT crossmatch).

8. SCHEME DEVELOPMENT AND QUALITY INDICATORS

8.1. Accreditation

Unconditional CPA accreditation of the Scheme has been maintained with the most recent inspection being in July 2010. The Scheme will be inspected by UKAS to ISO17043 standards from 2013.

8.2. IT and communications

- By the end of 2011, 96% of UK and 90% of non-UK laboratories had taken advantage of web-based entry of results and receipt of reports.
- On-line re-registration was launched in 2011.

8.3. Delegate fee in annual subscription

Participants from the UK and Ireland were offered the option to include one delegate fee (at a reduced rate) for the Annual Participants' meeting within the annual subscription for 2010/11 and again for 2011/12. The option was taken up by 224 (54%) of participants for 2011/12. This registration option will continue to be offered by the Scheme.

8.4. UI Submissions

A total of 114 UI submissions were received during this review period. On review of the panel sheets and explanations, the Scheme agreed with 86 submissions (75%) and disagreed with 28 (25%). There were seven appeals, six of which were upheld by the Scheme. Appendix 6 lists all the UI submissions, and provides further details on the 28 where there was no agreement; the current version of the 'Rules' are in Appendix 7. This data will be continue to be reviewed by the Steering Committee.

8.5. ABO titration Pilot

Following discussions with the Steering Committee, and collaboration with UK NEQAS for Histocompatibility and Immunogenetics, a small number of participants from the UK and overseas were recruited into an exploratory pilot exercise for titration of anti-A and anti-B antibodies, between December 2008 and March 2009. The Pilot was distributed in May 2009 and the report can be found in Appendix 8. A Specialist Advisory Group (SAG) was formed and agreed that a full Pilot Scheme should be started. Four exercises were distributed in between December 2010 and December 2011. These were open to laboratories where ABO titrations are undertaken to support the solid organ transplantation programme. Participation in this pilot scheme is being extended in 2012 to include laboratories where ABO titrations are undertaken for other purposes.

8.6. Performance Targets

All internal performance targets were met with the exception of initial contact with borderline performers and reported sample quality. See footnotes 3 to 5 in table 35 for details.

Table 35 – Performance targets from April 2009 to March 2011

Category	No. of Events/opportunities	Target	Target Achievement Rate	Actual Achievement Rate
Exercise Distributions	20	On schedule	100%	**100%**
Report Distributions	20	Within 6 days of C/D [1]	90%	**100%**
Complaints	22	Dealt with in 4 weeks	70%	**95%**
New Unsatisfactory Performers	89	Make telephone contact	90%	**90%**
		Within 5 days of C/D [1,2]	80%	**96%**
Borderline Performers	122	Make telephone contact	50%	**37%** [3]
		Within 10 days of C/D [1,2]	80%	**98%**
Reported Sample Quality – Plasma	69	≤2% unsatisfactory	90% of samples	**94%**
Reported Sample Quality – Whole Blood Samples	24	≤2% unsatisfactory	90% of samples	**42%** [4]
Reported Sample Quality – Red cells in Alsever's	21	≤2% unsatisfactory	90% of samples	**71%** [5]
Integrity of Samples	49433	<0.5% unsuitable for testing per exercise	90% (i.e. 9/10 exercises)	**90%**

[1] - C/D = Closing Date
[2] - Of those contacted
[3] - The vast majority of those not phoned were similar antibody identification errors, where the cause was evident and dealt with in the report, or where a UI submission was made and a letter written instead.
[4] - There are ongoing problems with haemolysis of the whole blood samples, particularly where the DAT is positive. Production of a simulated whole blood sample is part of the Scheme's quality improvement plan.
[5] - One of the red cell samples in 10R4 suffered major haemolysis, and the other two suffered minor haemolysis, due to a batch of contaminated Alsever's solution.

9. QUESTIONNAIRES AND NON-SCORING ELEMENTS

9.1. Mixed field ABO/D typing 10R7

Many laboratories recorded the use of multiple technologies and both automated and manual techniques, limiting the analysis of the mixed field detection by technology. A SurveyMonkey questionnaire was distributed after the closing date in an attempt to ascertain which technologies and techniques had first detected the mixed field reactions. Unfortunately the data obtained included too many confounding factors, and some contradictions with the initial data submitted. For these reasons, the questionnaire data was not used to report on the exercise. The full analysis and report can be found in Appendix 3

9.2. Emergency Exercise

10R9 was an 'emergency' exercise and included additional result sheets and questionnaires. Participants were requested to crossmatch blood from their stock fridge, so no 'donor' cells were provided. The aim was to establish what pre-transfusion testing is performed when blood is requested in an emergency situation. See Appendix 4 for full details.

9.3. Titration exercise and questionnaire

11E8 included a non-scoring antibody titration exercise and questionnaire. The aims of this element of the exercise were to:

- Monitor compliance with BCSH technical guidance in performing titrations.
- Make a direct comparison between methodology and results.
- Investigate triggers for referral to a fetal medicine unit (FMU)

The main points are summarized below and a detailed report can be found in Appendix 5.

- Approximately 80% of samples for titration are tested by a reference centre.
- A wide range of titration values was reported and there was variation within and between technologies.
- DiaMed technology is used for titration by 71% of participants
- Comparing results only from laboratories using DiaMed:
  - Using a weak reaction rather than 1+ as the endpoint of the titration increased the method median
  - Use of different red cell diluents did not appear to affect results.
- Titration results obtained in hospital laboratories are being used to make clinical decisions on testing protocols and referral to a Fetal Medicine Unit; however, the cut-off points used to make this decision are not always in line with BCSH guidance.
- A titre of 32 is widely used as a trigger for further action, but this result does not represent the same level of antibody in all laboratories.

9.4. Standard Practice questionnaire

A standard practice questionnaire was distributed with 09R9 (Appendix 9) and again with 11R1 (Appendix 10). The purpose of this questionnaire is to gather basic information to monitor trends in routine pre-transfusion testing (not necessarily the testing performed on the exercise with which it is distributed). Respondents were requested not to include information regarding testing performed on antenatal, cord or reference samples. This information will be updated on an annual basis.

10. TRENDS IN USE OF TECHNIQUES IN THE UK

Data prior to 2008 are taken from one exercise in each year and therefore only include laboratories returning results. Subsequent data are derived from questionnaires. Historically, questionnaire data have shown that some participants use different or additional techniques for UK NEQAS samples than for clinical samples.

Figure 1 – ABO/D grouping technology

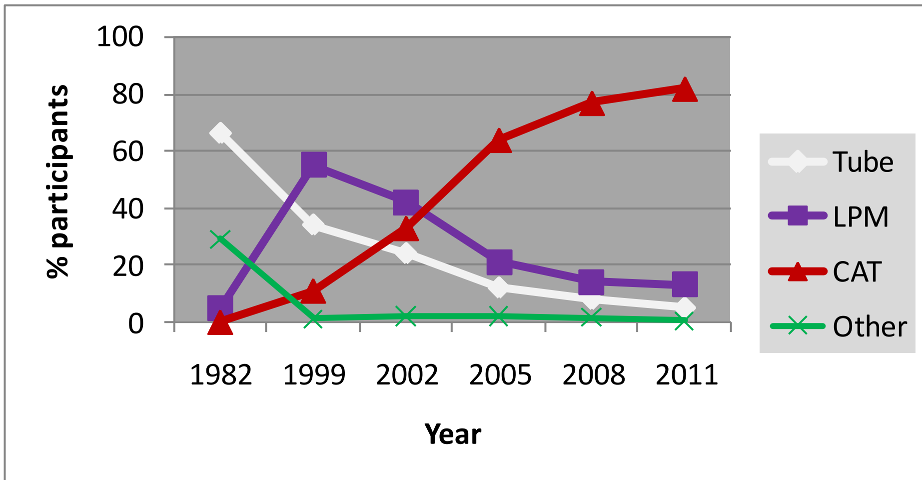


Figure 2 – IAT antibody screening technology

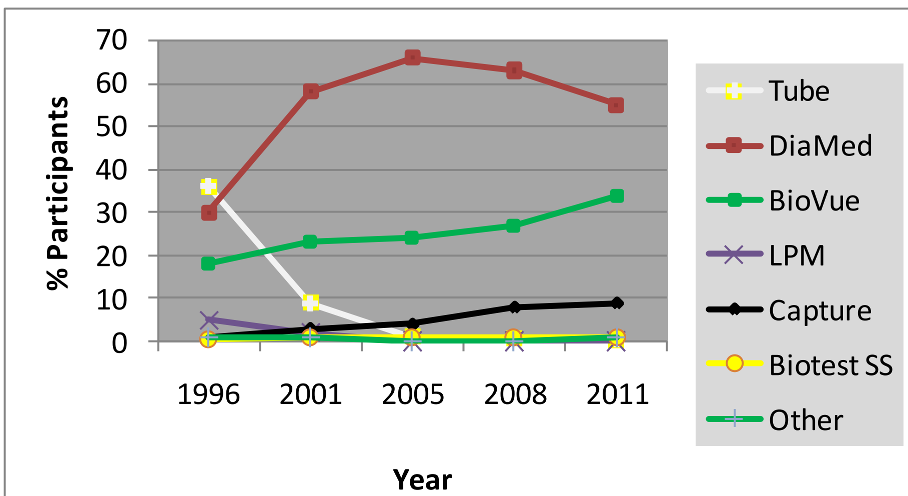


Figure 3 - Use of enzyme techniques in antibody screening

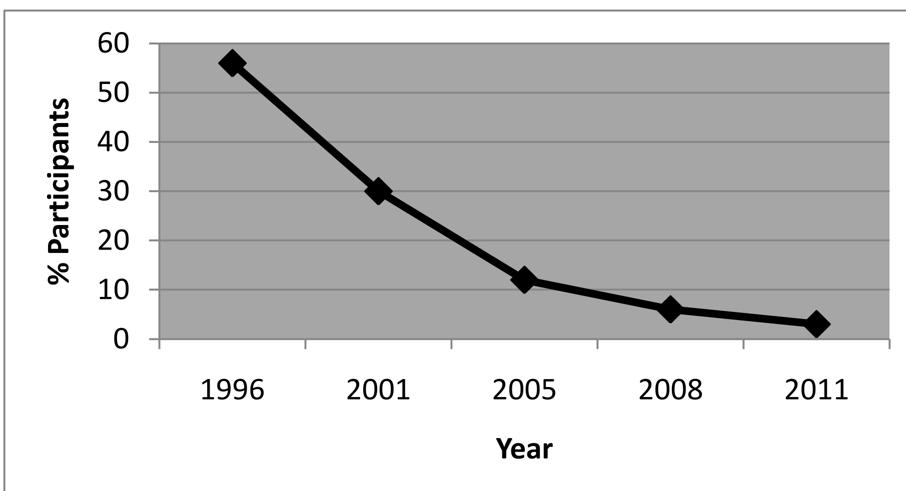


Figure 4 - IAT crossmatching technology

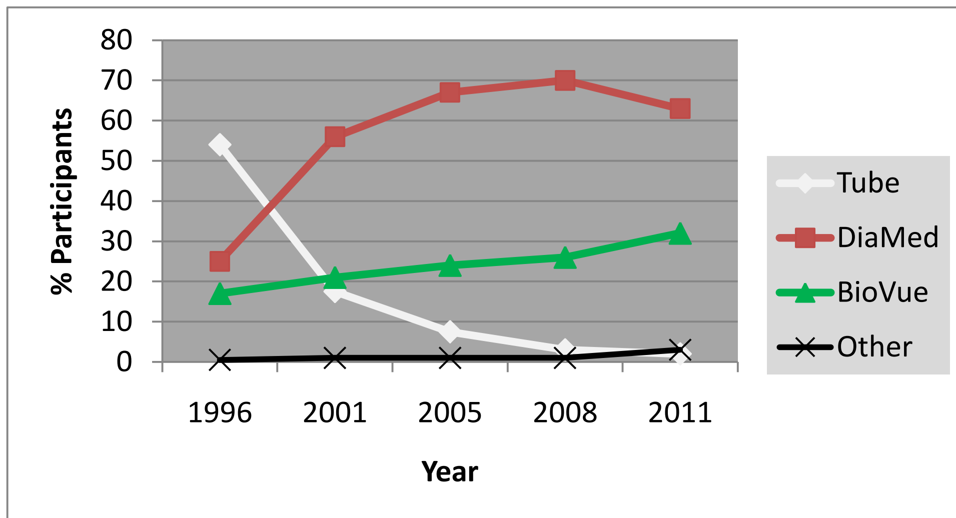
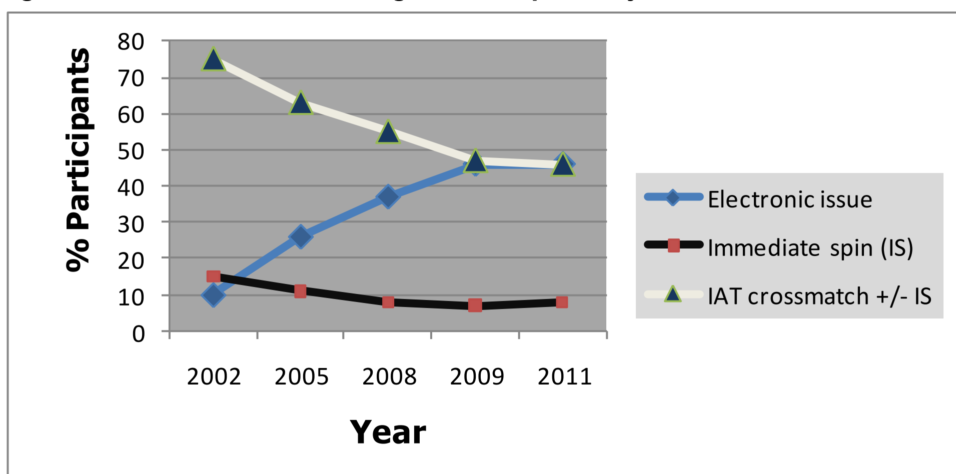


Figure 5 – Means of establishing final compatibility



Abbreviations used in figures 1-4
LPM – Liquid phase microplate
CAT – Column agglutination technology

11. INFORMATION, EDUCATION AND PUBLICATIONS/PRESENTATIONS

Education

- Annual meeting November 2009: See Appendix 11 for programme details.
- Annual meeting November 2010: See Appendix 12 for programme details.
- Annual meeting November 2011: See Appendix 13 for programme details.
- MRCPath teaching

Publications

UK Transfusion Laboratory Collaborative: minimum recommended standards for hospital transfusion laboratories. *Transfusion Medicine 2009,* 19*, 156-158.* B Chaffe, J Jones, C Milkins et al, on behalf of the Collaborative

Pre-transfusion testing. *ISBT Science Series,* ***4****, No 1, 37-44* . J White

UK NEQAS for Blood Transfusion Laboratory Practice - evolution or revolution? Article in Blood Matters Summer 2009, Issue 28. C Milkins

Detection of mixed field reactions in ABO/D typing – results of an EQA exercise and questions raised. *Transfusion Medicine 2010,* ***20****, Suppl 1.* White J, Benkhaled D, Milkins C.

Titrating anti-A and anti-B for ABO incompatible renal transplantation – results of an external EQA pilot exercise. *Vox Sang 2010,* ***99****, Suppl 1.* Milkins C, White J, Benkhaled D, Rowley M.

Trends in the use of electronic issue and other pre-transfusion testing in the UK. *Vox Sang 2010,* ***99****, Suppl 1.* White J, Milkins C, Benkhaled D, Rowley M.

Progress in developing external quality assessment (EQA) and standardization for titration of ABO antibodies in the context of ABO incompatible renal transplant. *Transfusion Medicine 2011,* ***21****, Suppl 1.* White J, Milkins C, Rowley M.

Detection of dual populations for ABO and D in a UK NEQAS exercise. *Vox Sang 2011, 101, Suppl 1*. White J, Milkins C, Rowley M.

The minimum requirements for red cell serological testing. *ISBT Science Series 2011, 6, No 1*. C Milkins.

Presentations/teaching

In addition to those already included in the publications section, Scheme staff made several contributions through oral presentations and teaching to many different organizations.

UK NEQAS (BTLP) was also represented on the following groups/bodies:

- *SHOT Working Expert Group and Steering Group*
- *UK Transfusion Laboratory Collaborative*
- *BCSH Blood Transfusion Task Force*
- *BBTS SIG for Blood Bank Technology*
- *Writing group for the BCSH Compatibility testing and IT guidelines*
- *Modernising Scientific Careers Curriculum Development*
- *Specialist Advisory Committee for Immunohaematology (SACIH)*
- *CMOs National Transfusion Committee IT Working Group (Joint with the NPSA)*

12. FINANCIAL STATEMENT

Income and Expenditure Summaries for the two-year period April 2009 to March 2011 (to the nearest £500)

Income:

Participant Type	2009/11
UK Clinical Laboratories:	611,500
Non-UK Clinical Laboratories:	330,000
Non-Clinical Laboratories:	6,000
Grand Total	**£947,500**

Expenditure:

Category	2009/11
Salaries:	562,000
Revenue:	241,500
Overheads:	162,500
Education/R&D (inc. books meetings etc.)	8,500
Grand Total	**947,500**

Appendix 1

Composition of BTLP Steering Committee at December 2011

Dr Ann Benton (Chair), Morriston Hospital, Swansea/Welsh Blood Service
Mrs Clare Milkins (Secretary), Scheme Manager, UK NEQAS
Dr Megan Rowley, Scheme Director, UK NEQAS
Ms Jenny White, Deputy Scheme Manager, UK NEQAS
Dr Peter Baker, Royal Liverpool University Hospital
Mrs Samantha Harle-Stephens, Derriford Hospital, Plymouth
Mrs Catherine Almond
Dr Rekha Anand, NHSBT, Birmingham
Mr Martin Maley, RCI, NHSBT, Newcastle
Ms Anna Capps-Jenner, UCLH (TDL)
Mr Stephan Bates (NQAAP representative), Cheltenham General Hospital
Mr Malcolm James (co-opted), NHSBT Reagents, Birmingham

Appendix 2

Supplementary Report – D typing
Exercise 09R7 – Distributed 20 July 2009

Introduction

The primary aim of this exercise was to assess proficiency in D typing rr DAT positive samples, and this report details the D typing results for:
'Patient' 1 - Group A D negative, DAT strong positive
'Patient' 3 - Group O D negative, DAT weak positive
The red cells in Patients' 1 and 3 whole blood samples were sensitised with IgG anti-c.

Results

Results of laboratories making D typing errors for Patient 1

There were seven results of D positive reported for 'Patient' 1; however two of these were due to transcription error, and these have not been included in further analysis. One of these was known at the time of the 09R7 report and one investigated subsequently, where follow up testing of anomalous results was undertaken and an interpretation of D negative recorded, but D positive reported during transcription to the website. The error rate for D typing was therefore 5/432 (1.2%). Individual results and interpretations for the five laboratories are detailed in Table 1.

Table 1 – Results of those reporting 'Patient' 1 as D positive

Lab.	Automated	Reaction grades recorded				Interpretation
		Anti-D 1	Anti-D 2	Reagent Control	DAT	
1	Yes	S	S	W	Positive	D Positive
2	Yes	MF	MF	W	NR	D Positive
3	Yes	S	NR	W	NR	D Positive
4	No	S	NR	W	NR	D Positive
5	Yes	S	S	S	Positive	D Positive

S=strong (3-4+), W=weak (w-2+), MF=mixed field, NR=no result

All used BioVue cassettes for initial testing, which contain anti-D reagent(s) and a reagent control potentiated with 2.5% PEG; one also used an ABD card (routinely included for samples requiring crossmatch).

- 4/5 used automated systems – the fifth had problems running the EQA samples on their automation and undertook manual testing.
- All obtained a positive reaction with the reagent control
- All recorded a strong positive reaction (or MF) with the anti-D reagent, and a weak positive reaction with the control; 2 also recorded a positive DAT.
- In 2 cases, the weak positive control was ignored because the laboratories had been experiencing problems with false positive reactions in the control column.
- In at least 4 cases, standard protocols were not followed with respect to repeat testing or to result interpretation; this was apparently because this was an EQA exercise, although it is not clear why this happens or how often protocols are not followed in clinical practice.
- One laboratory repeated the D tying using a manual DiaMed technique and liquid reagents, recording a 2+ reaction; however they inappropriately used an IgG card instead of a saline card, a protocol they also use to confirm weak D types.
- In at least one case, an ABD/ABD BioVue cassette was used inappropriately, as part of the confirmatory testing.
- In one case, the SOP for resolution of grouping anomalies was not clear, and is now being reviewed.

Results of laboratories making D typing errors for Patient 3

All five laboratories reporting D positive for 'Patient' 1 also reported D positive for 'Patient' 3, as did an additional five laboratories, giving an error rate of 10/434 (2.3%). Individual results and interpretations for these ten laboratories are detailed in Table 2.

Appendix 2

Table 2 – Results of those reporting 'Patient' 3 as D positive

Lab.	Automated	Reaction grades recorded				Interpretation
		Anti-D 1	Anti-D 2	Reagent Control	DAT	
1	Yes	W	NR	N	NR	D Positive
2	Yes	W	W	W	Positive	D Positive
3	Yes	MF	MF	W	NR	D Positive
4	Yes	W	NR	W [1]	NR	D Positive
5	Yes	W	W	W	Positive	D Positive
6	Yes	W	NR	W	NR	D Positive
7	Yes	W	NR	N	NR	D Positive
8	No	W	NR	N	NR	D Positive
9	Yes	W	NR	W	Positive	D Positive
10	Yes	S	S	W	Positive	D Positive

S=strong (3-4+), W=weak (w-2+), MF=mixed field, N = negative, NR=no result.
[1] negative on confirmatory testing using manual BioVue

As for 'Patient' 1 all used BioVue cassettes for initial testing.

- This sample generally gave weaker reactions with the anti-D reagent and the control than 'Patient' 1.
- 3 recorded a weak positive reaction with the anti-D reagent and a negative reaction with the control reagent; the other 7 recorded positive reactions with both the anti-D and the control reagent.
- 4 recorded a positive DAT; 2 performed a DAT on 'Patient' 1 but not 'Patient' 3.
- The same issues regarding following standard procedures discussed for 'Patient' 1 applied to 'Patient' 3.
- One laboratory has their automation set to assign a result of D positive to samples giving a reaction of ≥1+ with the anti-D reagent.

Overall results for 'Patients' 1 and 3

Tables 3 and 4 include data from laboratories that correctly reported D negative or UI for 'Patients' 1 and 3 respectively (excluding three laboratories - one with transcription error, one not D typing and UK NEQAS 'in-house' results). The numbers recording combinations of reaction grades for a reagent control and anti-D reagent are shown, and where more than one anti-D was used the results were identical in all cases, except where noted. The expected results are shaded, i.e. where the anti-D reagent and reagent control gave the same reaction grade, or where a control was not used and a negative reaction was recorded with one or more anti-D reagents.

Table 3 – Reaction grades from laboratories reporting 'Patient' 1 as D negative or UI

Control Reaction Grade	Anti-D Reaction Grade				
	Strong Pos	Weak Pos	Mixed Field	Negative	Total
Strong Positive	9 (2) [1]	1	2	7	19
Weak Positive	8 (1) [1]	9 (3) [1]	9 [2]	1	27
Mixed Field	1	0	16 (5) [1]	0	17
Negative	0	0	1 (1) [1]	267	268
No Control Recorded	2	0	0	91	93
Total	20	10	28	366	**424**

[1] Figure in brackets relates to the number of labs recording a negative reaction with a second anti-D reagent
[2] One recorded a weak reaction with a second anti-D reagent

Overall, (excluding the three laboratories detailed above) 69 laboratories reported a positive reaction with a reagent control (either weak, strong or mixed field) for 'Patient' 1 and made the following D typing interpretations:

- 30 D negative
- 33 unable to interpret (UI)
- 6 D positive

Appendix 2

Table 4 – Reaction grades from laboratories reporting ‘Patient’ 3 as D negative or UI

Control Reaction Grade	Anti-D Reaction Grade				
	Strong Pos	**Weak Pos**	**Mixed Field**	**Negative**	**Total**
Strong Positive	3	0	2	2	7
Weak Positive	0	25 (5) [1]	4 (2) [1]	6	35
Mixed Field	0	0	7 (3) [1]	0	7
Negative	0	8 (2) [1]	3	264	275
No Control Recorded	1 (1) [1]	0	0	96	97
Total	4	33	16	368	**421**

[1] Figure in brackets relates to the number of labs recording a negative reaction with a second anti-D reagent

Overall, (excluding the three laboratories detailed above) 56 laboratories reporting a positive reaction with a reagent control (either weak, strong or mixed field) for ‘Patient’ 3 made the following D typing interpretations:

- 26 D negative
- 23 unable to interpret (UI)
- 7 D positive

Results for ‘Patients’ 2 (Group B positive, DAT negative)

Seven laboratories reported a positive reagent control for ‘Patient’ 2 (two MF, one weak and four strong). However, all of these interpreted the D type as D positive, suggesting ‘tickbox’ error in recording the reaction grades.

Direct antiglobulin test (DAT)

The results of the DAT for ‘Patients’ 1, 2 and 3 (all laboratories, including results submitted after the closing date) are shown in table 5.

Table 5 - DAT results (n=438)

Sample	DAT positive	DAT negative	DAT not reported
‘Patient’ 1	171	6	261
‘Patient’ 2	1	101	336
‘Patient’ 3	156	10	272

Significantly more BioVue users reported a DAT than users of other techniques:

- P1 – 80% BioVue; 27% others
- P2 – 33% BioVue; 20% others
- P3 – 74% BioVue; 24% others

Discussion

There are certain limitations with this EQA exercise and with the data collected: firstly, the only options for reporting reaction grades are negative, weak positive, strong positive or mixed field, and therefore more subtle differences between reaction grades for anti-D and control cannot be determined from the data collected; secondly, there is a baseline level of error in recording reaction grades, as seen with seven laboratories reporting a positive reaction with a control reagent for ‘Patient’ 2 (D positive, DAT negative), presumably due to ‘tickbox’ error. However, all reaction grades and results detailed in tables 1 and 2 have been verified with the participating laboratories.

Samples for ‘Patients’ 1 and 3 were prepared to give differing strengths of DAT. The aim of this was to provide more information on the circumstances in which D typing errors occur, i.e. to differentiate between interpretive errors made where the reagent control was clearly positive, and those errors made where the anti-D reagent might give a weak reaction without a corresponding reaction in the reagent control. Excluding those occurring during transcription of results, there were 15 D typing errors made by ten laboratories, and in all but three cases a positive reaction was recorded with the reagent control during initial routine testing.

Where cells are sufficiently coated with IgG to cause a false positive reaction, a reagent control should give a similar reaction to the reagent it is designed to control. A positive reaction with the reagent control invalidates the test result, even where the reaction with the control is weaker than that obtained with the anti-D reagent.

A weaker reaction was recorded with the reagent control than with the anti-D reagent by 80% laboratories reporting ‘Patient’ 1 as D positive and 50% reporting ‘Patient’ 3 as D positive compared with only 3% of those reporting D negative or UI for ‘Patients’ 1 and 3. Although the numbers are small, and there are limitations within the data as

described above, this suggests that obtaining anomalous results of this type increases the risk of an incorrect interpretation being made.

In two cases the weak positive control was dismissed because the laboratories had been experiencing problems with false positive reactions in the control column for clinical samples. These situations should always be resolved as a priority, since the use of reagents or systems giving high levels of false positive reactions can lead to a culture where 'real' weak positive reactions are overlooked.

In three cases a weak positive reaction was obtained with the anti-D reagent for 'Patient' 3, whilst the reagent control gave a negative reaction in initial testing, and no follow-up was triggered. Even where the reagent control is found to be negative, or the reagents in use do not require a control, it is still not safe practice to assign a D type of D positive or D^{Var} based on a weak (<3) reaction with a single anti-D reagent (BCSH[1]). Ortho Clinical Diagnostics advise that (in addition to a positive reaction with the control invalidating the test) weak positive reactions (≤2+) with anti-D reagents in BioVue cassettes may indicate 'spontaneous agglutination' and should be confirmed using a different technology.

Potentiated reagents or techniques should be avoided in confirmatory testing of anomalous ABO/D typing results. This includes BioVue cassettes (and in particular ABD/ABD cassettes which do not include a control), enzyme techniques and antiglobulin techniques. It is also inadvisable to use these techniques to confirm apparent D negative or weak D positive samples, due to the possibility of false positive reactions in the presence of in-vivo IgG or complement coated red cells. When a positive reaction is obtained with the reagent control, testing should be repeated, where possible, with non-potentiated IgM monoclonal anti-D reagents by direct agglutination. If such reagents are not available, patients should be regarded as D negative until the D type has been confirmed by a reference laboratory.

In the majority of cases, automation highlighted the anomalous results and did not offer an interpretation for the D type, but follow-up testing was not always performed according to the SOPs in place for clinical samples, and an incorrect interpretation was made based on the original results. In order to gain the most value from EQA, the samples must be treated as closely as possible to patient samples. This includes decisions to refer to more senior members of staff, and the undertaking of further testing where anomalous results are obtained. Where samples would normally be referred elsewhere before an interpretation is made, the option of UI (unable to interpret) is the most appropriate response.

Conclusions

Misinterpretation of anomalous results and/or failure to adhere to local policy for follow-up played a part in all of the D typing errors in this analysis. It is also clear that there is an increased risk of interpretive error where anomalous results are obtained. It is vitally important to understand the characteristics and limitations of the anti-D reagents in use, even when they are sold as part of a 'testing system'. The principle that a discrepant result for a control invalidates the test results applies to all blood group serology testing and should be understood by all staff performing tests and interpreting results. Warnings given by automated systems should be acted upon and not overridden without careful consideration of the consequences. BCSH guidelines and manufacturers' instructions should be followed with respect to interpretation of weak reactions.

In order to gain the maximum benefit from EQA, samples should be treated as far as possible as clinical samples.

The implications of misinterpretation and reporting of a D negative patient as D positive are potentially very serious, especially for females with childbearing potential, as highlighted in the SHOT annual reports[2]. Until the D type is confirmed, no interpretation should be recorded (other than D negative, if essential to issue blood) and only D negative blood should be transfused, at least to women of child bearing potential.

References

[1] BCSH (2004) Guidelines for compatibility procedures in blood transfusion laboratories, sections 5.10.3 and 5.3.4. *Transfusion Medicine*, 2004. www.bcshguidelines.com

[2] Serious Hazards of Transfusion (SHOT) annual reports 1996/97 - 2008. http://www.shotuk.org/SHOT%20reports%20&%20Summaries.htm

Appendix 3

Supplementary Report for Exercise 10R7
Distributed 12 July 2010 - UK

Introduction

The samples provided for ABO/D grouping for all three ‘Patients’ were designed to simulate a dual population of red cells, arising from the clinical situation where red cells compatible but non-identical for ABO and/or D red cells are transfused. The aims were:
1. To assess recognition of dual populations for ABO and D.
2. Investigate the unexpected outcomes of exercise 08R8 (see discussion).
All three samples were non-scoring for ABO/D, and for the purposes of the EQA exercise, UI was the expected interpretation for ‘Patients’ 1, 2 and 3, since it was not possible to establish the true ABO and/or D type without clinical information to elucidate the cause of the dual population of red cells.

Material

Samples representing Patients 1 and 2 and 3 were prepared from the same pools of group A D positive red cells, group A plasma, and O D negative red cells, mixed in different proportions:

Patient 1 - Group A D positive / O D negative (10:90)
Patient 2 - Group A D positive / O D negative (25:75)
Patient 3 - Group A D positive / O D negative (50:50)

These whole blood samples showed varying degrees of haemolysis which was noted by the majority of participants; however, in a similar clinical scenario where a patient has been transfused with a different ABO group it is quite possible that some haemolysis would occur due to anti-A or anti-B (recipient or donor in origin), so the picture seen in this exercise is not necessarily unrepresentative of a clinical scenario. Six laboratories did not report ABO/D groups for ‘Patients’ 1 and 2, and five for ‘Patient’ 3, citing the reason as poor sample quality.

Data analysis

425/433 (98.2%) laboratories in UK and Ireland returned results for exercise 10R7 by the closing date. Results from laboratories registered only for ABO typing, those not recording reaction grades vs. anti-A and / or anti-D, and those that did not complete testing due to poor sample quality have been excluded from this analysis. The total number of results analysed was 412 for Patients 1 and 2, and 414 for Patient 3. Many laboratories recorded multiple technologies and used both manual and automated techniques, and a few did not record any details of the technology used. Where data has been analysed by technology, only laboratories recording a single technology (tested once, or by the same technology twice) have been included. Where data is analysed with reference to automated / manual testing, those recording the use of an automated technique +/- a manual technique, have been categorised as using automation. Where the term ‘primary’ technology is used it includes those using a single technology plus those using the technology on automation with an additional manual technology. The assumption has been made throughout, that if a MF reaction was not reported, then it was not detected.

Results

1. Overall detection of MF reactions

Table 1 shows the overall detection rate of the dual population in the three samples, and the reaction grades reported where a MF reaction was not recorded.

Table 1 – reaction grades recorded for Patients 1, 2, and 3 vs. anti-A and anti-D

Sample	Reaction strength vs. anti-A				Reaction strength vs. anti-D			
	Strong	**Weak**	**Negative**	**MF**	**Strong**	**Weak**	**Negative**	**MF**
Patient 1 (n=412)	2%	7%	10%	81%	<1%	7%	35%	58%
Patient 2 (n=412)	3%	7%	4%	86%	1%	13%[1]	15%	71%
Patient 3 (n=414)	17%	3%	<1%	79%	26%	2%	0%	72%

[1] This 13% includes 29/121 (24%) of those using BioVue as their primary technology compared with 8/210 (4%) of those using DiaMed as their primary technology.

Appendix 3

2. Detection rate by technology

Tables 2, 3 and 4 show the number (%) using a single technology (tested once, or by the same technology twice), the number (%) of each of these recording a MF reaction vs. anti-A and anti-D, and the subsets recording a MF reaction vs. only anti-A or only anti-D.

Table 2 – Patient 1 (10:90 A+/O-)

Technology	Total	Number (%) detecting MF vs:			
		Anti-A total	Anti-D total	Anti-A not anti-D	Anti-D not anti-A
BioVue	57	44 (77%)	12 (21%)	32 (56%)	0 (0%)
DiaMed	148	130 (88%)	102 (69%)	28 (19%)	0 (0%)
LPMP	14	8 (57%)	7 (50%)	1 (7%)	2 (14%)
Tube	27	12 (44%)	12 (44%)	1 (4%)	1 (4%)

Table 3 - Patient 2 (25:75 A+/O-)

Technology	Total	Number (%) detecting MF vs:			
		Anti-A total	Anti-D total	Anti-A not anti-D	Anti-D not anti-A
BioVue	55	50 (91%)	24 (44%)	27 (49%)	1 (2%)
DiaMed	151	138 (91%)	135 (89%)	3 (2%)	0 (0%)
LPMP	13	9 (69%)	8 (62%)	2 (15%)	1 (8%)
Tube	24	11 (46%)	11 (46%)	1 (4%)	1 (4%)

Table 4 - Patient 3 (50:50 A+/O-)

Technology	Total	Number (%) detecting MF vs:			
		Anti-A total	Anti-D total	Anti-A not anti-D	Anti-D not anti-A
BioVue	62	51 (82%)	30 (48%)	22 (35%)	1 (2%)
DiaMed	153	137 (90%)	138 (90%)	0 (0%)	1 (1%)
LPMP	17	6 (4%)	6 (4%)	0 (0%)	0 (0%)
Tube	27	9 (33%)	10 (37%)	0 (0%)	1 (4%)

3. CAT technology and automation

Table 5 shows the detection rate of MF reactions vs. anti-A and anti-D by manual and automated techniques for those using BioVue and DiaMed as a single technology.

Table 5 – % MF detection by DiaMed and BioVue – manual and automated

Sample	Ratio A+/O-	DiaMed Manual		DiaMed Auto		BioVue Manual		BioVue Auto	
		Anti-A	Anti-D	Anti-A	Anti-D	Anti-A	Anti-D	Anti-A	Anti-D
Patient 1	10:90	81%	76%	90%	67%	75%	42%	78%	16%
Patient 2	25:75	82%	82%	95%	92%	67%	58%	98%	40%
Patient 3	50:50	79%	82%	93%	93%	38%	23%	94%	55%

4. Interpretation of ABO/D typing results – Example: Patient 2

Patient 2 (25:75 A+/O-) had the highest detection rate for MF reactions (by a small margin), with 359 laboratories reporting at least one MF reaction. This sample has therefore been selected to demonstrate the blood grouping interpretations made based on MF reactions:

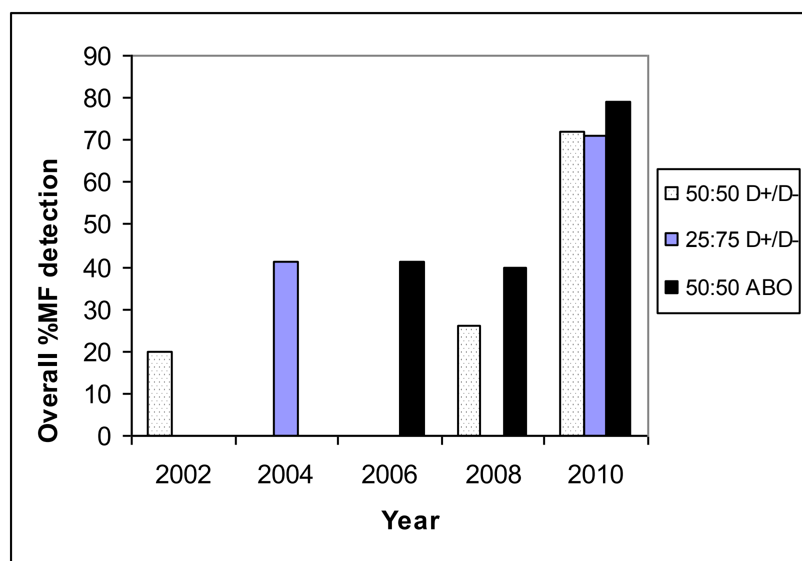
- 80/355 (22.5%) detecting the MF reaction vs. anti-A reported 'Patient' 2 as group A.
- 44/293 (15%) detecting the MF reaction vs. anti-D reported 'Patient' 2 as D positive or D variant.

Appendix 3

5. Trends in detection rate of MF reaction in UK NEQAS exercises

Figure 1 shows overall detection rates, over time, for mixed field reactions in samples with dual populations for ABO and / or D.

Figure 1



Discussion

Background and purpose of the exercise

Recognition of dual populations is clinically important, and EQA exercises have been distributed regularly to monitor the detection of mixed field reactions in samples with dual populations for ABO and / or D (see Fig. 1). The last exercise (08R8) included a 75:25 D+/D- sample, and for the first time, a sample with a dual population for both ABO and D (50:50) which gave some unexpected results. This exercise raised several questions around the low detection rate with the 75:25 D+/D- sample, the difference in detection of mixed fields for ABO and D in BioVue, and the low detection rate of an ABO mixed field by DiaMed, with reports of the 50:50 A+/O- sample giving strongly positive reactions on automation, but repeat testing using the same automation showing clear mixed field reactions.

The current exercise was designed to see if the unexpected findings with the 50:50 ABO/D dual population in 08R8 were reproducible, and to investigate the detection rate of ABO and D dual populations, in a range of samples with the proportion of cells positive for the A or D antigen at < 50%. The aim was to ensure that the ratio of A+/O- cells was the only variable in comparing the detection of the dual population in the three samples. To achieve this, the samples were made from two pre-prepared pools of A D positive and O D negative units, mixed in different proportions. Furthermore, the donor units would have had red cell parameters within normal ranges and were obtained from a single donor session, so that separation (on centrifugation) of cells of different ages and densities, as can sometimes be seen in samples from transfused patients, would not be an issue.

Overall detection of dual populations

The overall detection rate of each of the dual populations for ABO and D in this exercise was much higher than that observed when comparable samples were distributed in the past (see fig 1). In this exercise the detection rate of the A/O mixed field was similar for Patients 1, 2 and 3 at 81%, 86% and 79% respectively. This was not the case for the D+/D- mixed field, where only 58% recorded a mixed field reaction for Patient 1 (10:90) compared to 71% and 72% for Patients 2 and 3 respectively. Of those not recording a mixed field reaction with anti-D, the majority recorded a negative reaction for Patient 1 (10:90), approximately equal numbers recorded negative and weak reactions for Patient 2 (25:75), and the majority recorded a strong positive reaction for Patient 3 (50:50). This would suggest that there are different mechanisms for missing a dual population. However, the overall detection rates do not give the whole picture, as significant differences were observed in detection rate of the mixed field for D, both within and between technologies.

Appendix 3

Detection of dual populations by technology

The detection rate of the D+/D- dual population was a significantly higher by DiaMed than by BioVue (*p<0.001*) for all three samples. There was also a significant difference (*p<0.001*) between the detection rate of the A/O and D+/D- dual populations in each sample by BioVue. For 'Patient' 3 (50:50 A+/O-), 82% BioVue users recorded a mixed field reaction vs. anti-A but only 42% vs. anti-D, confirming the picture seen in a similar sample in exercise 08R8, where 59% BioVue users recorded a mixed field reaction vs. anti-A and 11% vs. anti-D.

The results of 08R8 gave rise to the theory that where a significant proportion of the cells are D positive, some or all of the 'negative' cells become trapped within the agglutinates formed by the reagent and the 'positive' cells, thereby affecting the proportion that pass through the gel or beads in column agglutination systems. It was also speculated that the avidity of the reagent and the presence of any potentiators might affect this process. This could account for the low detection rate of the mixed field with the potentiated anti-D reagent in BioVue cassettes compared with the anti-A, which contains a lower level of PEG than the anti-D reagent. However, for Patients 1 (10:90 A+/O-) and 2 (25:75 A+/O-), this theory cannot be applied, since the D positive cells are in the minority. Also, in Patient 1 the difference between detection of the ABO and D mixed fields was also reported by a small percentage of those using either DiaMed or liquid phase microplate technology, where potentiated reagents are not used.

Where the dual population was not detected in this exercise, unexpected weak reactions were recorded for all three patients vs. anti-A and anti-D, with this effect being most pronounced in Patient 2 by BioVue: 13% overall recorded a weak reaction vs. anti-D, including 29/121 (24%) of those using BioVue as their primary technology and only 8/210 (4%) of those using DiaMed as their primary technology (see Table 1). Results of our in-house testing showed a weak reaction with Patient 2 vs. anti-D by BioVue, but not by DiaMed or tube. The mechanism for these unexpected weak reactions is unknown, but it is thought that shear forces can disrupt agglutinates[1], and we have postulated that this might make them appear 'weak', and that the degree to which this happens might be influenced by the affinity of the reagents. Where these 'weak' reactions involve a very low proportion of 'positive' cells it might be that they are difficult to see by eye, or detect with automated readers, possibly accounting for the results for Patient 1 (containing only 10% D+ cells) not conforming with the overall trend for automation being better at detecting mixed field reactions.

There was no significant difference in the detection rate by DiaMed and BioVue of the A/O mixed field in the three samples. The unexpected finding in 08R8 (50:50 A/O), where a mixed field reaction vs. anti-A was recorded by only 32% of DiaMed users *cf.* 59% BioVue users, was not reproducible.

The clinical importance of recognising a dual population of red cells

There are three ways in which an inappropriate clinical decision can be made in transfusing a patient with a dual population of red cells. Firstly a mixed field reaction might not occur in the testing system used, secondly it might occur but not be recognised, or thirdly, although recognised it might not lead to the appropriate choice of blood components.

There are a number of clinical scenarios resulting in dual populations of red cells, with the most common being the transfusion of ABO/D compatible, non-identical blood. A rarer situation, but of utmost importance, is where the sample is from a post stem cell transplant recipient, either during the engraftment period or when the graft is failing. Failure to obtain or recognise a mixed field reaction in this situation could lead to blood components of the incorrect ABO/D group being transfused, and other special requirements being overlooked. This is also of clinical relevance to laboratories in non-transplant centres, where care is shared, or where transplant patients could present with unrelated conditions in routine or emergency settings. Rarely, a mixed field reaction may be attributed to factors such as permanent chimerisms or ABO subgroups; however, it is still important to identify the cause before making a decision on the most appropriate blood group to transfuse. A mixed field reaction may also be the first sign that a clinically unrecognised ABO incompatible transfusion has taken place. Its recognition is therefore critical, to avert the potential for additional ABO incompatible units being transfused. This is especially relevant where no reverse group is performed in the presence of a historical group, as is routine practice for 26% of laboratories (09R9 Pre-transfusion testing questionnaire).

Patient 2 was reported as D positive or D variant by 15% of those recording a mixed field reaction vs. anti-D, where without a clinical history the laboratory result would give no indication as to whether the original group was D positive or D negative. An interpretation of group A was made by 22% of those recording a mixed field reaction vs. anti-A for Patient 2; fewer than for similar samples in exercises 08R8 (43%) and 06R9 (60%). This may have been due to the lack of any anti-A in the reverse group, indicative of a 'group A' patient transfused with group O donor cells. However, without a history, it would have been prudent to defer drawing a conclusion or issuing blood other than group O.

Appendix 3

Conclusions

One of the limitations of this exercise was the degree of haemolysis of the whole blood samples, which may have affected the level of testing undertaken. In addition, the red cells in the pools were all donated on the same day, which whilst reducing the testing variables, does not reflect the composition of a sample from a transfused patient. However, the indication is that although the overall detection rates for dual populations have improved, and the detection rate of an A/O mixed field is >80% overall, it seems that the detection of a D+/D- mixed field is more variable. This is a concern, especially where this leads to a D negative female patient of childbearing potential being incorrectly grouped as D positive or D variant. The results of this, and previous exercises, suggest that a positive reaction rather than a mixed field reaction is being recorded more frequently where samples mixed field for D contain 50% or more D positive cells. Also, D typing misinterpretations are potentially being made even where mixed field reactions are obtained. Further investigation is required to look at possible mechanisms for not detecting a mixed field reaction where there are a minority of D positive cells, and for obtaining weak reactions where mixed field reactions would be expected.

Reference

[1] P Phillips et al. An explanation and clinical significance of the failure of microcolumn tests to detect weak ABO and other antibodies. Transfusion Medicine, 1997, **7**, 47-53

Appendix 4

Emergency Issue Questionnaire
Distributed with exercise 10R9 – October 2010
UK and Republic of Ireland

Aims

The aims of this 'emergency exercise' were to determine:

- The type of blood selected in an emergency out-of-hours situation
- The level of testing undertaken where blood is required within 10-15 minutes or within 60-90 minutes of sample receipt
- The level of retrospective testing undertaken, both out-of-hours and during the next session of core hours
- Whether any different choices are made where blood is required within 15 minutes for a group AB D positive patient.

A summary of the questions is attached as Appendix 1.

Material

A whole blood sample and a request form were provided for each of the patients listed below, with instructions for completing the exercise in the emergency format. A separate SurveyMonkey questionnaire was issued for each patient.

Patient 1: Dee Borched, female, age 40, group A D negative, inert, blood required within 10-15 minutes
Patient 2: Bea Haive, female, age 35, group AB D positive, inert, blood required within 10-15 minutes
Patient 3: Beau Nidle, male, age 60, group O D positive, anti-c, blood required within 60-90 minutes

Return Rate and data analysis

The return rate was slightly different for each patient, and the return rates and numbers analysed are shown in Table 1; these numbers exclude incomplete and duplicate returns and those with unrecognisable PRNs. Table 2 shows the reasons given for not undertaking emergency testing.

Table 1: Return rate by patient

Sample	Returned	Excluded[1]	Not testing as emergency	Number analysed[2]
Patient 1	385/429 (89.7%)	3	31	351
Patient 2	375/429 (87.4%)	2	27	346
Patient 3	374/429 (86.0%)	3	42	329

[1]Data from laboratories with more than one registration on one site were excluded
[2]Since not all respondents answered all questions, the totals in the following tables do not always equal this number.

Table 2: Reasons for not undertaking emergency testing

Reason for not testing in emergency format	Patient 1	Patient 2	Patient 3
Reference laboratory	12	10	8
No emergency testing	18	16	17
Scenario not considered an emergency	0	0	16[2]
Other	1[1]	1[1]	1[1]
Total (% returns)	31 (8%)	27 (7%)	42 (11%)

[1]Scenario considered improbable
[2] Provision of blood in 60- 90 minutes was achieved with routine procedures. This was not given as an option in the questionnaire, but data has been derived from comment fields.

Results

Both Patient 1 and Patient 2 required blood within 10-15 minutes and the testing protocols used by the 342 laboratories reporting results for both samples were similar. Therefore only data for Patient 1 has been shown, unless there were any differences to report. Data from Patient 3 has been reported separately, as the clinical scenario was different in that blood was required within 60-90 minutes.

Appendix 4

Patients 1 and 2 requiring blood within 10-15 minutes

ABO grouping undertaken within 10-15 minutes

Testing undertaken within 15 minutes is summarised in Table 3.

Table 3: Testing undertaken within 15 minutes

Procedure	Patient 1 - Number (%)
Recorded a group within 10-15 minutes	313/351 (89%)
Performed a 'rapid' group	280/311 (90%)
Completed 2 or >2 cell groups (+/-reverse group)	178/313 (57%)
Used a new aliquot of cells for subsequent groups	156/178 (88%)
Included a control with their forward group(s)	202/311 (65%)
Performed a reverse group before issuing blood	227/313 (73%)

ABO grouping results

The groups recorded within 15 minutes for Patients 1 and 2 are shown in Table 4. 309 (99%) reported the correct group for Patient 1 and 304 (97%) for Patient 2.

Table 4: Grouping results recorded for Patients 1 and 2 within 15 minutes

Group recorded within 15 minutes	Number of laboratories	
	Patient 1	Patient 2
A D negative	309	1
A D positive	0	1
B D positive	0	2
AB D positive	2	304
AB D negative	0	2
AB / UI	0	1
UI/UI (Unable to interpret)	2	2
Total	313	313

Incorrect and incomplete ABO groups

One laboratory transposed samples from Patient' 1 and 'Patient' 2 during testing and reported Patient 1 as AB D positive and Patient 2 as A D negative (issued group O D negative blood).
Two laboratories reported UI/UI for Patients 1 and 2; one performed a rapid forward group only, with no control (technique not specified), and the other a forward and reverse group including a control, that was not stated to be a 'rapid' group. Both issued group O D negative blood.

Patient 1 – The other laboratory reporting the group as AB D positive issued group A D negative blood, suggesting a transcription error.

Patient 2 – The two laboratories reporting the group as B D positive performed a single rapid forward group, with no reverse group or control. One of these issued group AB D positive red cells, again suggesting transcription error, and the other issued group O D negative red cells. The laboratory reporting the group as A D positive performed two forward groups with no control and one reverse group, and issued group A D positive red cells.

Use of controls and abbreviated grouping

The use of controls by laboratories performing 'full' groups and those omitting a reverse group for Patient 1 (group A) and for Patient 2 (group AB) are shown in Table 5. Table 6 shows the exclusion of a control and reverse group by technology for the 216 laboratories using a single technology.

Table 5: Use of controls Patients1 and 2

Level of testing	Negative control included - Number (%)	
	Patient 1 (group A)	Patient 2 (group AB)
Forward and reverse group	156/225 (69%)[1]	154/216 (71%)[2]
Forward group only	46/86 (53%)	52/93 (56%)
Overall	202/311 (65%)[1]	206/309 (67%)[2]

[1] Excludes 2 laboratories not stating whether a control was used
[2] Excludes 4 laboratories not stating whether a control was used

Overall, 40 laboratories did not include a control or a reverse group for Patient 1, with three of these including a control for Patient 2. 41 laboratories did not include a control or a reverse group for Patient 2, with three of these including a reverse group for Patient 1.

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Table 6: Exclusion of a control and reverse group for Patient 1 vs. grouping technology

Technology	Patient 1 - Number (%)		
	No control	No reverse group	No control or reverse group
Tube (n=150)	68[1](45%)	45 (30%)	21 (14%)
DiaMed (n=21)	7 (33%)	10 (48%)	3 (14%)
BioVue (n=25)	2 (8%)	3 (12%)	2 (8%)
Microplate (n=9)	3 (33%)	3 (33%)	2 (22%)
Slide / Tile (n=6)	4 (67%)	5 (83%)	3 (50%)
Other (n=5)	2 (40%)	3 (60%)	2 (40%)

[1] including 2 not stating whether a control is used

Further tests completed prior to labelling blood for collection in 10-15 minutes

38 laboratories did not record a group for Patient 1 prior to the issue of blood; however, four of these issued group A D negative blood, implying that a group had been done but not recorded. Table 7 shows additional tests / procedures undertaken before issue at 15 minutes by the 34 laboratories not performing a group. Table 8 shows additional tests / procedures taken by the 313 laboratories recording a blood group result within 15 minutes.

Table 7: Additional work undertaken by laboratories not performing a group within 15 minutes

Additional test / procedure	Patient 1 - Number (%)
Immediate spin crossmatch	2 (6%)
Check group of the donor units	4 (12%)
Sample donations for retrospective crossmatching	15 (44%)

Table 8: Additional work undertaken by laboratories recording a group within 15 minutes

Additional test / procedure	Patient 1 - Number (%)
Immediate spin crossmatch	118 (38%)
Check group of the donor units	36 (12%)
Sample donations for retrospective crossmatching	247 (79%)

Level of testing undertaken before issue of blood

Table 9 shows the level of testing undertaken by those selecting O D negative and A D negative blood for issue at 15 minutes. This table excludes 34 laboratories selecting group O red cells without performing a group, and four laboratories not recording a group but assumed to have performed one, as group A red cells were selected for issue.

Table 9: Testing undertaken before issue of O group or group A blood

Level of testing prior to blood issue in 15 minutes	Patient 1 - Number (%)	
	Selecting group O blood (n=60)	Selecting group A blood (n=252)
2 forward groups performed on separate aliquots	21 (35%)	133 (53%)
2 forward groups (same aliquot) + ISXM	1 (2%)	10 (4%)
2 forward groups (same aliquot) + ISXM or >1 reverse group	0 (0%)	8 (3%)
1 forward group (+/- reverse group) + ISXM	11 (18%)	45 (18%)
1 forward group (or 2 on same aliquot), reverse group, no ISXM	13 (22%)	37 (15%)
1 forward group, no reverse group or ISXM	14 (23%)	19 (8%)

Retrospective testing

Table 10 shows testing and follow up actions completed by the 351 laboratories, after the issue of blood (10-15 minutes), but before the next session of 'core' hours, and Table 11 any retrospective testing during the next session of core hours.

Table 10: Details of testing after issue at 15 minutes, but before next session of core hours

Further testing	Patient 1 - Number (%)
No further testing	3 (1%)
Forward and reverse group	251 (72%)
Forward group only	7 (2%)
Reverse group only	3 (1%)
Antibody screen	345 (98%)
IAT crossmatch on units issued	245 (67%)
ISXM on units issued	38 (11%)[1]
Other	9 (3%)

[1] 30 of these also performed an IAT crossmatch

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Table 11: Details of further testing during next session of core hours

Further testing	Patient 1 - Number (%)
No further testing	265 (75%)
Blood group	64 (18%)
Group and antibody screen	45 (13%)
IAT crossmatch	5 (1%)
Antibody ID panel	9 (3%)
Other[1]	10 (3%)

[1] eight reviewed previous testing, one requested a second sample, and another updated results on the IT system.

Patient 1 - 2/351 (<1%) laboratories did not undertake an antibody screen at any point during testing; both performed a retrospective IAT crossmatch (one before and one during next session of core hours).

Patient 2 - 6/346 (2%) did not undertake an antibody screen at any point during testing; two of these performed a retrospective IAT crossmatch before the next session of core hours.
4/346 (1%) would not perform any further testing after that completed in 10-15 minutes (all issued group AB D positive blood). One stated that they completed a forward and reverse group (microplate), an immediate spin crossmatch and an antibody screen within 15 minutes.

Units selected for transfusion - Patient 1 (group A D negative, female, aged 40)
Group O D negative blood was issued by 94/350 (27%):

- 58 (62%) issued blood designated as 'flying squad' or equivalent, with an additional 28 issuing K negative and 21 issuing rr (cde/cde).

Group A D negative was issued by 256/350 (73%):

- 244 (95%) issued K negative and 93 (36%) issued rr (cde/cde)

One laboratory did not state the group issued.

Units selected for transfusion – Patient 2 (group O D positive, female, aged 35)
Group O D negative blood was issued by 69/346 (20%), and a further 8/346 (2%) issued group O D positive:

- 52 (75%) issued blood designated as 'flying squad' or equivalent
- 40 (58%) issued rr (cde/cde)

269/346 (78%) issued non-group O blood (5 A D negative, 67 A D positive, 3 AB D negative, 184 AB D positive, 2 B D negative, 8 B D positive)

Patient 3 - requiring blood within 60-90 minutes (Group O D positive, anti-c)

Initial approach to testing
Table 12 shows the initial approach taken to providing blood for within 60-90 minutes, by the 329/374 (88%) laboratories completing the 'emergency testing' questionnaire for 'Patient' 3.

Table 12: Initial approach to testing 'Patient' 3

Initial approach to testing	Number (%)
Group and antibody screen to be followed by a serological crossmatch	101 (31%)
Group and antibody screen with a view to electronic issue	76 (23%)
Simultaneous group, antibody screen and serological crossmatch	151 (45%)
Other – group and screen followed by a second sample for EI	1 (1%)
Total	**329 (100%)**

- 92/318 (29%) did not undertake a second group
- 19/226 (8%) used the same aliquot of red cells for the second group
- 5/328 (2%) did not include a reverse group:
  - two used automation and three tested manually
  - two routinely omit the reverse group (data from 11R1 questionnaire).

Results reported within 60-90 minutes
328/329 (>99%) reported O D positive with antibodies present; the other reported B D positive with no antibodies detected. This laboratory completed an automated group and screen, a second group using a new aliquot of cells, antibody identification, patient phenotyping and crossmatch of two O D positive units (no stated phenotype) that were found compatible by IAT. No further testing would be undertaken either before of during the next session of core hours.

Appendix 4

Use of automation for 'group and screen'

- 222/329 (67%) completed an automated group and screen within 60 – 90 minutes
- 107/329 (33%) reported results based on manual testing at this stage:
  - 59 (55%) stated that they have no automation, however one uses a 'semi-automated' system and 2 have card readers
  - 7 (7%) have automation but do not use it outside of core hours
  - 31 (29%) have automation but do not use it for 'urgent' work (one also stated that it is not used for any work outside of core hours)
  - 2 (2%) test manually where there is no historical group, as EI is not possible and it is quicker to proceed to simultaneous manual G+S and crossmatch
  - 2 (2%) wanted to avoid the risk of delay due to a rejected group on the analyser
  - 3 (3%) stated that the analyser was unavailable when the EQA exercise was tested.

Crossmatching within the 60-90 minutes

- 276 (84%) stated that they performed an initial 2 unit IAT crossmatch, and 53 of these also performed a DRT crossmatch. A further 11 gave IAT crossmatching results, so presumably also performed an IAT crossmatch
- 6 (2%) performed a DRT crossmatch only, but 4 of these stated they had units suitable for issue in 60-90 minutes.

Additional testing undertaken

Table 13 shows additional testing undertaken

Table 13 - Additional testing

Further testing	Number (%)	
	Within 60-90 minutes	After 90 minutes but before the next session of core hours
Antibody identification	286 (87%)	24 (7%)
Patient phenotype	156 (48%)	44 (13%)
Phenotype of units already crossmatched	35 (11%)	10 (3%)
Crossmatch of additional units (not phenotyped)	24 (7%)	9 (3%)
Crossmatch of additional phenotyped units	91 (28%)	96 (29%)

Units selected for transfusion within 60-90 minutes

- 303/329 (92%) initially selected 2 units of O D positive blood for crossmatch – Table 14 shows the breakdown of phenotyped units based on initial approach. In total:
  - 108 (36%) selected K-
  - 100 (33%) selected R_1R_1 (or c negative)
  - 3 (1%) selected other antigen negative blood (E - or Jk(a-))
- 6/329 (2%) initially selected 2 units of O D negative blood for crossmatch, with 4/6 stating that this was 'flying squad' blood
  - 3 stated that they had two units suitable for issue within 60-90 minutes
    - 2/3 crossmatched additional units based on antibody ID results within 60-90 minutes whilst the other did so after 90 minutes but before the next session of core hours
- 3/329 (1%) did not state the group initially selected for crossmatch
- 17/329 (5%) did not undertake a crossmatch within 60-90 minutes for reasons including: "insufficient sample" (2), "unable to find antigen negative blood to crossmatch" (2) and "would not select units until antibody identification completed" (2).

Issue of blood at 60-90 minutes

- 141/283 (50%) reported both initial units selected as compatible, 46 (16%) reported one unit as compatible and 96 (34%) reported both as incompatible. This varied depending on whether the crossmatch was undertaken simultaneously with the antibody screen or retrospectively (see Table 14).
- 228 laboratories stated that they had blood suitable to issue within 60-90 minutes. Table 14 shows the breakdown depending on initial approach taken. In total:
  - 3 had completed antibody identification but stated that no crossmatch was undertaken
  - 88 selected either R_1R_1 or c negative for the initial two unit crossmatch
  - 140 did not initially select either R_1R_1 or c negative units. Of these: 58 crossmatched additional phenotyped units; 2 found the initial two units to be c negative; 15 crossmatched additional random units;16 phenotyped the units already crossmatched; 10 did not complete antibody identification.

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- 99 did not have 2 units to issue at 90 minutes
  - 11 of these did no further in-house testing, but all would try and negotiate delay of the surgery, 3 would refer to a consultant haematologist and 8 would refer samples to a reference laboratory.

Table 14: Selection of phenotyped red cells and red cells suitable to issue within 90 minutes

Outcome	Initial approach to testing – Number (%)	
	Simultaneous screen and IAT crossmatch (n=151)	IAT crossmatch or EI following result of antibody screen (n=177)
Selected K-	36 (24%)	75 (42%)
Selected R_1R_1	12 (8%)	99 (56%)
Both initial units compatible	25 (17%)	105 (59%)
2 units suitable for issue within 60-90 mins	92 (61%)	135 (76%)
Use of automation	72 (48%)	148 (84%)

Further actions taken before next session of core hours
Table 15 shows further action that would have been taken had this been a similar clinical situation out of hours. The options are not mutually exclusive.

Table 15: Actions completed after 90 minutes, but before the next session of core hours

Further actions	Number (%)
No further actions	100 (30%)
Refer to consultant haematologist	64 (19%)
Refer to a more senior BMS	35 (11%)
Try to defer surgery until next day	120 (36%)
Send sample to a reference centre	89 (27%)
Other	68[1] (21%)

[1] including informing clinicians of delay, ordering stock from blood services and requesting repeat samples for referral the next day

Repeat testing during next session of core hours
Data is shown in table 16. The options are not mutually exclusive.

Table 16: Details of repeat testing during next session of core hours

Further testing	Number (%)
None	223 (68%)
Blood group	43 (13%)
Antibody screen	26 (8%)
Antibody ID panel	21 (6%)
Retrospective crossmatch on units issued	5 (2%)
Retrospective phenotype on units issued	2 (1%)
Patient phenotype	19 (6%)
Other	26 (8%)

- 19/91 laboratories not undertaking any repeat testing after 60-90 minutes (either before or during the next session of core hours) performed manual testing within 60-90 minutes, although 10/19 had automation for use during core hours.

- Two laboratories reporting a positive antibody screen did not perform antibody identification or send the sample to a referral centre at any stage. One of these reported two units of group O D positive to be compatible by IAT and stated that the blood was ready within 90 minutes.

General Questions

Selection of blood for 'Unknown' patients
49/349 (14%) laboratories stated that units of a different blood group would have been selected for transfusion to Patient 2 within 10-15 minutes if the sample been from an 'unknown' patient.

Major haemorrhage policy
323/349 (92%) stated that they have a major haemorrhage policy. Of the 26 that do not, one stated that a policy is being introduced at the moment, and another refers to national guidelines for managing major haemorrhage.

Appendix 4

Discussion

Issue of group specific blood within 10-15 minutes

A blood group was reported within 10-15 minutes by 89% of laboratories for Patient 1, and 57% performed a second cell group (+/- a reverse group) within 10 –15 minutes; however, 12% of these performed the second test on the same aliquot of cells as the first group, potentially perpetuating any error in selecting the correct specimen for the first group. This compares with 6% sampling the same aliquot in a similar exercise in 2008 (08R10), 12% in 2006 (06R9) and 18% in 2003 (03R9); until the current exercise there appeared to be a downward trend in this practice.

For Patient 1, 19/351 (5%) laboratories performed a single forward group (or a second group from the same aliquot), with no reverse group or immediate spin crossmatch, before issuing group specific (A D negative) blood. BCSH guidelines state that 'a reverse group or a repeat cell group, in either case using re-sampling, or an immediate-spin crossmatch must also be carried out before ABO matched blood is issued'. Therefore, at least 5% are outwith BCSH guidelines, and since we did not ask whether the reverse group was undertaken by re-sampling, it is possible that a further 37/351 (11%) laboratories testing as above but including a reverse group, might also be non compliant.

Both Patients 1 and 2 were female patients <50 years old with no previous blood group, requiring blood within 10-15 minutes. One of the aims of the exercise was to determine whether emergency testing protocols differed where the patient was initially grouped as AB D positive. However, there was no difference in the level of testing undertaken on Patient 1 (A D negative) and Patient 2 (AB D positive).

BCSH guidelines[1] state that 'care should be taken when results indicate that the patient is group AB D positive, as anomalies such as cold agglutinins may not be detected without adequate controls'. Repeating the forward group in this circumstance would not increase the chances of detecting such an anomaly, but 41/309 (13%) included no reverse group or control for Patient 2 before issuing blood. Fewer laboratories issued group O blood for Patient 2 (22%) than for Patient 1 (27%).

Issue of group O D negative blood

In this exercise, 94/350 (27%) selected O D negative units for Patient 1.. However, at least 33/60 (55%) of those who performed a group within 10-15 minutes had completed a level of testing that would have allowed issue of group specific blood under BCSH guidance as outlined above. Laboratory policy for issue of O D negative or group specific blood in emergency situations should be based on a risk assessment, with factors including the frequency with which emergency testing is undertaken, differences in methodology between routine and emergency testing, level of blood stocks, skill mix and case mix. The NBTC recommends use of O D negative in emergency situations, only until the patient's blood group has been determined, with a limit of two units wherever possible[2].

Issue of blood within 60-90 minutes

Sixteen laboratories did not complete the questionnaire because they did not consider this request to fall into the category of urgent testing. There was a range of approaches to this transfusion request, with 45% undertaking a group, screen and IAT crossmatch simultaneously, 31% undertaking a group and screen followed by an IAT crossmatch, and 23% a group and screen with a view to electronic issue. The benefits of each approach are difficult to assess: this patient had anti-c, and since approximately 21% of D positive red cells are R_1R_1, it is unlikely that two randomly selected D positive units would be compatible. Had the patient had anti-K, there would have been a very good chance of randomly selecting two compatible units. Several respondents said that they selected R_1R_1 and/or K- red cells even before seeing the result of the antibody screen. 76% of laboratories awaiting the outcome of the screen before selecting red cells, had two units suitable for transfusion within 90 minutes, compared with 61% of those undertaking a screen and an IAT crossmatch simultaneously; however this may reflect the relative use of automation (see Table 14) in these groups.

More laboratories than would be expected based on the frequency of R_1R_1 units, found two compatible non-phenotyped red cell units. It is not clear whether this was a matter of luck or whether some of the results submitted were actually those for additional units crossmatched.

Use of automation

Fully automated systems change the balance of risk during 'out of hours' situations. They allow for simultaneous testing of several urgent samples, using routine (and therefore safer, and more secure) techniques. Even where time-constraints require initial manual testing as in the 10-15 minute scenarios in this exercise, results of repeat and additional tests can be available with less 'hands-on' time and greater security. In the 60-90 minute scenario, 67% laboratories performed an automated group and screen whilst 18% tested manually due to lack of automation. However, 15% (48 laboratories) had automation available but did not use it, with the majority of these having a policy to revert to manual testing for urgent and / or 'out of hours' testing. Ten laboratories with automated systems tested manually within 60-90 minutes, and did not repeat testing on the automation at any stage in the process.

Appendix 4

SHOT data has demonstrated that more laboratory errors occur out of hours and with manual testing[3]. The UK Transfusion Laboratory Collaborative[4] recommends that all laboratories have full walk away automation with a bidirectional interface to the laboratory information system, in use 24 hours, 7 days a week, with the exception of "where the workload does not warrant such technology, e.g. hospitals with a remote and rural location performing in the order of 10 group and screens per week then the collaborative expects all reasonable measures to be taken in order to mitigate laboratory errors".

Policy for managing major haemorrhage

The majority (92%) of laboratories have a major haemorrhage policy. Practice is changing rapidly in this area, and consequently, the 2006 BCSH guidelines for managing major haemorrhage have been archived. Current guidance includes guidelines from the Association of Anaesthetists of Great Britain and Ireland (AAGBI) entitled 'Blood transfusion and the anaesthetist: management of massive haemorrhage'[5] and an NPSA rapid response report NPSA/2010/017: the transfusion of blood and blood components in an emergency[6]. The 2010 SHOT report[3] includes a learning point stating 'Every Trust must review its Major Haemorrhage Protocol to ensure that it is compliant with the recommendations of the NPSA Rapid Response Report.

References

1. BCSH (2004) Guidelines for compatibility procedures in blood transfusion laboratories. Transfusion Medicine, 2004, 14, 59-73 and www.bcshguidelines.co.uk
2. NBTC: The appropriate use of group O RhD negative red cells http://www.transfusionguidelines.org.uk/docs/pdfs/nbtc_bbt_o_neg_red_cells_recs_09_04.pdf: (accessed 24/06/11)
3. SHOT reports, http://www.shotuk.org (accessed 11/07/11)
4. UK Transfusion Laboratory Collaborative: Recommended minimum standards for hospital transfusion laboratories *Transfusion Medicine*, 2009, **19**, 156–158
5. Association of Anaesthetists of Great Britain and Ireland (AAGBI) entitled 'Blood transfusion and the anaesthetist: management of massive haemorrhage' http://www.aagbi.org/publications/guidelines/blood-transfusion-and-anaesthetist-management-massive-haemorrhage (accessed 11/07/11)
6. NPSA Rapid Response Report NPSA/2010/017 http://www.nrls.npsa.nhs.uk/alerts/?entryid45=83659 (accessed 11/07/11)

Summary of scenario, instructions and questions

SCENARIO

You are working alone outside of core hours. You receive three separate requests for crossmatching; these **do not** arrive simultaneously and should be tested within separate time-frames. The request forms give patient details and transfusion requirements. Assume these requirements fall within your usual protocols for urgent provision of red cells (i.e. the request details would not just trigger groups and screens), but do not trigger your major haemorrhage protocol.

- Dee Borched (Patient 1) requires two units of red cells for emergency surgery in 10-15 minutes of sample receipt, and may need more later.
- Bea Haive (Patient 2) requires two units of red cells for emergency surgery in 10-15 minutes of sample receipt, and may need more later.
- Beau Nidle (Patient 3) requires two units of red cells for theatre within 60-90 minutes of sample receipt.

INSTRUCTIONS

- Book requests into computer (or manual equivalent if IT not available). Assume they arrive at different times, and do not overlap. You have no other urgent work competing for your time or other resources.
- Prepare two units of red cells each for Patients 1 and 2 (Borched and Haive) within 10-15 minutes, and two units for Patient 3 (Nidle) within 60-90 minutes, using your own blood supplies.
- Undertake whatever testing you would normally perform before the next session of core hours, but stop short of referring elsewhere, calling additional staff in, or ordering red cells from the Blood Centre.
- Document results in the same way as you would normally document emergency testing, e.g. on the computer or workbook and/or on the request form.
- Complete the SurveyMonkey emergency results sheet/questionnaire for each patient. These include questions about what testing would normally be repeated during the next session of core hours, so you will need this information before accessing the survey.

Appendix 4

QUESTIONS - Patients 1 and 2
Within 10-15 minutes:
How many forward groups were performed?
Did you consider one of these to be a ‘rapid’ group?
If more than one group, was the second performed on a new aliquot from the primary sample?
How many reverse groups were performed?
Was a reagent (diluents) control used for ABO/D typing?
Which technology was used for ABO/D typing?
Was any additional testing completed, e.g. immediate spin crossmatch, sample units for retrospective crossmatch, group check on donations?
Record ABO/D type (if performed).

After 10-15 minutes but before next session of core hours
Were any of the following completed (excluding those completed within 10-15 minutes)?
- Forward and reverse group
- Forward group only
- Reverse group only
- Antibody screen
- Antibody identification
- Retrospective IAT crossmatch
- Retrospective DRT crossmatch

During next session of core hours
Which of the following would be routinely performed?
- ABO/D group
- Antibody screen
- Antibody identification
- Retrospective crossmatch on units issued

QUESTIONS – Patient 3

Within 60-90 minutes
What was your initial approach to testing this sample?
If more than one group, was the the second performed on a new aliquot from the primary sample?
Was a reverse group performed?
Was an automated group and screen completed?
- If No, then reason why not

Record ABO/D type and antibody screening result.

Within 60-90 minutes
Were any of the following tests completed?
- Direct room temperature (DAT) crossmatch 2 units
- IAT crossmatch 2 units
- Antibody identification
- Patient phenotype
- Phenotype of units already crossmatched
- Crossmatch of additional units (NOT phenotyped)
- Crossmatch of additional phenotyped units
- Other

What was the ABO/D group of the initial two red cell units crossmatched?
Were these units selected on any of the following criteria?
- Emergency O D negative
- K negative
- CDE negative
- Other

Were two units suitable for issue within 60-90 minutes?
Record results of crossmatching of initial 2 units (if performed).

After 60-90 minutes but before next session of core hours
Were any of the following tests completed?
- Antibody identification
- Patient phenotype

Appendix 4

- Phenotype of units already crossmatched
- Crossmatch of additional units (NOT phenotyped)
- Crossmatch of additional phenotyped units
- Other

What else would you have done in a similar clinical situation?:

- Refer to consultant haematologist
- Refer to more senior biomedical scientist / technologist
- Try to delay surgery until next day
- Send sample to a reference centre
- Other

During next session of core hours

Which of the following testing would be repeated?

- ABO/D group
- Antibody screen
- Antibody identification
- Retrospective crossmatch on units issued
- Retrospective phenotyping on units issued
- Patient phenotype
- Other

QUESTIONS – General

Would your selection of blood for issue within 10-15 minutes have been different if the sample had been from an 'unknown' patient? (with Patient 2 questionnaire)

Does your hospital have a major haemorrhage (massive blood loss) policy?

Appendix 5

Report of titration exercise and questionnaire (11E8) Distributed September 2011 - UK and Republic of Ireland

Introduction

Antibody titration was included with exercise 11E8 as an optional, non-scoring element for laboratories undertaking titration of IgG alloantibodies as part of antenatal testing. The instructions were to titrate 11E8 Patient 4 plasma as if it were an antenatal booking sample, selecting appropriate red cells and using routine techniques. There was an accompanying on-line questionnaire for recording titration results and methods used as well as details of local policy regarding the management of antenatal cases with IgG alloantibodies.

Material

11E8 Patient 4 plasma: Anti-E (all participants returning titration results correctly identified anti-E in exercise 11E8).

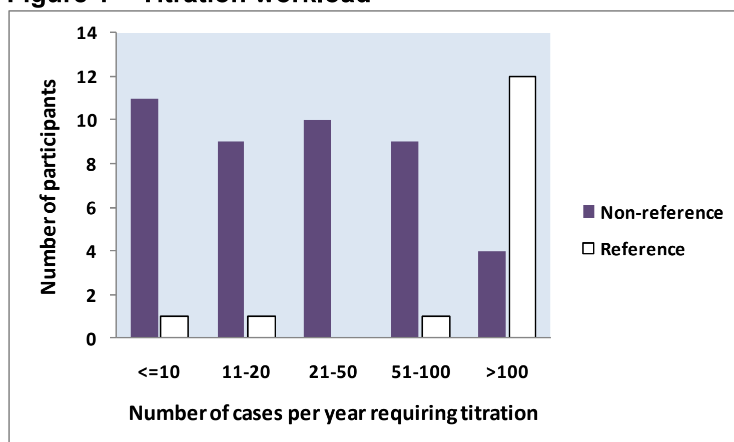
Return Rate and data analysis

The questionnaire was accessed by 172 participants, 66 of whom stated that they performed antenatal titrations in clinical practice. One of the 66 returns has been excluded since no titration results were recorded and no further questions were completed in the questionnaire. Two laboratories did not return reaction grades or a reported titration value, but did complete the questionnaire. Four laboratories reported titration reaction grades but no titration value, and in these cases an interpretation has been made based on the reaction grades recorded and the endpoint (weak or 1+) stated to be used in answer to the questionnaire. Where workload figures have been given as a range, the midpoint has been taken. As not all respondents completed all questions, the numbers in the result tables do not always equal 65; due to rounding, totals may not be exactly 100%. Reference laboratories were taken to be those within the blood services, and any others that stated that they tested referred samples. Three non-reference laboratories reporting >1000 cases were excluded from workload figures, as it is possible that the question could have been misinterpreted to mean general antenatal cases.

Workload

Figure 1 shows the number of antenatal cases requiring titration of IgG alloantibodies per annum in the 58 laboratories responding to this question (15 reference and 43 non-reference).

Figure 1 – Titration workload



Appendix 5

Titration Results

Table 1 shows the number of participants using each IAT technology and the overall titration values obtained by technology. Figure 2 shows the titration value reported vs. % of participants using each technology. Table 2 shows the plasma diluent used and Table 3 the numbers using each red cell diluent by technology.

Table 1 – Number (%) laboratories and titration results by IAT technology

Technique	Number (%)	Median titration result	Range
DiaMed	45 (71%)	8	2-128
BioVue	12 (19%)	8	1-16
Tube	3 (5%)	2	1-8
Immucor	3 (5%)	32	16-32
All technologies	63 (100%)	8	1-128

Of the 60 laboratories using IAT technologies where a standard IAT method is provided by the manufacturer, 58 stated that they used the recommended IAT method, one did not answer this question, and another stated that they did not use the recommended method but gave no further details.

Figure 2 - Titration value by IAT technology

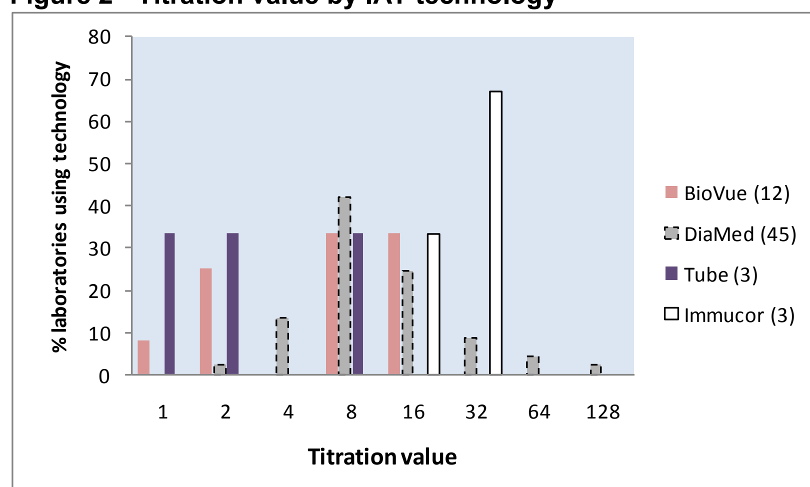


Table 2 – Plasma diluent used

Plasma diluent	Number (%)
PBS	48 (76%)
0.8% NaCl	7 (11%)
CellStab	1 (2%)
ID Diluent 2	5 (8%)
Other	2 (3%)

Table 3 – Red cell diluents used by technology

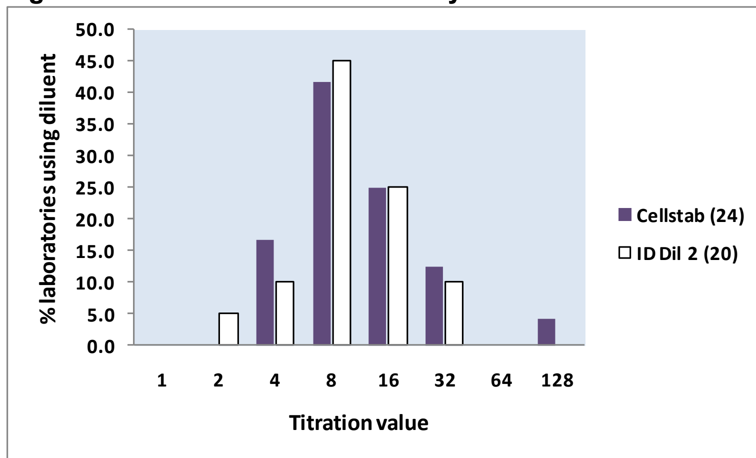
Technique	Number of participants using each red cell diluent					
	DiaMed CellStab	DiaMed Dil-2	Ortho 0.8%	LISS	PBS	Other
DiaMed	24	20	0	1	0	0
BioVue	1	0	9	0	1	1
Tube	0	0	0	2	1	0
Immucor	0	0	0	1	1	1
All technologies	25	20	9	4	3	2

Red cells heterozygous for the E antigen were selected for the titration by 61/63 (97%), whilst two selected homozygous cells.

Figures 3 and 4 show the titration values obtained using DiaMed, by red cell diluent and by stated endpoint of the titration (see section on titration policy), respectively. The stated endpoint for titration (weak or 1+) was

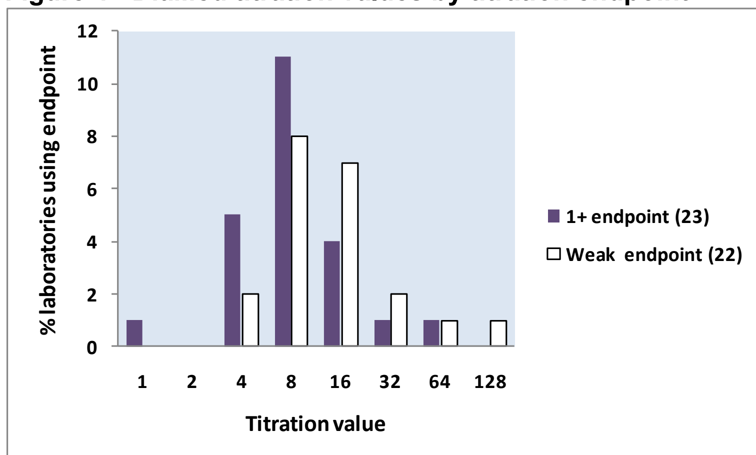
distributed evenly between the groups using CellStab and ID Dil-2. Numbers were too small to make similar comparisons for other technologies.

Figure 3 - DiaMed titration values by red cell diluents



	Method median
CellStab	8
ID Dil 2	8

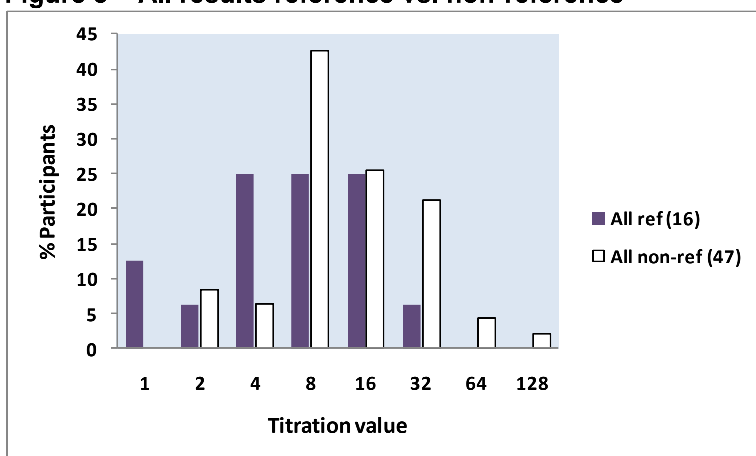
Figure 4 - DiaMed titration values by titration endpoint



	Method median
Weak endpoint	16
1+ endpoint	8

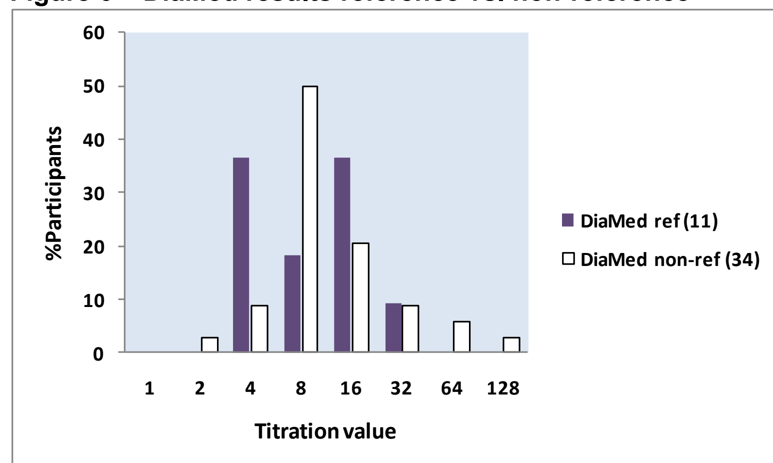
Figures 5 shows titration values reported by reference and non-reference laboratories using all technologies, and figure 6 includes only those using DiaMed technology. Each group contained approximately equal numbers of laboratories using weak and 1+ endpoints. Each group represented in figures 5 and 6 had a median titration value of 8.

Figure 5 – All results reference vs. non-reference



Appendix 5

Figure 6 – DiaMed results reference vs. non-reference



Results from 23 laboratories stating that they test >100 cases per annum (including 15/16 reference laboratories) encompassed the entire range of results reported (1 to 128).

A titration score was reported by only five laboratories.

Table 4 shows the percentage of participants reporting a titration value >=32 or below 32 for Patient 4, for whom this result would have triggered follow-up actions, had this been a clinical sample from a woman booking at an antenatal clinic at 12 weeks gestation.

Table 4 – Actions triggered by the titration result for Patient 4

Action undertaken	Titration value reported (number of participants)		
	<32 (n=54)	>=32 (n=9)	All (n=63)
Ascertain obstetric history	26 (48%)	7 (78%)	33 (52%)
Refer to FMU[1] regardless of history	13 (24%)	5 (56%)	18 (29%)
Refer to blood services for advice	6 (11%)	3 (33%)	9 (14%)
Request a paternal sample	37 (69%)	8 (89%)	45 (71%)
Request a repeat sample at 28 weeks	32 (59%)	4 (44%)	39 (62%)
Request a sample other than at 28 weeks	19 (35%)	5 (56%)	24 (38%)

[1] FMU = Specialist Fetal Medicine Unit

Of the 19 reporting a titre <32 who would have requested a repeat sample at a gestation other than 28 weeks:

- 14 would request the next sample at 16 weeks:
  - 4 would continue monthly to 28 weeks and then 2 weekly
  - 5 would continue to request a sample 4 weekly
  - 5 did not state when any further samples would be requested
- 3 would request the next sample at 20-22 weeks:
  - 1 would then request a sample 4 weekly
  - 2 did not state when any further samples would be requested
- 2 did not specify the timing of the next sample.

Of the 5 reporting a titre >=32 who would have requested a repeat sample at a gestation other than 28 weeks:

- 4 would request the next sample at 16 weeks:
  - 1 would continue monthly to 28 weeks and then 2 weekly
  - 1 would request a sample 2-4 weekly
  - 1 would request a sample 4 weekly
  - 1 did not state whether any further samples would be requested
- 1 would request the next sample at 20-22 weeks.

Titration policy

32/65 (49%) stated that a weak reaction is taken as the end point of a titration, whilst 33/65 (51%) use a cut-off of the last 1+ reaction.

63/65 (97%) use cells with heterozygous expression of the relevant antigen for titration where possible, whilst two select cells with homozygous expression.

50/65 (77%) state that the previous sample (if available) is titrated in parallel with each new sample.

6/65 (9%) titrate the NIBSC standard anti-D in parallel with each titration performed.

Referral based on titration values

Table 5 shows the titration values that participants stated would trigger referral to a specialist fetal medicine unit (FMU) if either anti-K or other IgG alloantibodies, e.g. anti-E, were detected in a sample at booking from a woman with no obstetric history.

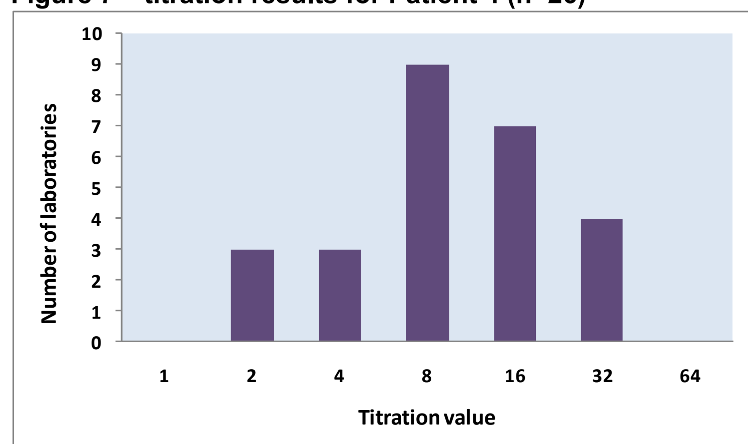
Table 5 – Titration values triggering referral to FMU

Titre at which a booking sample would be referred to a FMU	Number of participants (%)	
	Anti-K	Other IgG antibody, e.g. anti-E
Not referred	0 (0%)	1 (2%)
4	1 (2%)	0 (0%)
8	2 (3%)	3 (5%)
16	2 (3%)	3 (5%)
32	19 (32%)	27 (45%)
512	0 (0%)	1 (2%)
Any titre – all referred	19 (32%)	9 (15%)
Decision not made in laboratory	14[1] (23%)	13[2] (22%)
No policy	3 (5%)	3 (5%)
Total	60 (100%)	60 (100%)

[1] including two referring to NHSBT; [2] including one referring to NHSBT

Figure 7 shows the variation in titre reported for Patient 4 by 26/27 of the laboratories that would refer an IgG antibody such as anti-E to a FMU based on a cut-off titre of 32. One did not submit a titration result for Patient 4.

Figure 7 – titration results for Patient 4 (n=26)



Discussion

Workload

Of the 65 responses, 16 (25%) were from reference centres and 49 (75%) from other laboratories. Taking into account the higher estimated workload of the reference laboratories, approximately 80% of testing appears to be taking place by reference services. It is also likely that some of the work undertaken in hospitals is also referred for confirmation.

Appendix 5

Titration
The 2006 BCSH guidelines for blood grouping and antibody testing in pregnancy[1], recommend titration of antibodies by IAT using cells heterozygous for the corresponding antigen, titration of the National Institute for Biological Standards and Controls (NIBSC) anti-D standard in parallel with each test, and wherever possible 'reduction of variables'. Reference is made to the 1999 BCSH addendum for guidelines for blood grouping and red cell antibody testing during pregnancy[2] and although this document is now archived on the BCSH website, the advice has not changed. In this exercise, only 9% stated that the NIBSC standard is used as an internal control; however, one reference centre stated that a weak anti-Fy^a is titrated as a daily internal control for titrations. Some participants commented that a rising titre would be an indicator for referral to a FMU, highlighting the importance of testing the previous sample in parallel with a new sample to confirm a genuine change in titre rather than variation in testing. However, only 77% stated that they would titrate the previous sample in parallel, if it were available. In this exercise, the majority (97%) did select red cells heterozygous for the E antigen in line with BCSH guidance, but since red cells for titration were not provided as part of this exercise, some variation would have been introduced by the use of different examples of either r"r or R_2r cells.

A wide range of titration values was reported in this exercise (from 1 to 128), and there was also considerable variation within each technology. Further analysis was possible only for DiaMed (used by 71% participants), due to the small numbers in the other groups. The use of different red cell diluents does not appear to have had a significant effect on the endpoints obtained by DiaMed. As expected, analysis of the DiaMed data by whether it was policy to use a weak or 1+ reaction grade to denote the endpoint of the titration showed an increased median (from 8 to 16) for those using a weak endpoint. Overall titration results from reference centres have a lower range (1-32 vs. 2-128) but the same method median (8) as non-reference laboratories. Where only results by DiaMed are included (matched for endpoint), the reference centres have a tighter range of results compared to other laboratories (4-32 *cf.* 2-128), but again the same method median (8).

Testing protocols and referral to a Fetal Medicine Unit
The 2006 BCSH guidance[1] on the frequency of testing and referral to a FMU of women with clinically significant red cell antibodies in pregnancy depends on antibody specificity, titration value and whether or not there is a history of Haemolytic Disease of the Fetus and Newborn (HDFN) in a previous pregnancy. All women who have previously had an infant affected by HDFN should be referred before 20 weeks to a specialist unit for advice and for assessment of fetal haemolysis, irrespective of antibody level. Since the 2006 BCSH guidelines were published, it has become routine practice to establish the D, c, C, E or K status of the fetus by fetal genotyping using a maternal blood sample[3] (taken at 17 weeks for Rh and 20 weeks for K) which may alter the frequency of testing in those pregnancies where the fetus is predicted to be negative for the relevant antigen. The 2006 BCSH guidelines are currently under review to take account of this and other advances in the management of alloimmunised pregnancies.

Anti-K: In addition to the above, where anti-K is identified, it is recommended that the mother's transfusion history and the K type of the father are taken into account when deciding on protocols for testing and referral to a FMU. Current BCSH recommendations are that if the woman has not been transfused and the father is K positive then titration should be performed at monthly intervals to 28 weeks and then every 2 weeks to delivery, and that referral should be made to a FMU regardless of titre. It is acknowledged that because of the dual mechanism by which anti-K can cause HDFN (haemolysis and suppression of haemopoesis), the titre may not be a good measure of the potential for HDFN, but in most affected pregnancies the titre is at least 32.

There was a range of responses to the question regarding referral to a FMU based on the titre of anti-K at booking, possibly since the K type of the father was not indicated: 23% stated that the decision to refer to a FMU would not be made in the laboratory, 32% would refer regardless of titre, 8% at specific various titres below 32, and 32% if the titre were greater or equal to 32.

Other IgG antibodies, e.g. anti-E: Where antibodies associated with HDFN (other than anti-D, anti-c and anti-K) are detected in pregnancy, e.g. anti-C, anti-E, anti-Fy^a and anti-Jk^a, BCSH guidance is that titration at booking and 28 weeks generally provides sufficient information to determine management of the pregnancy, and a that only a titre greater or equal to 32 is likely to cause HDFN. However, the guidelines recognise that a clear-cut association between titre and HDFN has not been established. It is also recommended that a medical decision is made regarding the more frequent testing of women with a previous history of children with HDFN. The questionnaire data from this exercise shows that where the decision regarding referral to a FMU is made in the laboratory, 61% would refer to a FMU at a titre of 32. However, it is interesting to note that the titres reported for Patient 4 by this group ranged across 5 dilutions (2 to 32). A significant proportion (34%) would refer regardless of titre, or at a titre below 32.

Appendix 5

Conclusions

It appears that titration results obtained in hospital laboratories are being used to make clinical decisions on testing protocols and referral to a FMU; however, the cut-off points used to make this decision are not always in line with BCSH guidance. Furthermore, results of this exercise and questionnaire show that whilst a titre of 32 is widely used as a trigger for further action, this result does not represent the same level of antibody in all laboratories. There appears to more consistency in titration results from reference centres using the same technology (DiaMed), but the range still covers 4 doubling dilutions and the numbers are small too small to test the statistical significance of this observation.

References

[1]Guidelines for blood grouping and red cell antibody testing in pregnancy, 2006 www.bcshguidelines.com

[2]Addendum for guidelines for blood grouping and red cell antibody testing during pregnancy. Transfusion Medicine, 1999, **9**, 99 and www.bcshguidelines.com (archived guidelines)

[3]International Blood Group Reference Laboratory User Guide for the Blood Group Genotyping Laboratory : Fetal RhD, Kell, Rhc, RhE and Sex Genotyping from Maternal Blood 07 February 2011 http://ibgrl.blood.co.uk

Summary of Questions

General

- In which country is your laboratory based?
- Do you undertake titration of IgG antibodies as part of antenatal testing?
- If Yes, how many antenatal women per year does this apply to?

Titration – 11E8 Patient 4

- Record titration reaction grades for Patient 4, and titration score if used.
- Which IAT technology was used for the titration?
- Was your IAT method performed as described in the manufacturer's product insert?
- Which plasma diluent was used?
- Which red cell diluent was used?
- What was the zygosity (for the relevant antigen) of the red cells used for this titration?
- If this were a 12 week antenatal booking sample, what actions would be triggered by your result?

Titration policy

- What is the last positive reaction routinely taken into account to determine the end point of the titration?
- What is the preferred zygosity of cells routinely used for titration?
- Is the previous sample (if available) routinely tested in parallel each time a titration is performed?
- The NIBSC standard anti-D titrated in parallel each time a titration is performed?
- What is your cut-off titre for anti-K for referral to a FMU, in an antenatal booking sample on a patient with no obstetric history?
- What is your cut-off titre for other clinically significant antibodies (e.g. anti-E) for referral to a FMU, in an antenatal booking sample on a patient with no obstetric history?

Appendix 6

Summary of Data for UI submissions April 2009 to March 2011

Table 1 – Details by exercise (excluding samples not scored)

Exercise	Sample	Antibodies	No. UI returns	No. agreed	No. not agreed	No. Appeals (no. upheld)
09E5	P2	anti-c+K	59	49	10	4 (3)
09E6	P1	anti-S+PNSA	6	6	0	0
09E6	P4	anti-D+Jk^{b}	4	3	1	0
09E10	P1	anti-D+M	1	1	0	0
09E10	P2	anti-E+Jk^{b}	2	2	0	0
10R1	P1	anti-Fy^{a}	2	1	1	0
10E2	P4	anti-E+Fy^{a}	1	1	0	0
10E3	P3	anti-E+Jk^{a}	4	2	2	0
10E5	P1	anti-c+Jk^{b}	6	5	1	0
10E5	P3	anti-c	2	0	2	0
10E6	P3	anti-Jk^{a}	1	0	1	0
10R7	P1	anti-K+Fy^{a}	1	1	0	0
10E8	P3	anti-E+Jk^{b}	1	1	0	0
10R9	P3	anti-c	3	3	0	0
11R1	P3	anti-Jk^{b}	2	2	0	0
11E2	P1	anti-c+K	5	1	4	0
11R4	P2	anti-E+S	4	4	0	0
11E5	P1	anti-D	2	1	1	1 (1)
11E5	P2	anti-D	2	1	1	1 (1)
11E5	P3	anti-D	2	1	1	1 (1)
11R7	P3	anti-Jk^{a}	3	1	2	0
11E10	P1	anti-D+Fy^{a}	1	0	1	0
Total			114	86	28	7 (6)

Table 2 – Reasons for disagreeing with the UI submissions

Category	No. submissions
Could have identified the antibody with the IAT panel results submitted	9
False positive or false negative reactions recorded	2
Could have excluded additional antibody (ies) based on results submitted	1
Antibody not present positively identified	1
Did not consider the presence of an antibody (actually present)	3
No UI submission received	11
Total	**28**

Appendix 7

Acceptance of a result of UI for antibody identification

This process should only be used where antibodies of likely clinical significance cannot be fully elucidated or excluded.

<u>The following rules will apply</u>:

a. the following <u>will</u> incur penalties

- Misinterpretations contributed to by false negative or false positive reactions.
- If a specificity (actually present) is not entered as positively identified and we feel that it can be identified based on two positive and two negative reactions (as stated in BCSH guidelines) by whatever method is appropriate (e.g. IAT, OR enzymes in the case of Rh). This will be based on a maximum of 2 antibodies being present. (N.B: Serological reactions obtained with the antibody screening cells should be included in the interpretation).
- If a specificity not actually present is entered as positively identified.
- If a specificity is entered as 'cannot be excluded', but we feel that it can be excluded, either because of one or more negative reactions with an appropriate antigen positive cell, or because of one or more negative reactions by a particular method. For example, stating that an Rh antibody cannot be excluded from an antibody mixture in the presence of a negative result with an enzyme treated cell carrying the corresponding antigen would incur a penalty.
- If a specificity is entered as 'cannot be excluded', but the patient phenotype provided shows that the patient is positive for the corresponding antigen.
- Not positively identifying a clinically significant antibody in the presence of an enzyme non-specific antibody.

b. the following <u>will not</u> incur penalties

- Being unable to exclude a specificity in line with BCSH guidelines. E.g. having no homozygous cell available to exclude anti-Jk^a.
- Including a specificity (if actually present) even if the inclusion does not comply with BCSH guidelines (e.g. only one r'r cell).
- If an antibody (actually present) is not reacting with heterozygous cells, but with homozygous cells only, and is recorded as 'cannot be excluded', rather than as 'positively identified'. However, this would only apply if our in-house testing also found non-reactivity with heterozygous cells by the same technique; otherwise, this would be classed as a false negative result.

c. the following documentation is required for a UI submission to be considered

- The UI box should be marked in addition to any boxes for antibodies that you can confidently identify.
- Antibodies that cannot be positively identified, but cannot be excluded should be marked on the result sheet, and the result sheet must be completed with your explanation of why identification cannot be confirmed.
- Copies of all panel sheets showing the reactions recorded, (including those used for antibody screening) must be returned with your exercise result sheet and marked with your PRN.
- If supporting paperwork is not submitted, antibodies recorded as positively identified will be considered as your result for performance monitoring purposes.

Appendix 8

Exploratory pilot exercise for titration of anti-A and anti-B
Distributed 5th May 2009

Introduction

The primary aim of this pilot exercise and questionnaire was to gather information on titration of ABO antibodies in patients undergoing ABO incompatible renal transplantation. However, laboratories for which this clinical setting does not apply were also invited to participate, but were asked to indicate this on the on-line survey and result sheet. Laboratories were requested to titrate anti-A and anti-B in the plasma samples provided vs. the red cell samples provided, using the techniques normally used in the clinical setting of ABO incompatible renal transplantation, or if this was not applicable, in the most relevant other clinical setting.

Material

The following material was provided:

- 4 group O plasma samples for anti-A and anti-B titration, prepared from filtered fresh frozen plasma.
- 2 red cell samples, A1 rr and B rr, suspended to 30% in modified Alsever's solution.

Overall reported sample quality: 98.6% satisfactory.

Return of results

The pilot was distributed to 52 laboratories and 46/52 (88.5%) returned results. Each institution was able to return more than one set of results if more than one technique is routinely employed (e.g. depending on the whether the kidney is from a cadaver or a live donor, or to fulfil differing requirements of different referring institutions). One institution returned two sets of results and another three sets, making a total of 49 sets of results for analysis, although since not all respondents answered all the questions, the total numbers in the tables do not always equal 49.

Results

1. **Main purpose of undertaking titrations**
   - ABO incompatible renal transplantation: 20 (41%)
   - Stem cell/BMT transplant: 13 (27%)
   - ABO HDN: 11 (22%)
   - HLA matched thrombocytes: 1 (2%)
   - Other: 2 (4%)
   - No answer: 2 (4%)

2. **Methods used for titrations in this exercise**
   - 36 (73%) performed titration by direct agglutination at room temperature (DART)
   - 33 (67%) performed the titrations by indirect antiglobulin test (IAT)
     - 24 (73%) using untreated plasma
     - 6 (18%) using DTT treated plasma
   - 8 performed titration by other / additional techniques and of these:
     - 1 DTT treated pre testing by DRT
     - 1 DTT treated pre testing by flow cytometry
     - 2 neutralised the complete antibodies with AB substance
     - 1 tested after incubation at $4^{O}C$ for 2 hours in tubes
     - 2 specified that they used untreated plasma in parallel to DTT treated
     - 1 tested by direct agglutination at $37^{O}C$

Table 1 shows the technology used for testing by Indirect Antiglobulin Test (IAT) and Direct Agglutination at Room Temperature (DART). Table 2 shows the plasma diluents used and Table 3 the red cell diluents.

Table 1 – Technology used

Technique	Tube	DiaMed	BioVue
DART	21	13	2
IAT	12	20	1

Appendix 8

Table 2 - Plasma diluent

Diluent	Number
PBS	38
LISS	1
AB plasma/serum	1
Other	7*

*3 NaCl 0.9%; 2 DiaMed diluent 2; 2 2% BSA

Table 3 - Red cell diluent

Technique	PBS	DiaMed diluent 2	Ortho 0.8% diluent	DiaMed CellStab	0.9% NaCl	LISS
DART	17	7	1	3	3	0
IAT	5	12	1	9	0	4

- *Red cell concentration*:
    - Range for testing by DART: 0.8% to 5%
    - Range for testing by IAT: 0.8% to 5%
- *Plasma/red cell suspension ratio*
    - Range for testing by DART: <1:1 to 4:1
    - Range for testing by IAT: <1:1 to 4:1
- *Incubation time*
    - DART: immediate spin to 60 minutes
    - IAT: 15 to 60 minutes

Wide variation in red cell concentration, plasma/red cell suspension ratio and incubation time was also apparent within groups using the same technology (i.e. CAT or tube).

3. Titration Results

Table 4 shows the method median titration results by DART, IAT using untreated plasma, and IAT using DTT treated plasma for samples 1 – 4.

Table 4 – titration results (method medians)

Technique	P1 anti-A	P1 anti-B	P2 anti-A	P2 anti-B	P3 anti-A	P3 anti-B	P4 anti-A	P4 anti-B
DART	32	16	32	16	8	2	16	4
IAT untreated	256	16	128	16	32	4	64	32
IAT DTT	256	32	128	3	32	4	64	24

Titration results for ‘Patient’ 1 are shown in figures 1 – 4, results for ‘Patient’ 2 in figures 5 – 9, for ‘Patient’ 3 in figures 10 – 13 and for ‘Patient 4 in figures 14 - 17. For all but one sample the histograms for titration by IAT include all IAT results (DTT treated and untreated plasma) as there was no significant difference in the results obtained by either technique. However, ‘Patient’ 2 gave a significantly reduced anti-B titre by IAT with DTT treated plasma *cf.* untreated plasma, so these are displayed separately.

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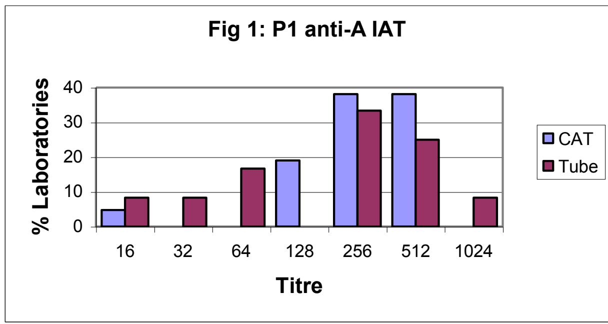

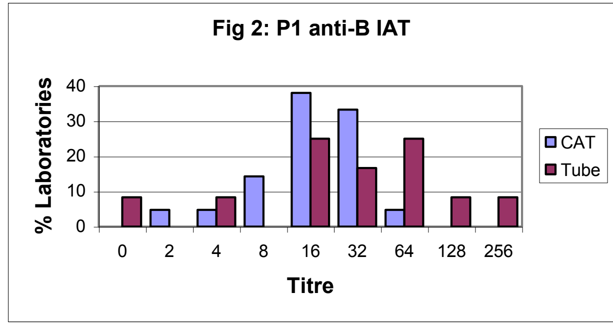

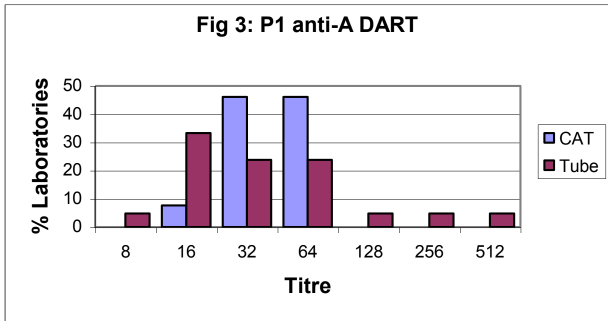

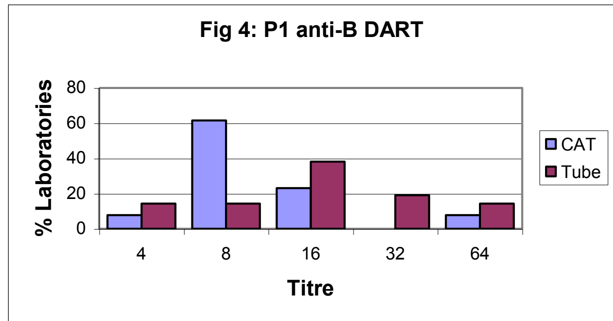

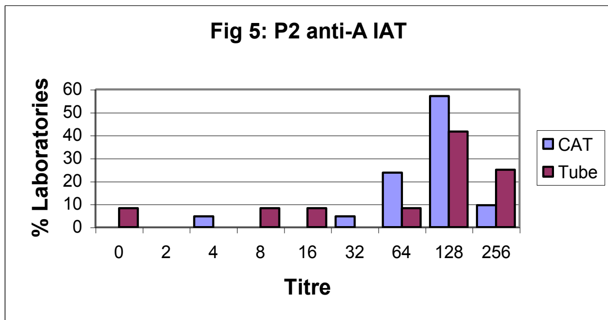

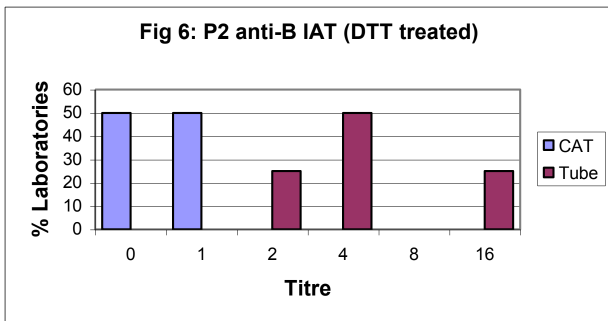

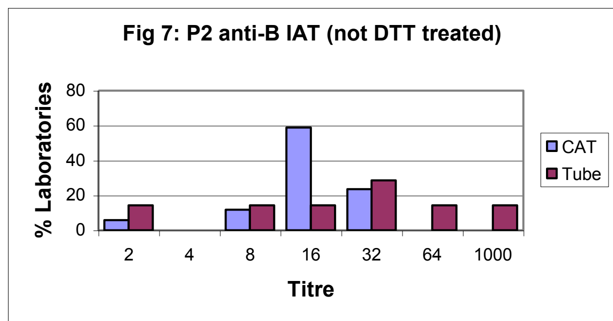

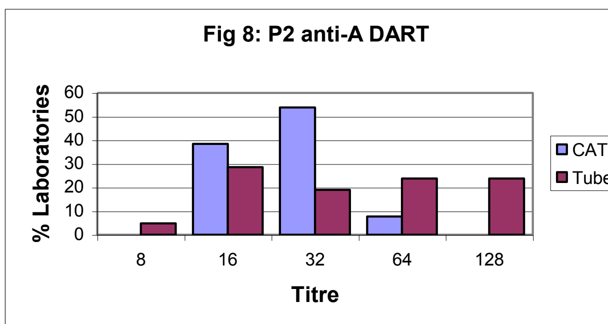

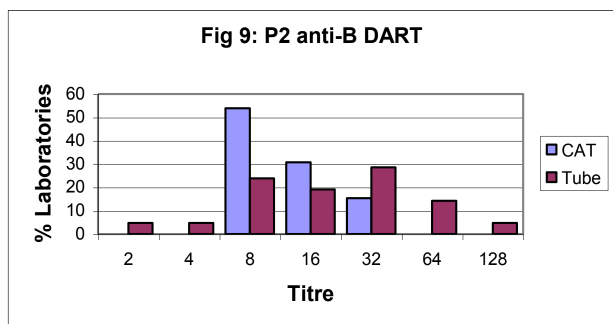

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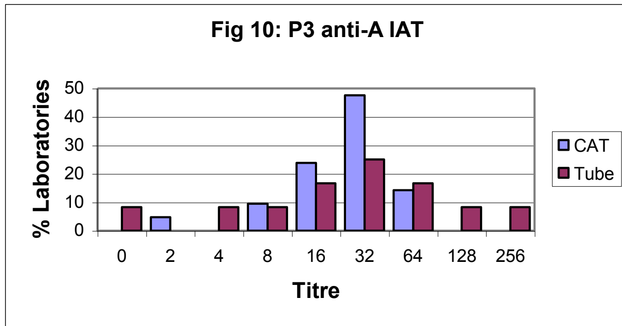
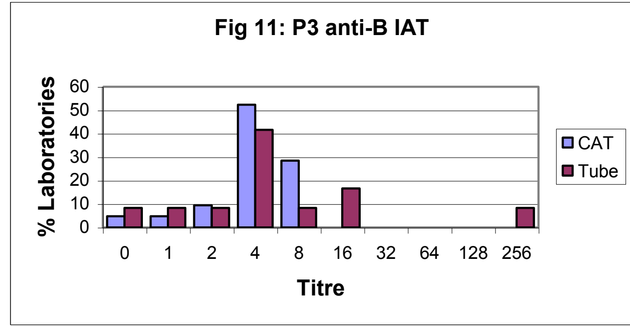
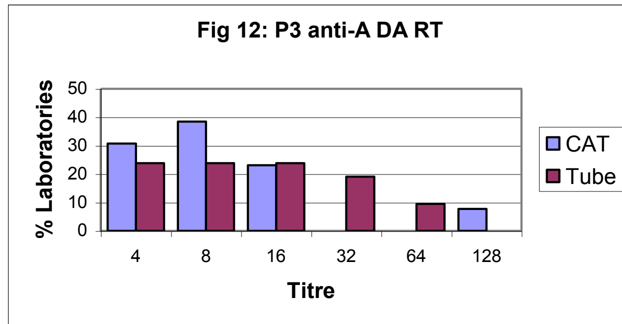
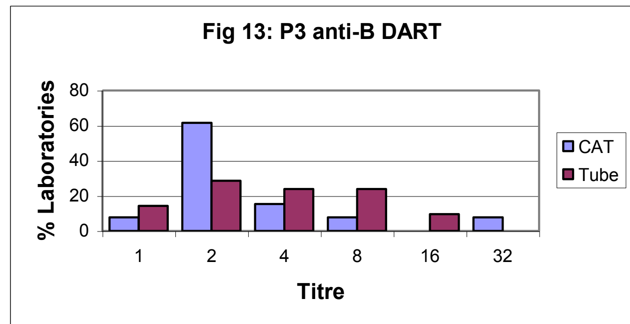
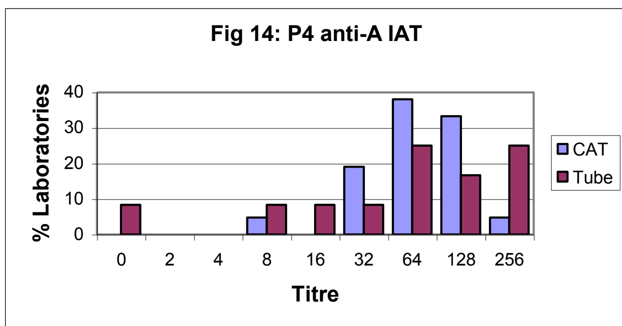
Figures 10 – 17:

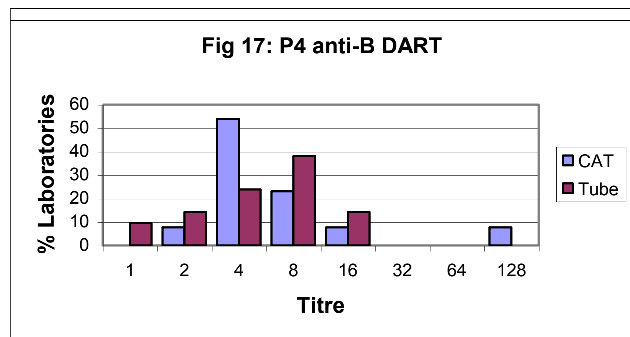


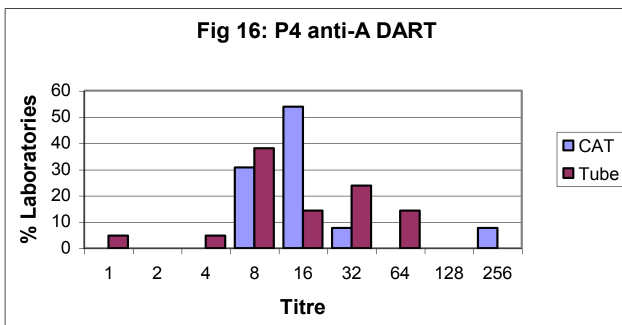












4. Titration policy

The reaction grades routinely used as the cut off point for determining titration value are shown in Table 5.

Table 5 – Reaction grade at endpoint of titration

	Weak	1+	2+	NA/other
DART	14	19	2	14[2]
IAT	11 [1]	19	2	17
Other	0	2 [2]	0	47

1 – includes one 'microscopic'
2 – a negative reaction (1)

Appendix 8

- The most recent patient sample is retested in parallel with the current sample for titration by 10/45 (22%) laboratories responding to this question, including 6/20 (30%) that undertake testing for ABO incompatible renal transplant.

Table 6: Red cells for titration

Red cells selected	Total	Renal transplant
Pool A1 cells	17	11
Single A1 cell	14	5
Single A cell	6	3
Pool A cells	2	0
Pool A2 cells	1	1
Total	40*	20**

* Nine did not answer
** Six of these would use donor cells where available, in preference to those stated

The following information was requested only from the 20 institutions undertaking ABO incompatible renal transplant.

- The maximum titration value at which a patient is considered suitable for an ABO incompatible renal transplant is determined using an IgG titration value by nine respondents, an IgM titration by three and a 'total antibody' titration by four. Four did not answer this question or stated that they do not provide comments to clinicians.

  - IgG (9 responses):
    - 2-8 (1)
    - <4 (1)
    - 8 (2) – (one 16 for A2)
    - 16 (2)
    - 256 (2)
    - 512 (1)

  - IgM: (3 responses):
    - 8 (2) – (one 16 for A2)
    - 512 (1)

  - Total antibody (4 responses):
    - <8 (1)
    - 8 (2) – (one 16 for A2)
    - 16 (1)

Discussion

The titration results for samples 1-4 show wide variation depending on the technology used (e.g. CAT and tube), and also inter-laboratory variation where the same technology is used. This is consistent with data from previous UK NEQAS titration exercises. The range of results obtained by CAT was narrower than that for results obtained by tube, although still significantly wide. Details of the titration method (e.g. diluent used) vary considerably amongst those using the same technology, and this is likely to be contributing to the poor correlation of results; however, once all these variables are applied the numbers are too small to analyse.

There also appears to be little consensus on policy with regard to the clinical use of results for ABO incompatible renal transplantation, with suitability for transplant being established based on results of titrations for IgG, IgM or total levels of anti-A and anti-B. The titration value used as a cut off point for suitability for transplant also varies considerably (ranging from <8 to 512).

Conclusions

Data from this exploratory exercise reveals a wide variation in practice and consequent variation in titration results obtained. This demonstrates a need to standardise methodology and policy for ABO titrations. The current situation is a particular cause for concern where titration results, and protocols for decision-making based on these results, are shared between treatment centres.

Thank you for your contribution to this exploratory pilot. We plan to develop a pilot Scheme for ABO titration and hope that you will take part.

Appendix 9

Pre-Transfusion Testing Questionnaire
Distributed with exercise 09R9 – October 2009

Introduction

The purpose of this questionnaire was to update basic information on routine pre-transfusion grouping and antibody screening procedures, gathered in 2008. We will continue to update this information on an annual basis.

Return Rate

Initially, 282/452 (63%) laboratories responded, and since this was significantly lower than for previous questionnaires, the closing date was extended and participants sent a reminder by e-mail. A further 59 laboratories responded, giving a final return rate of 341/452 (75%) *cf.*86% in 2008. Thirteen incomplete sets of results have been excluded. Thirteen reference laboratories returned results and sections of these have been analysed separately, where applicable. The main analysis includes data from 315 hospital transfusion laboratories, but since not all respondents answered all the questions, the numbers in the tables do not always total 315.

1. Summary and trend data

Table 1 shows a summary of current data compared to historical data where available

Table 1 – Trends in routine pre-transfusion testing	**2009 (n=332)**	**2008 (n=392)**	**2005 (n=426)**	**2002 (n=446)**
Automation for 'group and screen'				
Used during core hours[1]	73%	68%	60%	41%
Proportion of full automation used 24/7[2]	79%	82%	NDA	NDA
Proportion of full automation interfaced to LIMS	96%	89%	NDA	NDA
Routine ABO/D Grouping				
Liquid phase microplates	13%	14%	21%	41%
Column Agglutination Technology (CAT)	80%	77%	65%	33%
Omit reverse group on patients with historical groups	26%	25%	20%	13%
Omit reverse group on patients without historical group	<1%	<1%	1%	1%
D typing reagents				
Single anti-D used once for patients with a historical group	44%	45%	41%	15%
Single anti-D reagent used once for patients with no historical group	22%	25%	23%	5%
Routinely include IAT for D typing on apparent D negatives	8%	6%	5%	3%
Include and anti-CDE reagent	5%	1%	6%	≥ 10%
Routine method of establishing compatibility				
Electronic issue	46%	37%	26%	10%
'Immediate' spin	7%	8%	11%	15%
IAT (± other technique(s))	47%	55%	63%	75%
IAT technology antibody screening				
CAT	89%	90%	92%	85%
SPMP	10%	9%	8%	4%
IAT technology crossmatching				
CAT	96%	96%	81%	77%[3]
Tube	3%	3%	7%	17%[3]

[1] Full automation in 2008 and 2009 *cf.* full or 'semi' automation in 2005 and 2002
[2] 2009 data includes only those '*always* used out of hours' whilst 2008 includes 'used out of hours'
[3] 2001 exercise data. NDA = no data available

Appendix 9

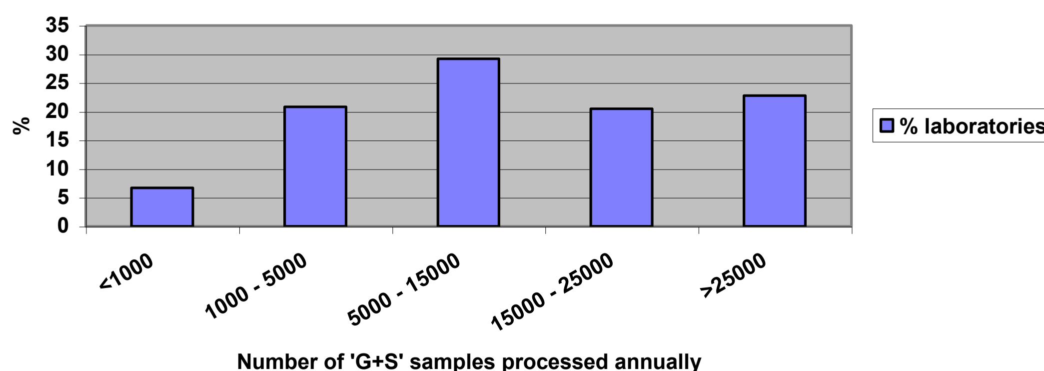
2. Analysis of 2009 data (excluding reference laboratories)

Sections 1 and 2: General information /Automation

Workload

Figure 1 shows the percentage of laboratories within workload categories based on the approximate number of group and screens performed per year.

Figure 1 - Workload



IT and automation

- 314/315 (99%) have an IT system for recording and reporting results of blood grouping tests.

Table 2 shows the use of automation for routine group and saves within core hours.

Table 2 – Number (%) laboratories using automation for group and saves during core hours

Testing	Number (%) of laboratories
Full automated	229 (73%)
Semi-automated (i.e. not walkaway)	17 (5%)
No automation	69 (22%)
Total	**315 (100%)**

- During core hours, approximately 90% of group and screens are tested with full automation (taking the number of group and screens performed by each laboratory to be the midpoint where the category is a range, to be 500 for the <1000 category and 30000 for the >25000 category).

Table 3 shows the number (%) of laboratories with an interface between the automation and laboratory information management system (LIMS).

Table 3 – Number (%) laboratories with automation – LIMS interface

Interface between automation and LIMS	Number (%) with full automation	Number (%) with semi-automated testing
Bi-directional	131 (57%)	2 (12%)
Uni-directional	90 (39%)	13 (76%)
Not interfaced	7 (3%)	2 (12%)
Total	**228* (100%)**	**17 (100%)**

*One laboratory using full automation did not answer this question

Testing outside core hours

- 296/315 (94%) undertake pre-transfusion testing outside core hours
    - 218/296 (74%) have full automation
        - 172/218 (79%) always use the automation for out of hours testing
        - 33/218 (15%) sometimes use the automation out of hours
        - 12/217 (6%) never use the automation outside core hours

Appendix 9

Section 3. Details of testing

ABO/D typing technology

Table 4 shows the number (%) of laboratories using each technology as their primary ABO/D typing technique for patients with a previous group, and the percentage of each using full automation, semi-automated systems and manual testing.

Table 4 – ABO/D typing techniques and use of automation

Technology	All laboratories	Full automation	Semi-automation	Manual testing
DiaMed	161 (51%)	120 (75%)	7 (4%)	34 (21%)
BioVue	90 (29%)	77 (86%)	2 (2%)	11 (12%)
Liquid Phase Microplate (LPMP)	41 (13%)	29 (71%)	7 (17%)	5 (12%)
Solid phase microplate	3 (1%)	3 (100%)	0 (0%)	0 (0%)
Tube	20 (6%)	N/a	N/a	20 (100%)
All techniques	**315 (100%)**	**229 (73%)**	**16 (5%)**	**70 (22%)**

Inclusion of a reverse group

- 82/315 (26%) omit the reverse group for patients with a previous group, including four laboratories undertaking manual testing, and four using semi-automated systems (all with a unidirectional interface to the LIMS).
- 2/315 (<1%) do not include a reverse group for new patients; both use DiaMed manual techniques and one undertakes electronic issue.

D typing

Table 5 shows the number (%) using one anti-D reagent once, or testing for D in duplicate, either with different reagents or with one reagent twice, for patients with and without a previous group.

Table 5 – D typing protocol for patients with and without a previous group

D typing reagents	Patients with a previous group	Patients with no previous group
Use a single anti-D reagent once	137 (44%)	70 (22%)
Test in duplicate	177 (56%)	242 (78%)
Total	**314**	**312**

- Three of those using a single anti-D once for patients with no previous group, undertake manual testing.
- 17/315 (5%) laboratories incorporate an anti-CDE reagent into routine testing.
- 26/315 (8%) routinely confirm D negatives using an IAT anti-D reagent.

Method of establishing compatibility

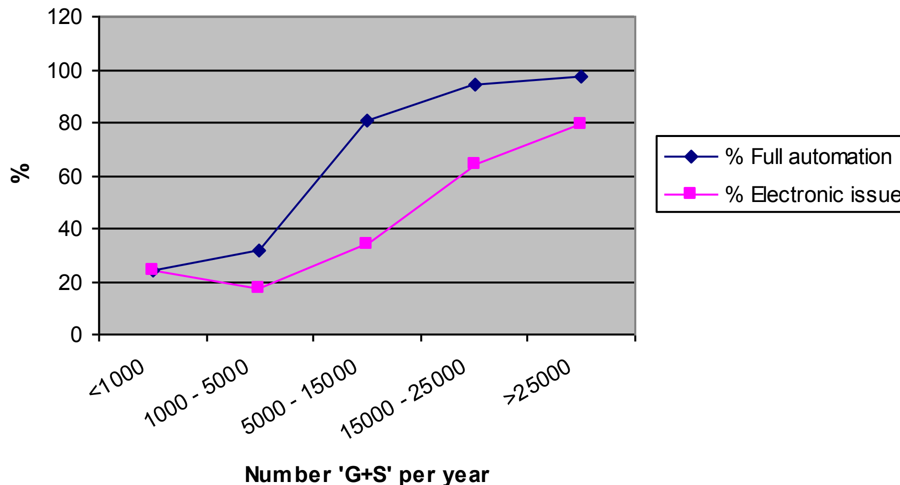
Table 6 shows the number (%) of laboratories using electronic issue (EI), 'immediate spin' (IS) or IAT +/- IS as their primary method for establishing compatibility.

Table 6 – Method of establishing compatibility – number (%) laboratories

Method of establishing compatibility	Number (%)
Electronic issue	143 (46%)
'Immediate spin' (IS)	26 (8%)
IAT (+/- IS)	145 (46%)
Total	**314 (100%)**

Appendix 9

Figure 2 shows the relationship between laboratory workload, automation and use of EI.



Of those using EI as their primary method for establishing compatibility:

- 8/143 (6%) are not using full automation
- 51/143 (36%) do not perform a reverse group on patients with one or more previous groups, and one of these also omits the reverse group on patients who do not have a historical group.

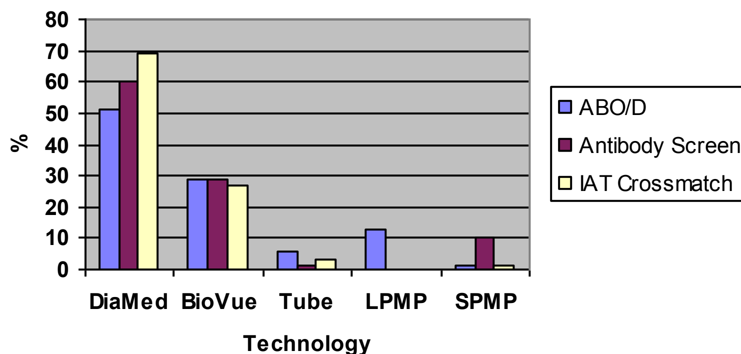
Technology used for antibody screening and crossmatching

Table 7 shows the number (%) using each IAT technology for antibody screening and crossmatching.

Table 7 – IAT technology used for antibody screening and crossmatching

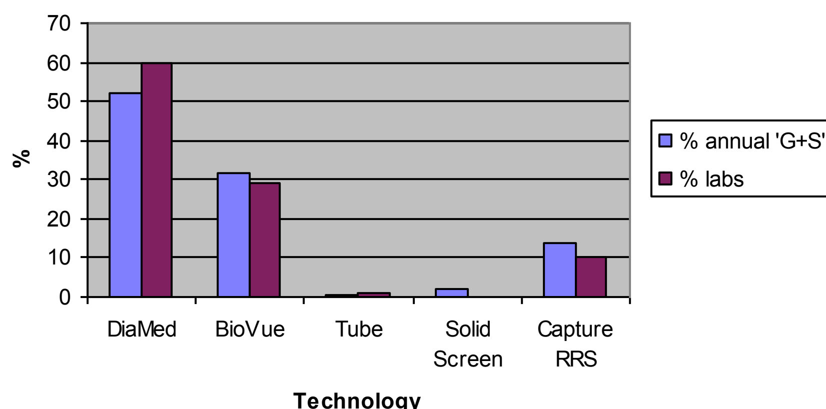
Technology	Number (%) laboratories IAT antibody screen	Number (%) laboratories IAT XM
DiaMed	190 (60%)	214 (69%)
Ortho BioVue	91 (29%)	86 (27%)
Immucor Capture	28 (9%)	3 (1%)
Tube	3 (1%)	8 (3%)
Biotest Solid Screen	3 (1%)	0
Total	**315 (100%)**	**311 (100%)**

Fig 3 shows the percentage of laboratories using each technology for ABO/D typing, antibody screening (by IAT) and crossmatching (by IAT).



Appendix 9

Figure 4 shows an estimation of the proportion of antibody screens performed annually using each IAT technology (based on midpoint of workload range as described in section 2), compared to the number of laboratories using each technology for antibody screening.



Use of an enzyme technique

- 12/315 (4%) routinely perform an antibody screen with enzyme treated cells.
- 278/315 (88%) have access to an enzyme panel for antibody identification.

3. Analysis of 2009 data from reference laboratories

13 responses were received; two from Ireland and 11 from UK reference centres. However, one was incomplete and two were based on donor testing; these have been excluded from the analysis. Not all laboratories answered all questions.

- All have an IT system for recording and reporting results of blood grouping tests
- 8/10 (80%) undertake testing outside core hours
- Four use full automation, and six undertake manual testing
  - 4/4 using full automation have an interface to LIMS
  - 2/3 using full automation and undertaking testing outside core hours, use the automation 24/7

Table 8 – Technology used by reference laboratories for primary testing

Technology	Number (%) laboratories ABO/D typing	Number (%) laboratories IAT antibody screen	Number (%) laboratories IAT XM
DiaMed	8 (80%)	6 (67%)	5 (56%)
Tube	2 (20%)	3 (33%)	4 (44%)
Total	**10 (100%)**	**9 (100%)**	**9 (100%)**

- 6/10 include a reverse group for patients with a previous group.
- 10/10 include a reverse group for patients with no previous group.
- 3/10 use a single anti-D reagent (once) for patients with a previous group.
- 1/10 uses a single anti-D reagent (once) for patients with no previous group.
- 1/10 incorporate an anti-CDE reagent into routine testing.
- 3/10 use an anti-D reagent by indirect antiglobulin test (IAT) to confirm all apparent D negative patients.
- 7/10 perform an enzyme screen.
- All have access to an enzyme panel for antibody identification.

4. Discussion (based on results from hospital laboratories)

Analysis of this questionnaire data and comparisons with previous data are made with the proviso that the significantly lower return rate in 2009 than in previous years might be skewing the data.

Full automation is used by 73% of laboratories for routine group and screens within core hours cf. 68% in 2008, with a further 5% using semi-automated systems. The bias towards automation in larger laboratories means that an even higher percentage of samples (estimated at 90%) are tested using full automation. Of those using full automation, 96% have an electronic interface between the automation and laboratory information management system (LIMS), affording security against transcription / transposition error. However, of those using semi-automated systems, only 88% have an interface between the automation and the LIMS. Of the 73% using full automation during core hours, only 79% continue to use it at all times outside core hours, whilst a further 15% sometimes use it.

The majority (80%) use CAT for routine ABO/D typing. Of the major users of automation, BioVue users are most likely to have full automation (86%), followed by DiaMed users (75%), and LPMP users (71%). A reverse group was included by 74% where the patient has a previous group (cf. 80% in 2005), and where the patient has no previous group on record, all but two laboratories perform a reverse group.

The use of a single anti-D reagent for pre-transfusion testing remains essentially unchanged since 2008. In 2008 the use of an anti-CDE reagent was at an all time low (<1%), in line with 2004 BCSH guidelines for pre-transfusion compatibility testing1, which recommend that anti-CDE is not used for patient testing. However, in 2009, 5% state that they use an anti-CDE reagent; the reason for this change is not known. Although the numbers are small, the trend seen in 2008 where the use of an anti-D reagent by IAT to confirm the D status of apparently D negative patients seems to be increasing over time, with 8% doing so in 2009 (cf. 6% in 2008). BCSH guidelines contraindicate the use of an IAT anti-D for routine patient testing1 because of the risk of misinterpretation of a DAT positive sample or a DVI positive sample as D positive.

The proportion of those establishing compatibility by electronic issue has increased since 2008 from 37% to 46%. Of these, 6% do not have full automation (cf. 5% in 2008), and of those with fully automated systems undertaking testing outside core hours, 8% do not use the automation 24/7. However, it is not evident from the data available whether these laboratories revert to serological crossmatching rather than continuing with EI using manual systems.

The information in this questionnaire will be updated annually.

5. References

1 BCSH (2004) Guidelines for compatibility procedures in blood transfusion laboratories.
Transfusion Medicine, 14, 59-73. These guidelines are currently under review.

Appendix 10

Pre-Transfusion Testing Questionnaire - UK and Republic of Ireland Distributed with exercise 11R1 – January 2011

Introduction

The purpose of this questionnaire was to update basic information on routine pre-transfusion grouping and antibody screening procedures, gathered at the end of 2009. The questionnaire was delayed until January 2011 to ensure that as many participants as possible had the opportunity to complete it with an 'R' exercise. We will continue to update this information on an annual basis.

Return Rate

329/426 (77%) laboratories responded, compared with 75% in 2009 and 86% in 2008. Twenty-two respondents stated that their laboratory does not undertake routine pre-transfusion testing, so data has been analysed from 307 hospital transfusion laboratories. Four of these did not answer any questions from page 4 onwards, and throughout some participants responded with 'unable to answer – these have been removed from the denominator data for the relevant questions.

Summary and trend data

Table 1 shows a summary of current data compared to historical data where available

Table 1 – Trends in routine pre-transfusion testing	2011 (n=307)	2009 (n=332)	2008 (n=392)	2002 (n=446)
Automation for 'group and screen'				
Used during core hours[1]	74%	73%	68%	41%
Proportion of full automation used 24/7[2]	84%	79%	82%	NDA
Proportion of full automation interfaced to LIMS	98%	96%	89%	NDA
Routine ABO/D Grouping				
Liquid phase microplates	13%	13%	14%	41%
Column Agglutination Technology (CAT)	82%	80%	77%	33%
Omit reverse group on patients with historical groups	24%	26%	25%	13%
Omit reverse group on patients without historical group	<1%	<1%	<1%	1%
D typing reagents				
Single anti-D used once for patients with a historical group	52%	44%	45%	15%
Single anti-D used once for patients with no historical group	31%	22%	25%	5%
Routinely include IAT for D typing on apparent D negatives	6%	8%	6%	3%
Include and anti-CDE reagent	3%	5%	1%	≥ 10%
Routine method of establishing compatibility				
Electronic issue	46%	46%	37%	10%
'Immediate' spin	8%	7%	8%	15%
IAT (± other technique(s))	46%	47%	55%	75%
IAT technology antibody screening				
CAT	90%	89%	90%	85%
SPMP	10%	8%	9%	4%
IAT technology crossmatching				
CAT	96%	81%	96%	77%[3]
Tube	2%	7%	3%	17%[3]

[1] Full automation from 2008 onwards *cf.* full or 'semi' automation in 2002
[2] 2009/11 data includes only those '*always* used out of hours' whilst 2008 includes 'used out of hours'
[3] 2001 exercise data. NDA = no data available

Appendix 10

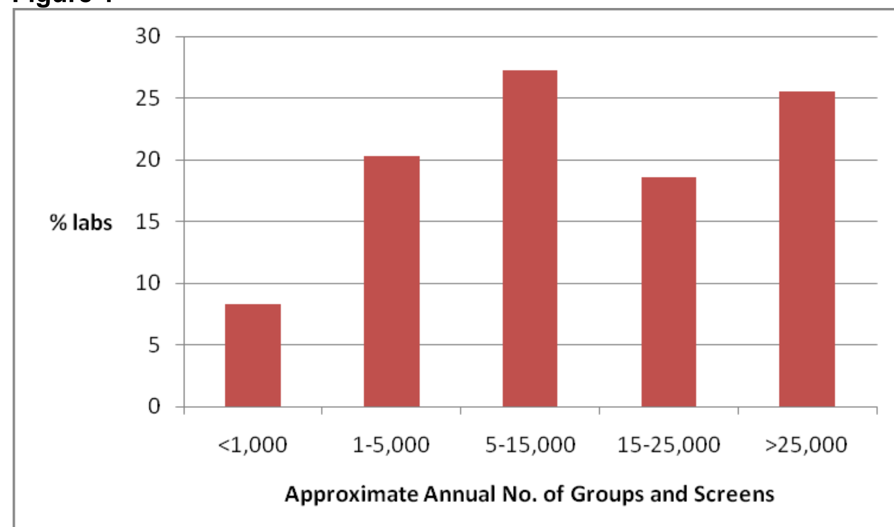
Analysis of 2011 data

General information /Automation

Workload (n=301)

Figure 1 shows the percentage of laboratories within workload categories based on the approximate number of group and screens performed per year.

Figure 1



IT and automation

- 305/307 (99%) have an IT system for recording and reporting results of blood grouping tests. The two laboratories with no IT system process <1000 groups and screens per annum.

Table 2 shows the use of automation for routine group and screens within core hours.

Table 2 – Number (%) laboratories using automation for group and screens during core hours

Testing	Number (%) of laboratories
Full automated	228 (74%)
Semi-automated (i.e. not walkaway)	15 (5%)
No automation	64 (21%)
Total	**307 (100%)**

- During core hours, approximately 95% of group and screens are tested with full automation (taking the number of group and screens performed by each laboratory to be the midpoint where the category is a range, to be 500 for the <1000 category and 30000 for the >25000 category). This does not take account of urgent testing which may be undertaken manually in a laboratory with automation.

Table 3 shows the number (%) of laboratories with an interface between the automation and laboratory information management system (LIMS).

Table 3 – Number (%) laboratories with automation – LIMS interface

Interface between automation and LIMS	Number (%) with full automation	Number (%) with semi-automated testing
Bi-directional	146 (64%)	3 (20%)
Uni-directional	76 (34%)	10 (67%)
Not interfaced	5 (2%)	2 (13%)
Total	**227* (100%)**	**15 (100%)**

*One laboratory using full automation did not answer this question

Appendix 10

Testing outside core hours

- 293/307 (95%) undertake pre-transfusion testing outside core hours
    - 220293 (75%) have full automation
        - 185/220(84%) always use the automation for out of hours testing
        - 29/220 (13%) sometimes use the automation out of hours
        - 6/220 (3%) never use the automation outside core hours

Details of testing

ABO/D typing technology

Table 4 shows the number (%) of laboratories using each technology as their primary ABO/D typing technique for patients with a previous group, and table 5 the percentage of each using full automation, semi-automated systems and manual testing.

Table 4 – ABO/D typing techniques

Technology	All laboratories
DiaMed	144 (48%)
BioVue	101 (33%)
Liquid phase microplate	38 (13%)
Solid phase	2 (<1%)
Tube	15 (5%)
Grifols	3 (1%)
All techniques	**303 (100%)**

Table 5 – Use of automation by technology

Technology	Full automation	Semi-automation	Manual testing
DiaMed (n=144)	107 (74%)	5 (4%)	32 (22%)
BioVue (n=101)	86 (85%)	2 (2%)	13 (13%)
Liquid phase microplate (n=38)	26 (68%)	8 (21%)	4 (11%)
Solid phase (n=2)	2 (100%)	0 (0%)	0 (0%)
Tube (n=15)	N/A	N/A	15 (100%)
Grifols (n=3)	3 (100%)	0 (0%)	0 (0%)

Inclusion of a reverse group

- 74/303 (24%) omit the reverse group for patients with historical groups, however 5 of these include a reverse group if there is only one historical group record.
- 2/303 (<1%) also omit the reverse group for new patients; both use manual DiaMed techniques and one undertakes electronic issue.

D typing

Table 6 shows the number (%) using one anti-D reagent once, or testing for D in duplicate, either with different reagents or with one reagent twice, for patients with and without a historical group.

Table 6 – D typing protocol for patients with and without a previous group

D typing reagents	Patients with a historical group	Patients with no historical group
Use a single anti-D reagent once	156 (52%)	93 (31%)
Test in duplicate	144 (48%)	207 (69%)
Total	**300**	**300**

- Six of those using a single anti-D once for patients with no previous group, undertake manual testing.
- 9/299 (3%) laboratories incorporate an anti-CDE reagent into routine testing, although one of these is only for female patients of childbearing potential.
- 17/297 (6%) routinely confirm D negatives using an IAT anti-D reagent.

Appendix 10

IAT technology used for routine antibody screening and crossmatching
Table 7 shows the number (%) using each IAT technology for antibody screening and crossmatching.

Table 7 - IAT technology used for antibody screening and crossmatching

Technique	IAT technology					
	BioVue	**DiaMed**	**Capture RRS**	**Solid Screen**	**Grifols**	**Tube**
Antibody screening (n=303)	103 (34%)	168 (55%)	26 (9%)	2 (1%)	3 (1%)	1 (<1%)
Crossmatching (n=296)	94 (32%)	188 (63%)	5 (2%)	0 (0%)	4 (1%)	5 (2%)

Method for establishing final compatibility
- 138 (46%) use electronic issue (one during core hours only)
- 141 (46%) use an IAT crossmatch (with or without an immediate spin)
- 24 (8%) use an immediate spin crossmatch

Electronic issue details
- Where a pregnant woman requiring transfusion has a positive antibody screen due to prophylactic anti-D, 21/128 (16%) would still use electronic issue, and one would issue 'group specific blood'.
- 77/137 (56%) require two samples taken at separate times before a patient is eligible for electronic issue
    - Seven of these only require one sample if the patient groups as O.

Of those using EI as their primary method for establishing compatibility:
- 4/138 (3%) are using manual systems
- 6/138 (4%) are using semi-automated systems

Use of an enzyme technique
- 10/302 (3%) routinely perform an antibody screen with enzyme treated cells.
- 269/300 (90%) have access to an enzyme panel for antibody identification.

Conclusions

Last year's report included a full discussion. Most of the discussion points are generally still pertinent and will not be repeated on an annual basis unless significant changes are apparent. This data will be collected and analysed on an annual basis.

Appendix 11

Joint meeting of UK NEQAS (BTLP) and the BBTS Blood Bank Technology SIG

Role of the Hospital Transfusion Laboratory in Improving Clinical Outcomes – Education, Communication and Empowerment

Wednesday 11th November 2009, National Motorcycle Museum, Birmingham

Session 1 – UK Transfusion Laboratory Collaborative - Reducing Laboratory Errors

Chair: Catherine Almond

10.10 Overview of the recommendations and implications for hospitals – Bill Chaffe

10.20 Opportunities for education and training in transfusion laboratory practice – Jenny White

10.40 How to implement the recommendation - Open Forum led by Bill Chaffe and Jenny White

11.10 – 11.30 Coffee

Session 2 – Extension of Practice – The Power of Communication

Chair: Richard Gray

11.30 Widening the scope of practice for patient benefit - Karen Madgwick

11.50 Empowerment of the BMS: effective strategies for challenging clinicians – Ken Mcloughlin

12.10 Decision making in transfusion medicine – what influences the decision to transfuse? – Simon Stanworth

12.30 Discussion

12.50 – 14.00 Lunch

Session 3 - Responsibilities of the transfusion laboratory in coordinating the care of pregnant women with alloimmunisation – education and empowerment

Chair: Rekha Anand

14.00 NEQAS update – Clare Milkins

14.20 DGH perspective – setting the scene - Steve Tucker

14.40 Reference lab perspective – titrating on the brink - Mark Williams

15.00 Communicating between laboratories and clinicians; examples of where it succeeds and fails - Vicky Woodhead

15.30 Fetal medicine unit – diagnostic tools in sensitised pregnancies – Sailesh Kumar

16.00 Discussion

16.15 Close

Appendix 12

Joint meeting of UK NEQAS (BTLP) and the BBTS Blood Bank Technology SIG

Documents, decisions and dilemmas for the new decade

Gatwick Hilton Hotel, Tuesday 23 November 2010

Session 1 – Decisions: Immune or prophylactic? ***Chair: Fiona Stribling***

10.10	Anti-D prophylaxis survey; Laboratory practice survey	Megan Rowley/ Clare Milkins
10.30	Where/how errors arise, including case studies from SHOT	Tony Davies, SHOT
11.00	NBS policy and algorithms for decision making	Paul Fleetwood
11.20	What is a weak reaction? Relevance: grading; titration endpoints; D typing	Mark Williams
11.40	Overlooking HDN: Case studies	Steve Tucker/ Malcolm Needs
12.00	Discussion	
	12.30 to 1.45 lunch and commercial exhibition	

Session 2 – Dilemmas: Coalition or collision? **Chair: Martin Maley**

1.45	NEQAS updates and learning points	Clare Milkins/Jenny White
2.20	CAPA CPA/MHRA differences	Richard Haggas

Session 3 – Documents: How big is your filing cabinet? **Chair: Ann Benton**

2.35	Document retention – different perspectives	Jonathan Wallis (Consultant Haematologist) Peter Maddox (Coroner)
2.55	Discussion	

Session 4 – A new Decade: The Collaborative driving change **Chair: Bill Chaffe**

3.05	Drivers and barriers: a brief update on toolkit	Bill Chaffe
3.10	Compliance in the East of England	Allan Morrison
	Practical solutions:	
3.20	Specialist support out of hours	Stephan Bates
3.30	Solutions in the private sector	Tim Woolley
3.40	Cross-trained out of hours staff.... competent or confident working?	Catherine Almond
3.50	**Discussion and close 16.15 with REFRESHMENTS**	

Appendix 13

Joint meeting of UK NEQAS (BTLP) and the BBTS Blood Bank Technology SIG

'Planning for the Worst and Delivering the Best
National Motorcycle Museum, Birmingham, Thursday 17 November 2011

Coffee, Registration and Commercial Exhibition 09.00 to 11.55

09.55 Opening Remarks by Ann Benton (Chair UK NEQAS Steering Committee)

Session 1 10.00 to 11.15 **Chair: Professor Adrian Newland**

Pathology Modernisation – What does this mean for the Transfusion Laboratory?

10.00 A user's view of the value of hospital transfusion services
Dr Mike Desmond, Consultant Anaesthetist, Liverpool Heart and Chest Hospital

10.10 to 11.15 Questions to the Panel:
Mr John Barker, Blood Transfusion Laboratory Manager QE Hospital, Gateshead
Ms Elaine MacRate, Regional Customer Service Manager, NHSBT
Ms Sasha Wilson, Lead Transfusion Practitioner, University College London Hospitals NHS Trust
Dr Ann Benton, Consultant Haematologist, Morriston NHS Trust, Swansea

Coffee and exhibition 11.15 to 11.40

Session 2 – 11.40 to 13.00 **Chair: Mr Steve Tucker**

Getting a handle on competency assessment

11.40 The difference between competency , CPD, knowledge and training
Mrs Joan Jones, Head of Quality Assurance & Regulatory Compliance, Welsh Blood Service

12.00 Modernising Scientific Careers: managing the competency process using an e-portfolio
Ms Susan Hamilton, Principal Clinical Scientist, West Midlands Regional Genetics Laboratory Birmingham Women's NHS Foundation Trust

12.20 Managing and putting competency assessment into practice in a busy laboratory
Mr Daniel Pelling, Training and Workforce Development Manager, St Mary's Hospital, London

12.40 Discussion

Lunch and Exhibition 13.00 to 14.15

Session 3 14.15 to 15.30 **Chair: Ms Samantha Harle-Stephens**

Haemolytic Transfusion Reactions – Do we know or do enough?

14.15 The laboratory investigation
Mr Richard Haggas, Quality Manager, Leeds teaching Hospitals NHS Trust

14.35 SHOT case studies
Mrs Clare Milkins, Scheme Manager, UK NEQAS

14.50 Testing for high titre haemolysins – what does this mean?
Mr Lionel Mohabir, Head of Automated Testing, WBS

15.05 NEQAS update including ABO titration pilot
Ms Jenny White, Deputy Scheme Manager, UK NEQAS (BTLP)
Dr Megan Rowley, Scheme Director, UK NEQAS (BTLP)

Session 4 15.30 to 16.30 **Chair: Dr Rekha Anand**

Contingency planning for the Olympics

15.30 NHS London planning for the Olympics
Dr Chloe Sellwood, NHS London

16.00 Olympic planning: NHS blood and Transplant
Dr Heidi Doughty, Consultant in Transfusion medicine, NHSBT

Close 16.30