Using EQA to improve practice - highlights 2017/18

Richard Haggas
UK NEQAS
Blood Transfusion Laboratory Practice
- Look at the front sheet
  - No penalties

- May look to the graphs
MAIN AIMS OF THE EXERCISE
Assessment of crossmatch sensitivity, detection and identification of a weak antibody and Jk(α) phenotype.

RETURN RATE
376/384 (98.4%) laboratories returned results by the closing date.

SAMPLE QUALITY
Satisfactory sample quality was reported by >90% of laboratories for plasma, donor and whole blood samples.

ABO TYPING
One laboratory, making a data entry error, recorded an incorrect D group for Patient 1.

ANTIBODY SCREENING AND ANTIBODY IDENTIFICATION
There were no errors in this exercise.

COMPATIBILITY TESTING
Twenty laboratories made a total of 43 errors in compatibility testing.

Four laboratories switched the results for Patients 1 and 2 vs. Donor Y with either Donor W or Z during data entry. One laboratory recording their results in a testing grid, rotated these results through 90 degrees during data entry, resulting in the three missed incompatibilities and three missed compatibilities.

Four laboratories missed one or both of the ABO incompatibilities between Patients 1 and 2 vs. Donor Y. One assumed that all donations provided were O D negative and chose the theoretical selection for both patients. The remaining three laboratories, all recording a negative reaction in the IAT crossmatch, missed the incompatibility between Patient 1 (B positive) and Donor Y (A negative), resulting after the closing date, gave a weak positive reactions for two laboratories and for one the result remained negative. One of these laboratories also missed the incompatibility between Patient 3 (anti-Fy) and Donor W (Fyα+β+)

Six other laboratories, all recording a negative reaction by IAT, missed the incompatibility between Patient 3 (anti-Fy) and Donor W (Fyα+β+). One laboratory appears to have transposed Donors W and Z during testing or reporting. Three laboratories, recording negative results vs. all three donors, appear to have used the whole blood samples for compatibility testing. The final laboratory recorded Donor Z as incompatible by theoretical diagnosis.

PHENOTYPING
Fourteen laboratories made a total of 23 errors in phenotyping.

Two laboratories appear to have transposed the samples or results for Donors Y and Z during testing or reporting, and two other laboratories obtained the correct results but made data entry errors.

Three laboratories recorded false negative Jk(α) types for one or both Donors W and Y. The final seven laboratories recorded false negatives Jk(α) types for one or more of the donors. Five of these laboratories were using the same anti-Jk(α) reagent (Biolocus & Anti-Jk(α) Cell Line: MS-B); three of these were following the manufacturer’s instructions for use, whilst the other two performed the test by IAT rather than direct agglutination. One of the two laboratories using other anti-Jk(α) reagents was also using a method that deviated from that recommended by the manufacturer, and the other was not able to confirm the method used. Two of the nine laboratories had used a Jk(a-b+) cell as a positive control to validate phenotyping results for this exercise.

Continued overleaf

DISCUSSION
In most laboratories avoiding reservation of ABO incompatible red cells is prevented by the LIMS system. However, during LIMS downtime or failure, it is important for laboratories to have robust systems and processes for ensuring that ABO incompatibility is detected. The IAT crossmatch is not the technique of choice for detection of ABO incompatibility and in the rare situation where a serological crossmatch is used without IT support to prevent ABO incompatibility, it is advisable to include a crossmatch by direct agglutination at room temperature.

In this exercise all laboratories detected and correctly identified the weak anti-Fy present in Patient 3. However seven laboratories failed to detect the incompatibility between Patient 3 and an Fyα+β+ cell in a serological crossmatching, this demonstrates the critical importance of an antibody screen as part of the pre transfusion process, together with the selection of antigens negative blood for crossmatching in cases where a clinically significant antibody has been identified.

Jk(α) and Jk(β) phenotyping was requested in this exercise as a follow up to exercise 18RQ where ~20% of laboratories obtained an incorrect Jk(α) type for a Jk(a-b+) donation (see supplementary report for exercise 18RQ that was distributed with reports for exercise 18RQ). In this current exercise nine (4%) laboratories recorded an incorrect Jk(α) type, with seven obtaining false negative results; the majority of these were using the Biolocus & Anti-Jk(α) Cell Line: MS-B reagent, and not all errors using this reagent were due to deviation from the recommended method.

It is important that manufacturer’s instructions are followed and that the limitations of reagents in use are considered. Commercial phenotyping reagents generally give ‘strong’ reactions with antigen positive cells, and it is advisable to repeat tests and question results where a weaker than expected reaction is obtained with either the positive control or with an individual test.

When performing red cell phenotyping, it is good practice to select a ‘positive’ control cell with heterozygous expression of the relevant antigen to demonstrate that the weakest normal antigen expression can be detected on the test cells.

To reduce the potential for procedural errors, checks are required at critical points in the pre-transfusion process, e.g. sample labelling, performing and interpreting manual tests and transmitting information.
Common themes in reports (1)

• Transcription errors / data entry errors

• Transposition errors
  ï Samples in exercise switched
  ï Samples tested from a previous exercise
Common themes in reports (2)

- Antibody ID inclusion / exclusion criteria
  - Distinguishing antibody mixtures
  - ‘Hidden’ antibodies
  - Differentiation between anti-M and anti-S
  - What can be excluded in an enzyme panel
    - Use of saline enzyme
    - Use of enzyme IAT
Technical issues

Your device did this?

No, the user made an error!
<table>
<thead>
<tr>
<th>Donor W</th>
<th>Overall Results</th>
<th>Jka+</th>
<th>Jkb+</th>
<th>65.49%</th>
<th>n=(148)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jka+ Jkb-</td>
<td>20.80%</td>
<td>n=(47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka+ NT</td>
<td>12.83%</td>
<td>n=(29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka- Jkb+</td>
<td>0.44%</td>
<td>n=(1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka- Jkb-</td>
<td>0.44%</td>
<td>n=(1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor Y</th>
<th>Overall Results</th>
<th>Jka-</th>
<th>Jkb+</th>
<th>85.46%</th>
<th>n=(194)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jka- Jkb-</td>
<td>13.28%</td>
<td>n=(3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka- NT</td>
<td>12.78%</td>
<td>n=(29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka+ Jkb-</td>
<td>0.44%</td>
<td>n=(1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Donor Z</th>
<th>Overall Results</th>
<th>Jka+</th>
<th>Jkb-</th>
<th>86.78%</th>
<th>n=(197)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Jka+ NT</td>
<td>12.78%</td>
<td>n=(29)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Jka- Jkb+</td>
<td>0.44%</td>
<td>n=(1)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Exercise 18R2 report

Â Possible link with one reagent (Bioscot Cell line MS-8)
   ï New reagent supplied by a reagent company but some labs did not check product insert (available on-line only)
   ï Tube method (IgM monoclonal) – many used IAT CAT in error (previous reagent IgG polyclonal)

Â Investigation of material – Donor W Jk(a+b+)
   ï Single donation from NHSBT
   ï Within 35 days limit for patient use during 18R2 testing window
   ï Confirmed by IBGRL to have normal expression of the Jk^b antigen with range of anti-Jk^b reagents, but weak reaction vs. BioScot (MS-8)
Learning points

1. To reduce the potential for procedural errors, checks are required at critical points in the pre-transfusion process, e.g. sample labelling, performing and interpreting manual tests and transcribing information.

2. When performing red cell phenotyping it is good practice to select a ‘positive’ control cell with heterozygous expression of the relevant antigen; this demonstrates that the weakest normal antigen expression can be detected on the test cells.

3. It is important that reagent manufacturer’s instructions are followed and that the limitations of reagents in use are considered.

4. Commercial phenotyping reagents generally give ‘strong’ reactions with antigen positive cells, and it is advisable to repeat tests and question results where a weaker than expected reaction is obtained with either the positive control or with an individual test.
Surveyed all UK&ROI phenotyping labs (197)

Survey developed in collaboration with Merck Millipore to investigate details of how their reagent was used and to gather denominator data from all UK labs reporting phenotyping results in 18R2
Additional survey report

Å 49% of Bioscot users did not follow the manufacturer’s method
Å 29% of those following the correct method obtained a negative result
Å Problem not just one reagent?
Å General problems with phenotyping also identified
  Å 25% selected a Jk(a-b+) cell as the positive control for Jk\(^b\) typing
  Å Typing reported on weak reactions obtained for test and/or control
Exercise 18R8

• 7 false negative Jk\(^b\) types
• 2 x Jk(a+b+) samples
• 5 using same reagent (Bioscot \(^{®}\) Anti-Jk\(^b\) Cell Line: MS-8)
  • 3 following manufacturer’s instructions
  • 2 not following manufacturer’s instructions
• 2 using other reagent
  • 1 not following manufacturer’s instructions
  • 1 method unknown
Example CAPA - EQA phenotyping error: anti-Jk\textsuperscript{b} reagent is found not to be working as expected

Remedial action

Consider risk of clinical samples typed using this anti-Jk\textsuperscript{b} reagent

? Re-test

Immediate action to protect patients

Å Depends what you use the anti-Jk\textsuperscript{b} for
Å Typing donors
Å Typing patients to confirm antibodies
Å Typing patients for red cell selection
Example CAPA - EQA phenotyping error: anti-Jk\textsuperscript{b} reagent is found not to be working as expected

**Corrective action**

- Replace anti-Jk\textsuperscript{b}
- Validate and document method including controls required

Action taken following investigation / root cause analysis

- Depends on the findings
- Change reagent
- Follow the method
- Refer Jk\textsuperscript{b} typing

If you do perform a CAPA we are always happy to receive a copy as it helps guide our understanding and shape future reports.
Example CAPA - EQA phenotyping error: anti-Jk\text{b} reagent is found not to be working as expected

Preventive action

- Review policy for selecting, validating, receipt, controlling and using all reagents

For those with an error and those labs without an error

- Review of whole reagent selection process
- Improving the process for other reagents
MHRA reporting

- Encourage all labs to report potential issues with IVDs early
- UK NEQAS has discussed weighting for reports from EQA providers
Report to MHRA

- Reported through yellow card process
- Uploaded 18R2, Q and 18R8 reports
- MHRA ref: 2018/010/025/401/011
  Your ref: 18R8
- ‘It can take 3 months or longer to investigate and so you might not hear from us during this time.’!
- Manufacturer has been in contact following report

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**Adverse Incident Report**

**About you**

- Your name: Jenny White
- Position/Occupation: Other healthcare professional
- Organisation: UK NEQAS STLP
- Your address: PO Box 133, Watford, Hertfordshire, WD18 9NP
- Your telephone number: 01923 179793
- Your email address: jenny.white@whht.nhs.uk
- Email Copy To:
  - Jenny White
  - Jonathan White
- Local reference number: 18R8

**Device & Incident details**

- Type of injury: None
- Type of device: Red cell phenotyping reagent
- Model: Bisiscet anti-Abo reagent (MS-6)
- Manufacturer name: Medic Medical
- Catalogue number: 2017/010250
- Serial number: various
- Lot or batch number: various
- Date of manufacture: 2016/010250
- Expiry date: 2017/010250
- Quantity defective: various
- Current location of device: various
- Has the manufacturer / supplier been contacted? Yes
- Is the device CE Marked? Yes
- Date of incident: various

**Details of incident / nature of device defect test**

UK NEQAS for Blood Transfusion Laboratory Practice has noted an increased EIA error rate for ABO phenotyping using this reagent, in two EIA exercises.
Concerns raised

Discussed survey findings in detail and asked them to consider:

- **Change to method (non-standard and too complex)**
  - unnecessary 2 step incubation and spin
  - Incubation temperature not optimal for an IgM reagent

- **Making instructions available with the reagent**
An opportunity for preventive action

The supplementary report issued with each exercise may have useful information even if you don’t have errors.

We provide summary slides to help put this information in a teachable format.
An opportunity for preventive action

We have a reflection sheet currently for R exercises which you can use internally to review reports even if there are no errors.

https://www.ukneqasbtlp.org/documents.php
UKNEQAS BTLP

https://www.ukneqasbtlp.org/

Email: btlp@ukneqas.org.uk

Tel: +44 (0)1923 217933