

# ANNUAL SHOT REPORT 2016



working with

**SERIOUS HAZARDS OF TRANSFUSION**

Affiliated to the Royal College of Pathologists

# SHOT



## Serious Hazards of Transfusion (SHOT)

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# Foreword and SHOT Update

# 1

## 1 Foreword and SHOT Update

*Authors: Paula Bolton-Maggs and Dafydd Thomas*

Overall, transfusion components themselves are very safe, but there is clearly room for improvement in practice. The pattern of reports in 2016 was much the same as in previous years, however the absolute number and percentage related to error has increased; 87.0%, 2688/3091. Similarly 98.1% of serious adverse event (SAE) reports to the Medicines and Healthcare Products Regulatory Agency (MHRA) resulted from error.

The number of ABO-incompatible red cell transfusions has continued to reduce with 3 reported in 2016 but there were nevertheless 264 near misses which could have resulted in incompatible transfusions had they not been detected. The number of ABO or D mismatches following allogeneic haemopoietic stem cell transplants continues to cause concern. Despite acknowledgement 17 years ago of the need to learn from errors (Department of Health 2000), a recent House of Commons committee noted that the National Health Service (NHS) still falls short in this area (House of Commons Public Administration and Constitutional Affairs Committee 2017). In 2016 the Healthcare Safety Investigation Branch was set up and their expert advisory committee noted that ‘all of this evidence points unequivocally to the unsatisfactory nature of the current system: it is seen as threatening by staff; untrustworthy by those affected; and fails to identify many opportunities to prevent future harm’ (HSIB 2016). This branch began work in April 2017 and will review about 30 incidents a year. It is essential that it remains fully independent and does not pass information to regulators or courts (Macrae and Vincent 2017). Transfusion incident-reporting may have been adversely affected by the recent trial of a nurse and her conviction of manslaughter for death resulting from an incompatible red cell transfusion. This error could have been prevented by a correctly completed bedside check.

Following SHOT’s focus on human factors, a number of questions were added to the error reporting questionnaires in order to learn more about why things go wrong. The text added in these fields adds to the evidence that staff are working under pressure with inadequate staffing levels, lack of training and feeling overwhelmed.

These factors are widely recognised and reported in the press with an NHS which is at capacity with bed occupancy above the recommended safety limit, and ‘in the face of ever increasing demand, care quality is unavoidably being eroded’ (Maynard 2017). The Care Quality Commission (CQC), in its report on the findings of the first round of hospital inspections, noted that ‘safety remains a real concern, often due to a failure to learn when things go wrong.’ Sir Mike Richards also noted that ‘the NHS now stands on a burning platform – the need for change is clear, but finding the resources and energy to deliver that change while simultaneously providing safe patient care seems almost impossible’ (CQC 2017).

This is at a time when enthusiasm for entering medical training is reduced (a 3.6% reduction in applications to medical schools), and for the first time some foundation year posts will not be filled in 2017 (Rimmer 2017). Additionally the proportion of doctors who have been through the foundation programme who then enter into speciality training has reduced from 71.6% in 2011 to 50.4% in 2016 (Rimmer 2017). Concerns about medical education and training have been expressed by the General Medical Council (GMC): ‘there is a state of unease within the medical profession across the UK that risks affecting patients as well as doctors. The reasons are complex and multifactorial, and some are long standing. The signals of distress are not always easy to interpret but they are unmistakable. This should

not be seen as a counsel of despair but as a message to governments, employers, regulators, and the profession itself' (GMC 2016). Robert Francis has also recorded his concerns about the NHS pressures (Lintern 2017). Concerns about laboratory staffing are widespread and also noted by the UK transfusion laboratory collaborative (UKTLC) survey performed in 2015. The Royal College of Nursing (RCN) notes in polling for a strike that 'the 1% cap on nursing pay is putting patient care at risk. RCN members are taking second jobs and using food banks. They are exhausted, morale is low and it's affecting the care they are able to provide' ([www.smartsurvey.co.uk/s/5FNLO](http://www.smartsurvey.co.uk/s/5FNLO) poll now closed).

Reflecting the current climate in our health service, SHOT is concerned by increasing numbers of reports, both from clinical areas and laboratories, where investigation of the error or near miss has concluded that the root cause, or a significantly contributing factor, was lack of adequately trained staff, either due to vacancies or increased workload and 10.0% (103/1027) of SAE reported to the MHRA were noted to be related to resource issues (staffing, workload, skill mix).

The majority of errors result from failures of communication, documentation and failure to follow procedures both in the laboratory and clinical areas. Many could be prevented by the final bedside check if it was done properly. This is our main recommendation for 2017. At worst a patient may die (ABO-incompatible transfusion reported last year) and the health care worker be convicted of manslaughter. For much of medical practice some flexibility and resilience is essential, but the bedside check is one process which should now follow a strict adherence to the checklist, as pilots do before take-off. There is new evidence that the World Health Organisation surgical checklist reduces mortality: there was a reduction in the 30 day post-surgery mortality in hospitals that completed a quality improvement programme to implement this (Haynes et al. 2017).

Pulmonary complications, particularly transfusion-associated circulatory overload (TACO), remain the most commonly reported cause of death and major morbidity and are most common in elderly patients who are noted to be particularly vulnerable 'the growth of multi-morbidity has been significant across all age groups, and especially the elderly' (Maynard 2017). Our second main recommendation is to use the TACO checklist which has been modified slightly from last year.

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# Participation in UK Haemovigilance Reporting

# 2

Authors: Debbi Poles and Paula Bolton-Maggs

## Reporting organisations 2016

Participation in United Kingdom (UK) haemovigilance remains at 100% with all National Health Service (NHS) organisations registered to report directly, or indirectly, to SHOT. In the calendar year 2016 only one registered NHS organisation did not make any reports to SHOT. There were 20 non-NHS organisations that made reports during 2016.

Despite the fact that 2016 has seen the lowest number of non-reporting NHS organisations for a number of years, this is the first year that overall report numbers have decreased slightly. Part of this decrease can be accounted for with the end of alloimmunisation reporting, but it could be that reporting levels have reached a plateau.

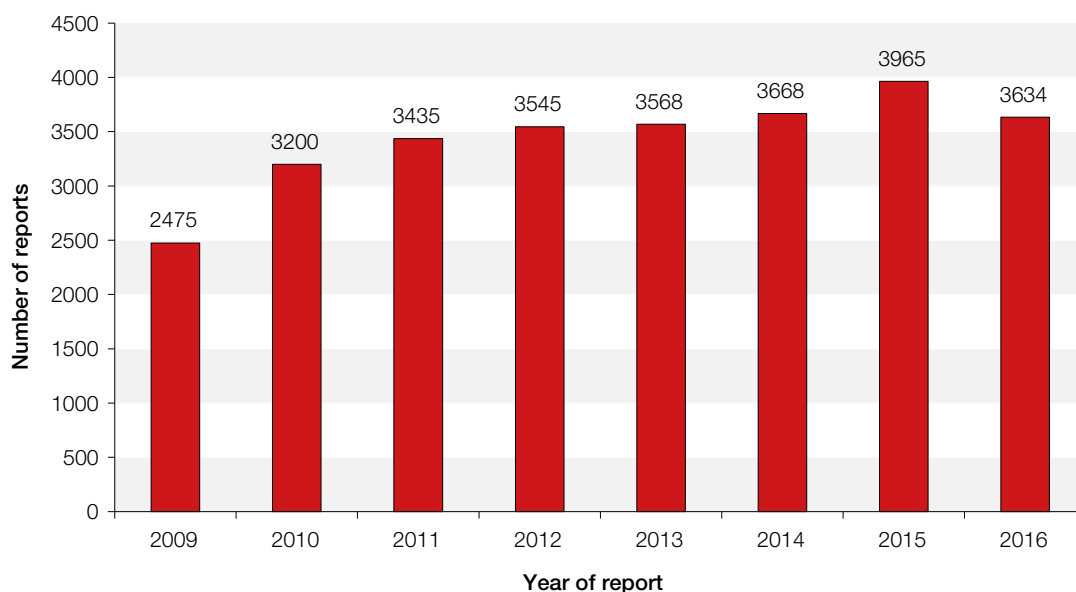


Figure 2.1:  
Number of reports submitted to SHOT 2009-2016

## Number of SHOT reports by UK country

A total of 3634 reports were submitted to the SHOT database in 2016 and the breakdown by country is shown below.

	2013		2014		2015		2016	
	Number	%	Number	%	Number	%	Number	%
<b>England</b>	2975	83.4	3119	85.0	3431	86.5	3035	83.5
<b>Northern Ireland</b>	129	3.6	98	2.7	100	2.5	102	2.8
<b>Scotland</b>	285	8.0	278	7.6	259	6.6	274	7.5
<b>Wales</b>	179	5.0	173	4.7	175	4.4	223	6.2
<b>United Kingdom</b>	<b>3568</b>	<b>100</b>	<b>3668</b>	<b>100</b>	<b>3965</b>	<b>100</b>	<b>3634</b>	<b>100</b>

Table 2.1:  
Total number of reports to SHOT by UK country 2013-2016

*Betsi Cadwaladr University Health Board comes under Wales rather than England from April 2016*

## Blood component issue data

**Table 2.2:**  
Total issues of blood components from the UK Blood Services in calendar year 2016

	Red cells	Platelets	FFP	SD-FFP	MB-FFP	Cryo	Totals
NHS Blood & Transplant	1,532,416	262,548	180,738	83,392	7,705	38,920	<b>2,105,719</b>
Northern Ireland Blood Transfusion Service	47,923	8,766	5,353	3,060	329	1,352	<b>66,783</b>
Scottish National Blood Transfusion Service	153,976	24,310	18,345	2,730	1,270	2,113	<b>202,744</b>
Welsh Blood Service	83,709	11,346	9,124	3,289	0	433	<b>107,901</b>
<b>Total</b>	<b>1,818,024</b>	<b>306,970</b>	<b>213,560</b>	<b>92,471</b>	<b>9,304</b>	<b>42,818</b>	<b>2,483,147</b>

Paediatric/neonatal MB-FFP are expressed as single units; cryoprecipitate figures are expressed as pools and single donations as issued; all other components are adult equivalent doses

FFP=fresh frozen plasma; SD=solvent detergent-sterilised; MB=methylene blue-treated; Cryo=cryoprecipitate

SD-FFP data supplied by Octapharma

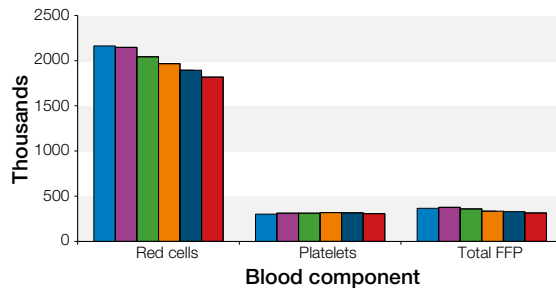
Betsi Cadwaladr University Health Board comes under Welsh Blood Service rather than NHS Blood & Transplant from April 2016

**Table 2.3:**  
Total number of reports per 10,000 components by UK Blood Services 2013-2016

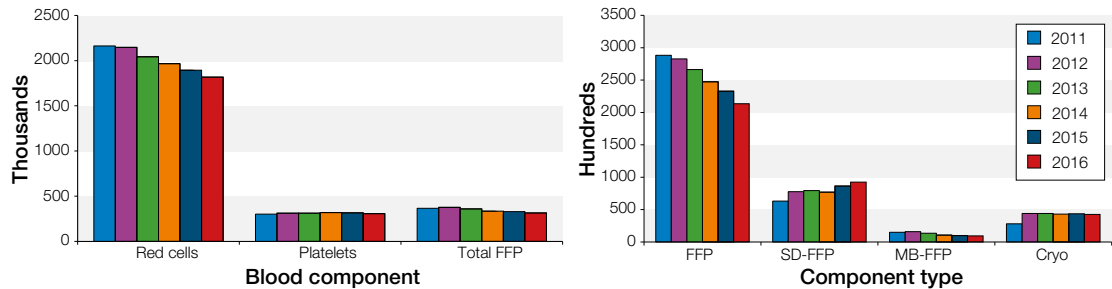
	2013	2014	2015	2016
NHS Blood & Transplant	12.7	13.7	15.5	14.4
Northern Ireland Blood Transfusion Service	18.7	14.6	15.0	15.3
Scottish National Blood Transfusion Service	11.8	12.4	12.3	13.5
Welsh Blood Service	17.2	18.2	20.1	20.7
<b>Total (rate for all Services combined)</b>	<b>12.9</b>	<b>13.8</b>	<b>15.4</b>	<b>14.6</b>

Analysis of the last few years' UK data for components issued indicates a marked downward trend in red cell usage, and a small decrease in overall FFP issues. However, there is little change in platelet issues.

**Figure 2.2 (left):**  
Issue data trends for red cells, platelets and total FFP 2011-2016



**Figure 2.3 (right):**  
Issue data trends for FFP, SD-FFP, MB-FFP and cryoprecipitate 2011-2016



A further breakdown of FFP data demonstrates a more pronounced decrease in standard FFP, but an increase in SD-FFP.

## Cases included in the 2016 Annual SHOT Report n=3091

The total number of reports analysed and included in the 2016 Annual SHOT Report is 3091. This is a decrease of 197 from the 3288 reports analysed in the 2015 Annual SHOT Report. Part of this decrease can be attributed to the cessation of alloimmunisation reporting, which accounted for 236 reports in 2015.

The overall number of errors has increased in 2016 (2688 total errors in 2016 compared to 2555 in 2015) and this, along with the reduction in reaction report numbers (due to the removal of alloimmunisations) means that the percentage of errors has increased considerably this year and now stands at 87.0% (2688/3091) of total reports.

The number of reports excluding near miss and right blood right patient (RBRP) is 1581 (1858 in 2015).

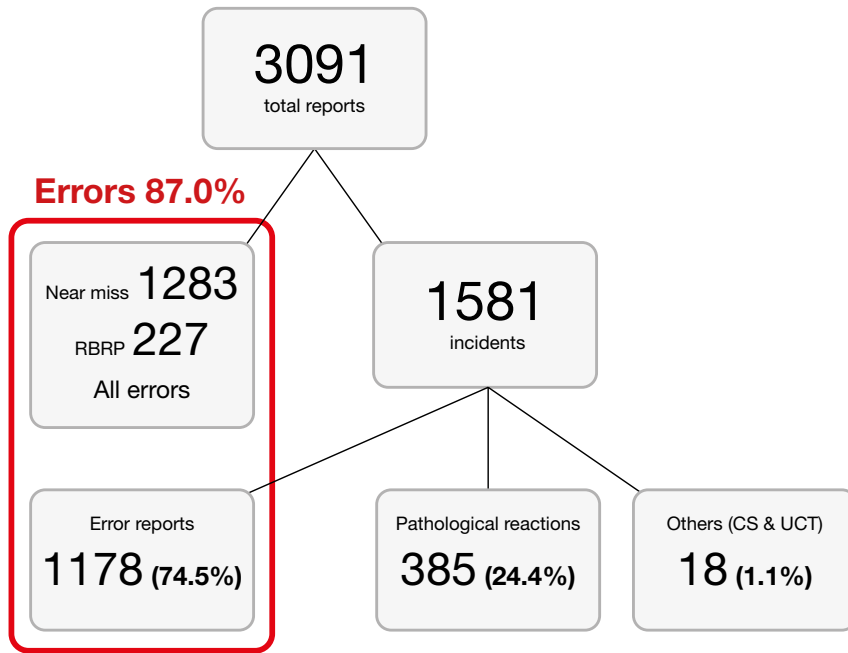


Figure 2.4: Categorisation of reports analysed in 2016

CS=cell salvage; UCT=unclassifiable complications of transfusion

### Error rates by category

To understand where and why errors overall have increased, they are compared in Table 2.4 by category to the previous year. Red indicates an increase and green a decrease. Laboratory errors are described in Chapter 7, Laboratory Errors. Although there is a reduction overall, there has been an increase in testing and component selection errors in 2016 compared with 2015.

Category	2015	2016
Near miss	1243	1283 (300 L)
RBRP	187	227
HSE	254	192
Laboratory	455	378
IBCT (clinical and laboratory)	280 (148 C, 132 L)	331 (161 C, 170 L)
Anti-D immunoglobulin (Ig) errors	350	409
Avoidable transfusions	116	114
Delayed transfusions	94	101

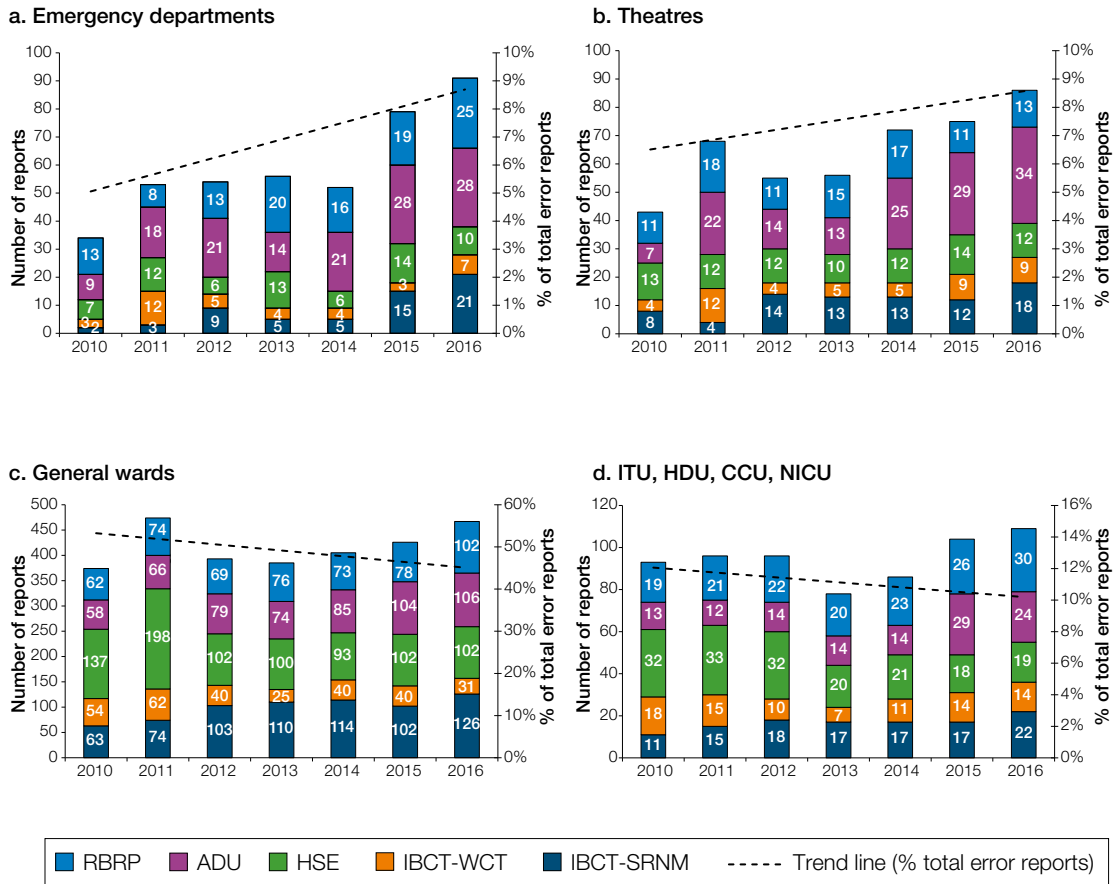
Table 2.4: Error rates 2015 and 2016 by category - red indicates an increase and green a decrease

HSE=handling and storage errors; IBCT=incorrect blood component transfused; C=clinical; L=laboratory

### Analysis of errors by location

Examination of the trend of error reports by different location (Figure 2.5a-d) demonstrates some differences. The errors in emergency departments and theatres have increased year-on-year, and these errors are an increasing percentage of all reported errors, so not simply due to an increase in reporting. Most transfusions take place in wards where there has been a decrease in percentage of all error reports, but overall there has been an increase in several categories, particularly a steady increase in specific requirements not met.

Figure 2.5:  
Trend of error reports from different departments



ADU=avoidable, delayed or undertransfusion; IBCT-WCT=IBCT wrong component transfused; IBCT-SRNM=IBCT specific requirements not met

ITU=intensive therapy unit; HDU=high dependency unit; CCU=coronary care unit; NICU=neonatal intensive care unit

## Monthly participation data

Details of monthly participation are now published on the SHOT website for general information, and can be found at <http://www.shotuk.org/reporting/monthly-participation-data/>.

Information included here are the numbers of reports submitted to the SHOT database each month, and a running total of the number of reports completed in each SHOT category. These data are updated each month and are subject to change following review of the completed cases.



# Headline Data: Deaths, Major Morbidity and ABO-Incompatible Transfusions

# 3

Author: Paula Bolton-Maggs

## Key SHOT messages

- ABO-incompatible transfusions are the tip of the iceberg and result from failure to identify the patient at the time of blood sampling (wrong blood in tube) or administration to the wrong patient. A bedside checklist will prevent administration errors
- Pulmonary complications, particularly transfusion-associated circulatory overload (TACO), cause the most deaths and major morbidity. Deaths related to TACO n=14, major morbidity n=18
- Delayed transfusions are an important cause of death, 25/115 (21.7%) 2010 to 2016
- Information technology (IT) systems are not always reliable. They must be properly set up and validated. IT suppliers need to work together to standardise their products across the UK
- Many errors in transfusion, some with serious clinical consequences, relate to poor communication between teams, shifts and interfaces. The infrastructure needs improvement to facilitate exchange of results within and between hospitals

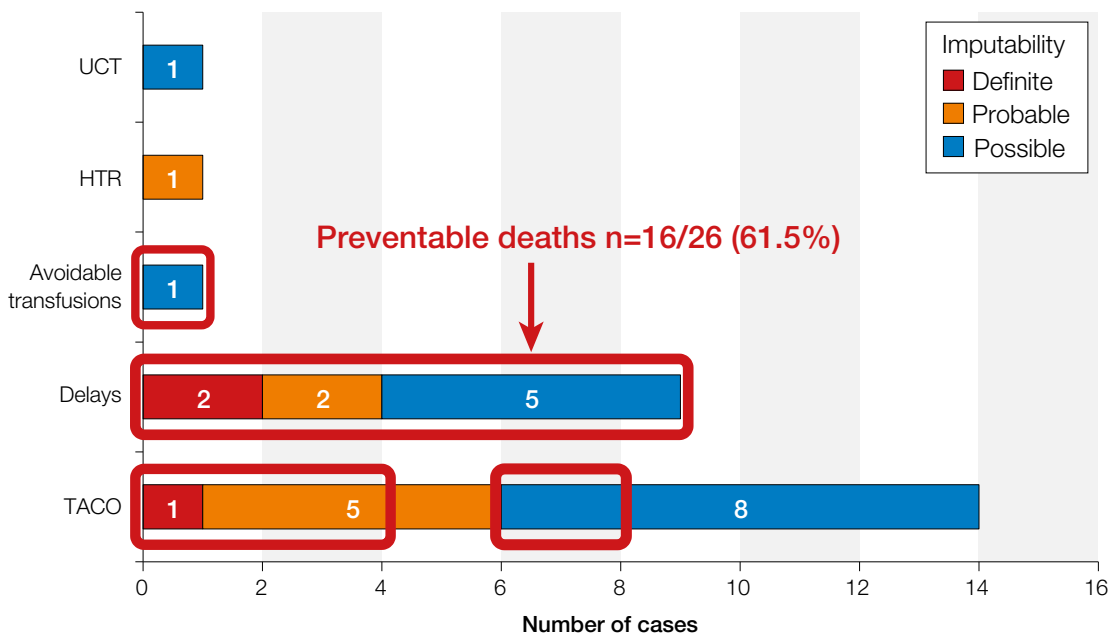


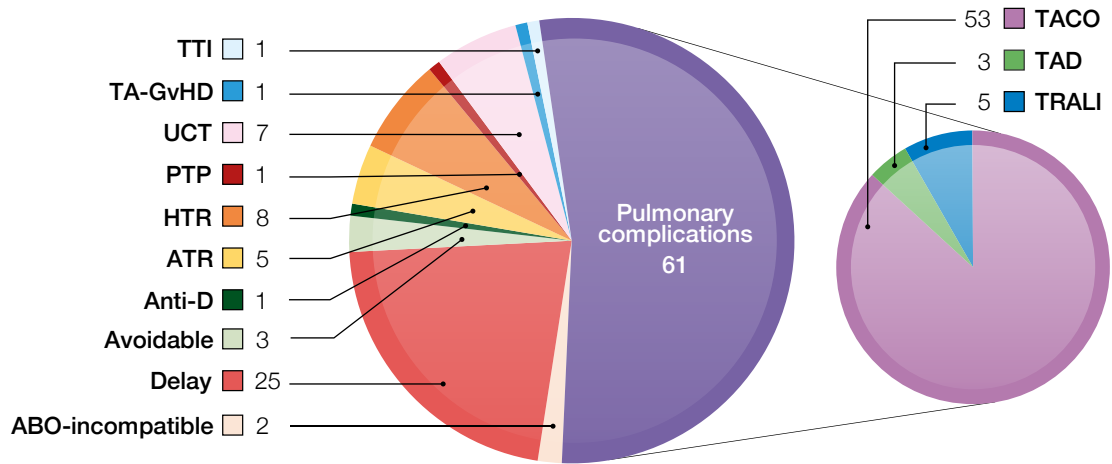
Figure 3.1:  
Deaths related  
to transfusion  
(with imputability)  
reported in 2016  
n=26

TACO=transfusion-associated circulatory overload; UCT=unclassifiable complications of transfusion, this one was related to granulocyte infusion; HTR=haemolytic transfusion reaction

More than half the deaths, 14/26, were related to TACO, compared to 7/26 in 2015. Delays in transfusion contributed to 9 deaths compared to 6 in 2015. Review of these reports shows that 16/26 (61.5%) were potentially preventable.

Review of cumulative data (2010-2016, Figure 3.2) for deaths shows that pulmonary complications are the leading cause of death in 61/115 (53.0%). Delayed transfusions accounted for 25/115 (21.7%).

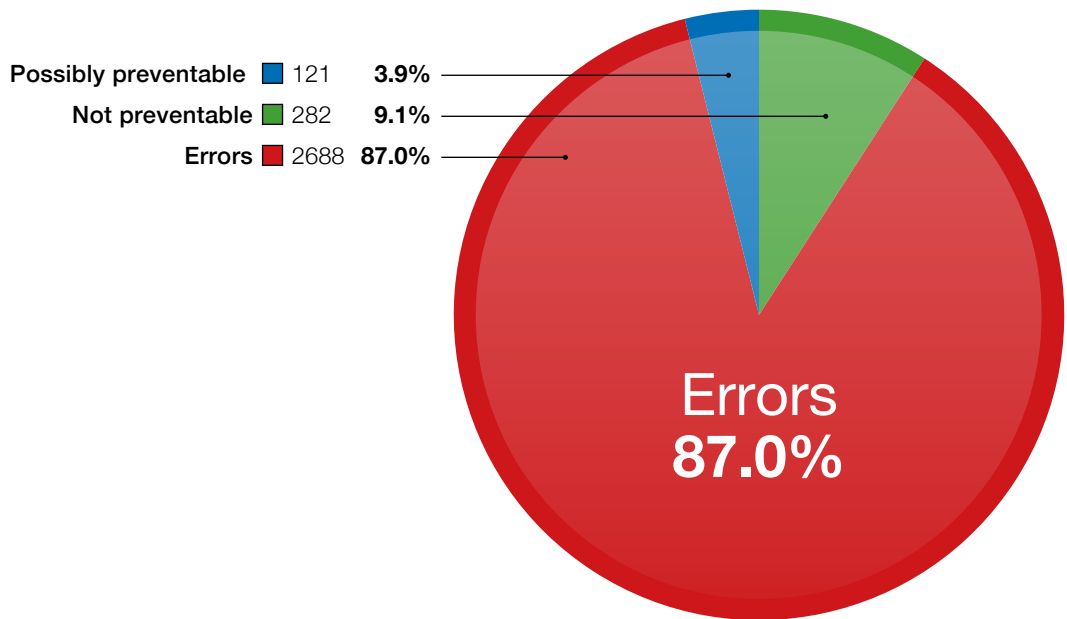
**Figure 3.2:**  
Transfusion-related deaths 2010 to 2016 n=115



For key to abbreviations please see Figure 3.4

In keeping with previous years, errors account for the majority of reports, Figure 3.3. These are a larger absolute number and proportion in 2016.

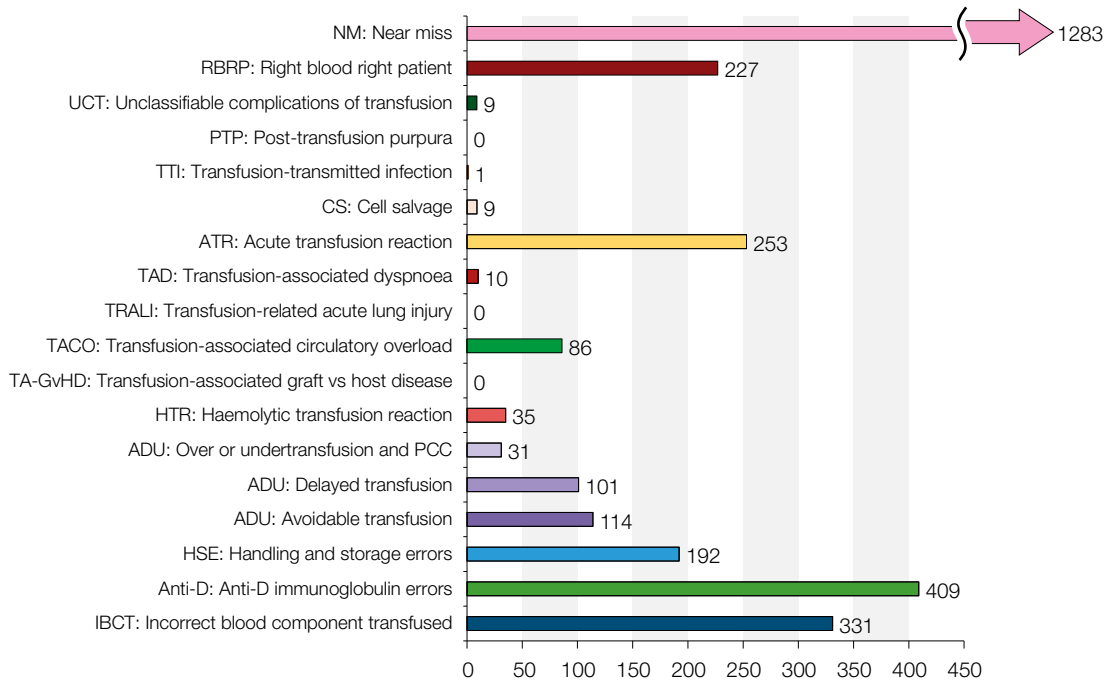
**Figure 3.3:**  
Errors account for the majority of reports



Errors with no harm to patients n=1510 (near miss and right blood to right patient reports).

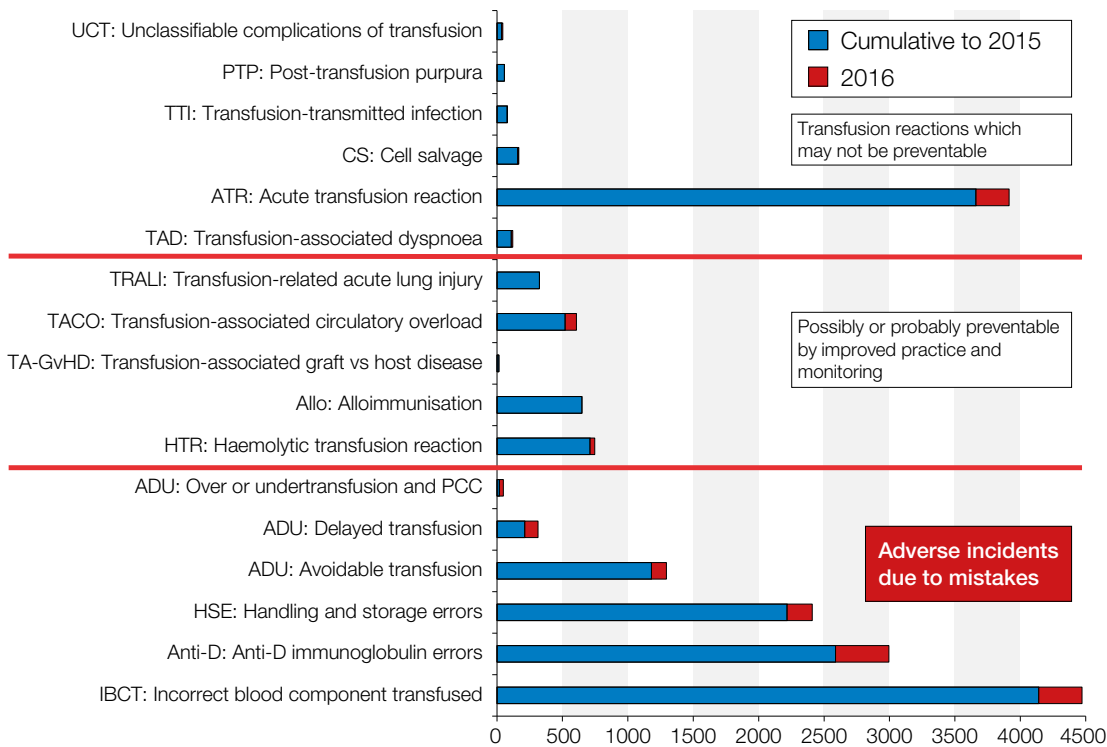
Other errors with actual or potential harm n=1178 (handling and storage errors, avoidable and delayed transfusions, anti-D immunoglobulin errors and incorrect blood components transfused).

Irradiation of cellular components was missed in 95 cases and in 73/95 (76.8%) the clinical areas were responsible. The cumulative number of reports of missed irradiation since 1999 is now 1310.

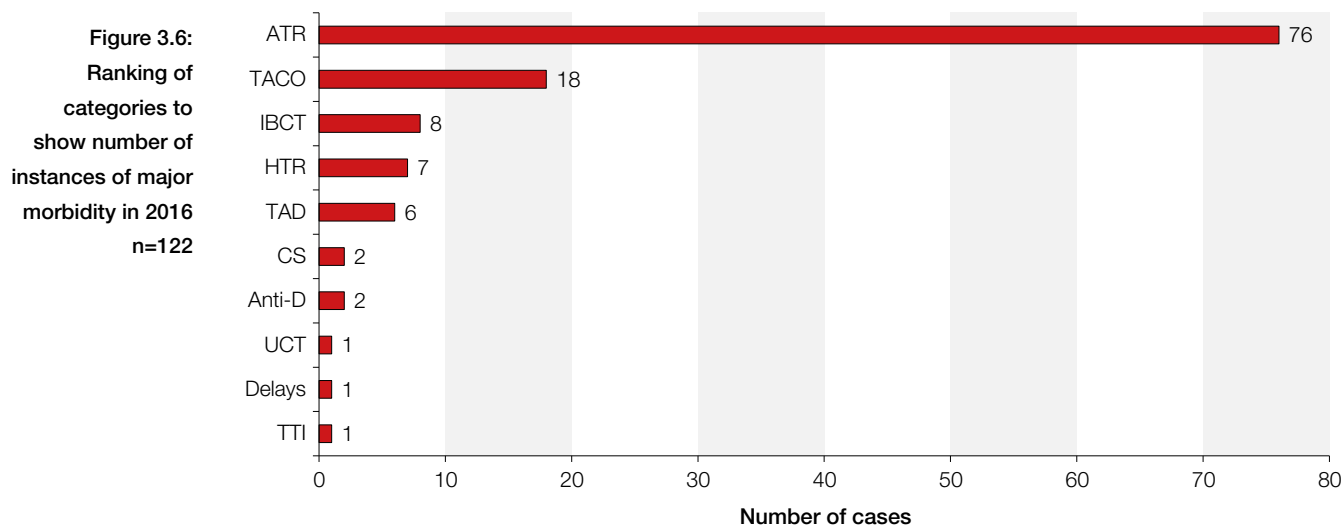


**Figure 3.4:**  
Summary data for 2016, all categories n=3091 (including near miss n=1283, and right blood right patient n=227)

PCC=prothrombin complex concentrate



**Figure 3.5:**  
Cumulative data for SHOT categories 1996 to 2016 n=18258



For key to abbreviations please see Figure 3.4

### Risk of major morbidity and mortality per 100,000 components issued in 2016

Table 3.1: Risks per 100,000 components issued in 2016

<b>Total morbidity</b>	<b>4.91</b>
<b>Total mortality</b>	<b>1.05</b>

	Mortality	Major morbidity	Total cases
All errors	0.40	0.44	<b>47.4</b>
ATR	0.00	3.06	<b>10.2</b>
HTR	0.04	0.28	<b>1.4</b>
TRALI	0.00	0.00	<b>0.0</b>
TACO	0.56	0.72	<b>3.5</b>
TAD	0.00	0.24	<b>0.4</b>
TA-GvHD	0.00	0.00	<b>0.0</b>
PTP	0.00	0.00	<b>0.0</b>
CS	0.00	0.08	<b>0.4</b>
TTI	0.00	0.04	<b>0.0</b>
UCT	0.04	0.04	<b>0.4</b>
Paediatrics	0.00	0.72	<b>5.5</b>

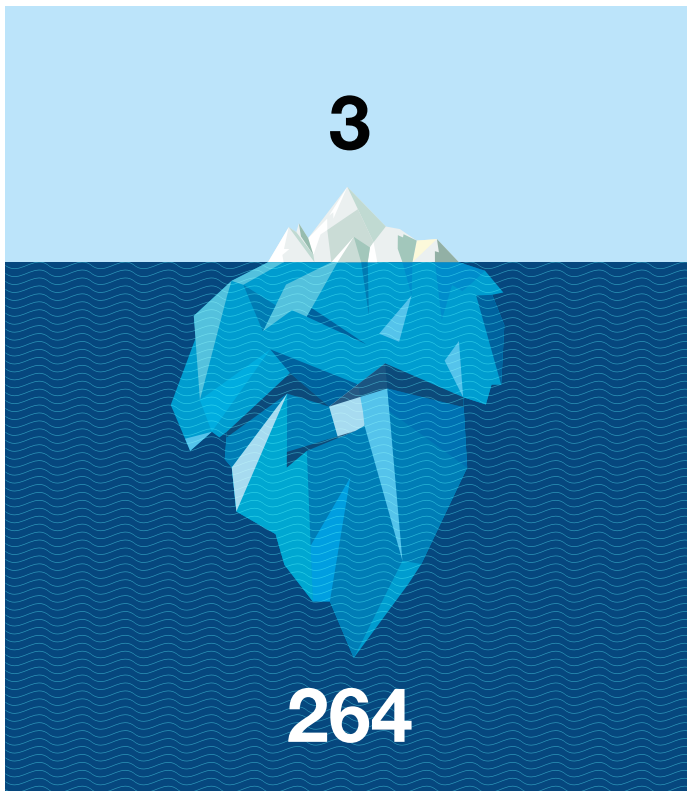
These numbers translate approximately into a risk of death of 1 in 100,000 components issued, a risk of death from error of 1 in 250,000 and a risk of major morbidity of 1 in 20,400. The international haemovigilance database (ISTARE) reported information collected from 25 countries 2006-2012 (Politis et al. 2016). The incidence of all adverse reactions was 77.5 per 100,000 components issued of which 25% were severe. The total components issued in this period were 132.8 million. The death rate was 0.26 per 100,000 with more than half (58%) due to pulmonary complications (TACO 27%, TRALI 19% and TAD 12%). Trending in 13 countries that reported every year showed a progressive increase in TACO and decrease in TRALI similar to the trend noted in SHOT (Chapter 18, Pulmonary Complications).

ABO-incompatible transfusion was reported in 511 cases with 305 (59.7%) reactions. There were 6333 wrong patient samples reported, 94.6% near misses.

## ABO-incompatible transfusions

Three ABO-incompatible red cell transfusions were reported, two of which resulted in major morbidity, but no deaths were reported in 2016. In addition there were 3 ABO-incompatible fresh frozen plasma infusions (now included in England as 'never events'). These are fully described in the chapter on incorrect blood component transfused (Chapter 10, Incorrect Blood Components Transfused (IBCT)). Although there were only 3 ABO-incompatible red cell transfusions, there were 264 potential ABO-incompatible transfusions which were avoided because the near miss incidents were detected (Figure 3.12 below, and Chapter 12, Near Miss Reporting (NM)). This is a reminder that the actual incidents are the tip of a considerable iceberg demonstrating much wider unsafe practice, Figure 3.7.

In addition to very serious clinical outcome (death) the consequences for hospital staff are severe. In December 2016 the nurse who administered an ABO-incompatible transfusion to a patient who then died (in 2014, included in the 2015 data) was convicted of manslaughter. This death would have been avoided if she had performed the final check. A bedside checklist is recommended again by SHOT this year, as in the Annual SHOT Reports for events reported in 2011 and 2015. This should become habit just as all pilots do formal checks before taking off. However, WBIT samples may not be detectable later in the transfusion process as demonstrated by two cases this year, a reminder that correct identification of the patient at the initial step is essential, and a group-check policy would reduce these errors.

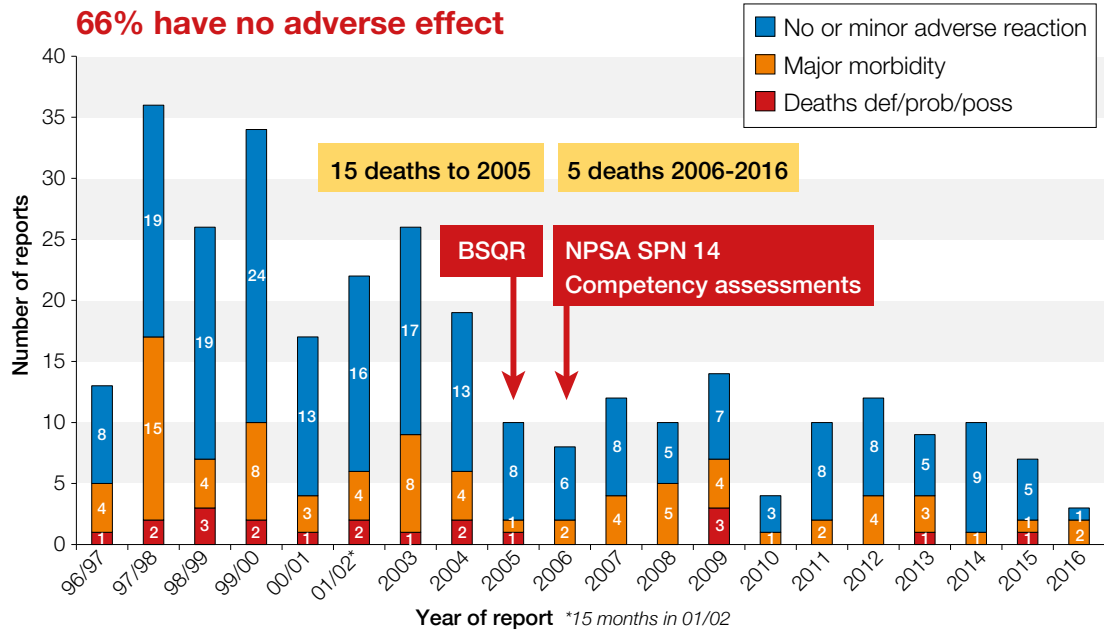


**Figure 3.7**  
ABO-incompatible transfusions: few events (n=3) but many ABO near misses (n=264)

Two of the incompatible red cell transfusions were caused by WBIT incidents in hospitals where there was a two-sample policy that was not followed; the third was a combination of collection and administration errors which could have been detected had the bedside check been performed.

Cumulative data for ABO-incompatible red cell transfusions have shown a decrease over time but each one of these has the potential to cause death. Review of 196 cases where wrong components were transfused 2012-2016 inclusive resulting from errors at administration showed that 141 (71.9%) would have been prevented had the administration checks been done correctly. This includes 26/39 (66.7%) ABO-incompatible red cell transfusions. In 72 cases the bedside check was performed by two people, in 33 cases by one (no details given in 36 cases). It is clear that a bedside checklist has potential to prevent wrong transfusions and death.

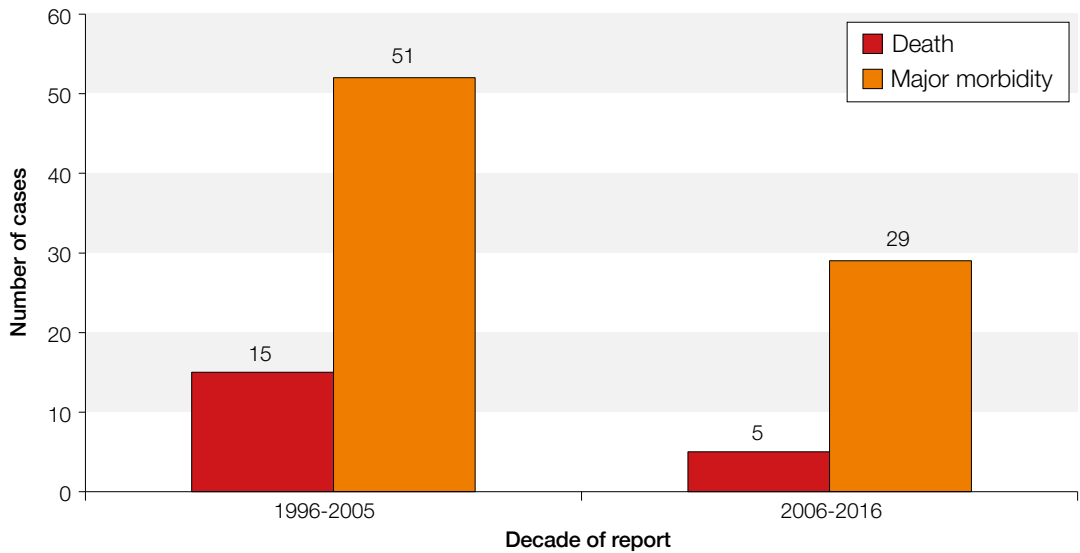
**Figure 3.8:**  
Outcome of ABO-incompatible red cell transfusions in 20 years of SHOT reporting



BSQR=Blood Safety and Quality Regulations: NPSA SPN 14=National Patient Safety Agency Safer practice notice 14 'Right patient, right blood' ([www.nrls.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?allid=60046](http://www.nrls.npsa.nhs.uk/EasySiteWeb/GatewayLink.aspx?allid=60046))

In the first decade of SHOT reporting, 1996 to 2005, 15 deaths were reported, but in the next decade, 2006 to 2016 there were 5. The overall reduction in ABO-incompatible red cell transfusions reflects safer practice perhaps as a consequence of the advent of the Blood Safety and Quality Regulations and introduction of mandatory competency-assessments in 2005.

**Figure 3.9:**  
Reduction in ABO-incompatible transfusions resulting in death or major morbidity in two decades of SHOT reporting



Review of the ABO-incompatible groups transfused in years 2010 to 2016 shows that the most frequent combination is group A units transfused to patients of group O, as would be expected from the distribution in the population. In 2 cases information on the groups was not available.



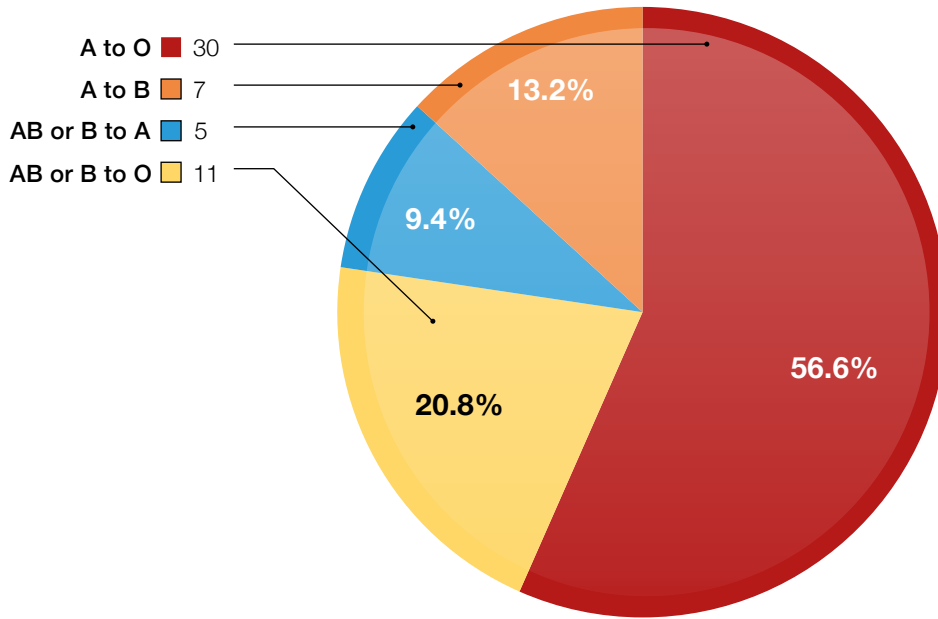


Figure 3.10: Combinations of groups in ABO-incompatible red cell transfusions n=53 (2010 to 2016)

Transfusion of group A red cells to group O patients was associated with the greatest risk of major morbidity (11/30, 36.7%), but both deaths occurred in group O patients receiving group AB red cells (Figure 3.11).

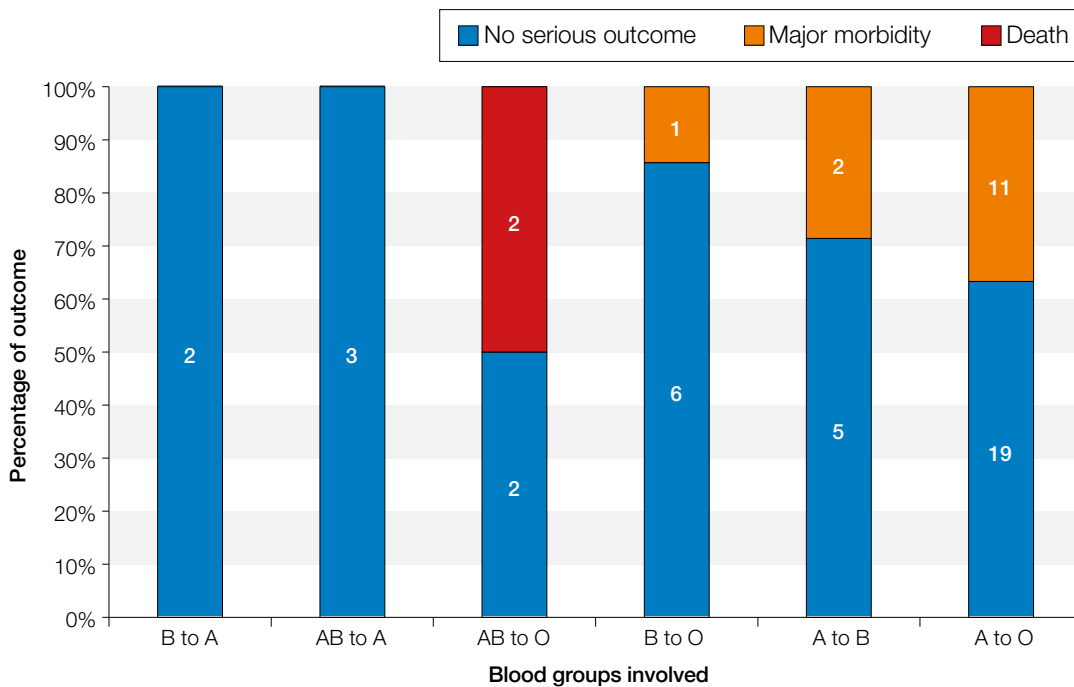
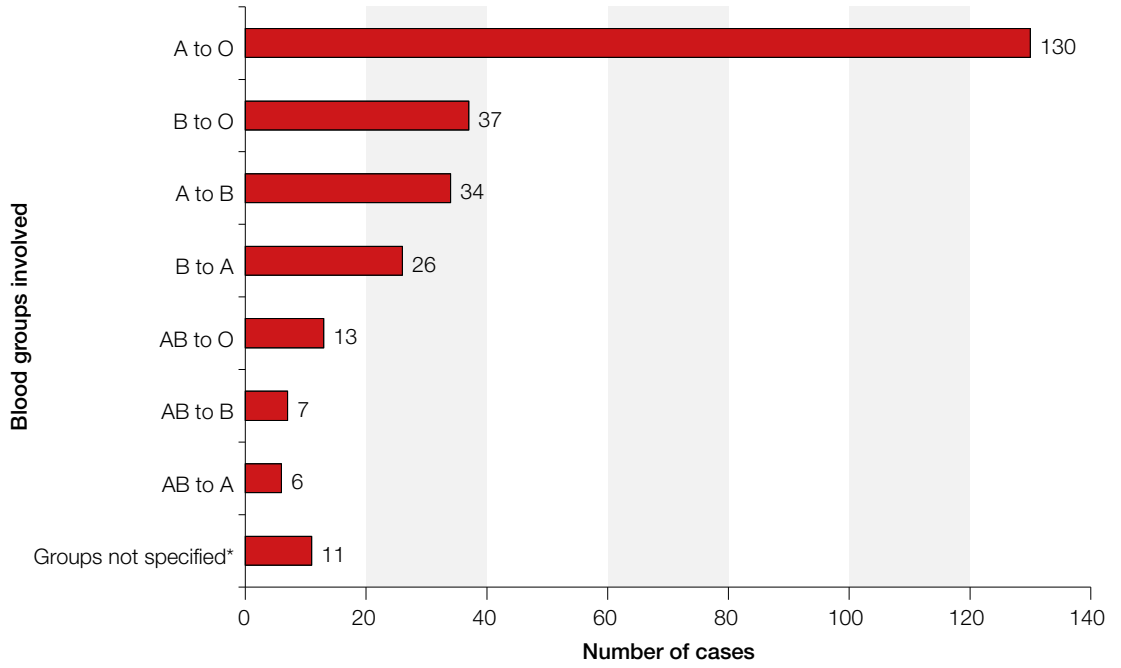


Figure 3.11: ABO-incompatible transfusions by groups (2010-2016) showing outcome n=53

### Near miss incidents

Review of near miss incidents in 2016 where WBIT samples were detected and no transfusion took place shows that there were 249/264 incidents where ABO-incompatible transfusions could have resulted had the WBIT not been detected. Other causes are given in Chapter 12, Near Miss Reporting (NM), Table 12.2. More than half of these would have been group A or group AB red cells transfused to group O patients (143/264, 54.2%) which are the most dangerous, Figure 3.11.

**Figure 3.12:**  
Possible impact  
if 264 near miss  
events (detected)  
had resulted in red  
cell transfusions



\*Reporters stated the combination would have been incompatible but did not specify the ABO groups

### Reference

Politis C, Wiersum JC et al. (2016) **The international haemovigilance network database for the surveillance of adverse reactions and events in donors and recipients of blood components: technical issues and results.** Vox Sang 111, 409-417

# Key Messages and Recommendations

# 4

Authors: Paula Bolton-Maggs and Dafydd Thomas

## Key SHOT messages

- **Errors** continue to be the source of most SHOT reports (87.0%). While component safety is very good, mistakes continue to put patients at risk. Many of these are caused by poor communication and others by distraction. A better understanding of human factors may help to reduce these
- **Training:** All staff participating in transfusion must have the knowledge and training to undertake the role. This is their personal responsibility. Information technology (IT) is not always reliable and does not replace the need for knowledge
- **Laboratory staffing** should ensure that there are adequate numbers of appropriately trained staff; there should be contingency planning for staffing levels below a minimum level and for times of high workload. Lone working is a concern and staff who are new to a laboratory should be trained and competency assessed
- **Adverse incidents should always be investigated**, and all organisations adopt sharing of incidents: to understand, learn lessons and for staff themselves to come up with resolutions to bring about ownership of the solutions put forward
- **Equipment and IT** must be fit for purpose. Software and equipment providers should market test and listen to transfusion staff and tailor development programmes accordingly. IT providers should standardise their products across the UK. People move between organisations so alerts, warnings and flags need to work in a similar way in different systems
- **Anti-D immunoglobulin administration** continues to be a source of numerous incidents. All healthcare providers involved in the care of pregnant women should review their policies and ensure regular refresher training for all staff, both clinical and laboratory

Transfusion practice requires improvement in safety. The components are very safe. There was a single transmission of infection (hepatitis E virus) reported in 2016 in nearly 2.5 million components issued, and no cases of transfusion-related lung injury, transfusion-associated graft versus host disease or post-transfusion purpura. Adverse reactions were reported in a total of 385 cases, 12.5% of all reports. Allergic, hypotensive and severe febrile reactions continue to be the most common cause of unpredictable reactions (253/385, 65.7%). Errors are responsible for the majority of SHOT reports (n=2688, 87.0% of all reports) and 98.1% of the 1027 serious adverse events reported to the Medicines and Healthcare Products Regulatory Agency (MHRA). This is an increase in SHOT error reports compared to 2015 (cessation of alloimmunisation reporting will have affected this).

There is clear evidence of the impact of laboratory staffing and workload issues on errors. The MHRA notes that these factors contribute to 10.0% of serious adverse event reports. The human factors questions added to SHOT error report categories have similarly provided evidence in 83 cases, including clinical areas, (Chapter 6, Human Factors) with staffing problems identified in 27/83 (32.5%) and workload in 18/83 (21.7%).

## The bedside checklist – be like a pilot

The regular use of a bedside checklist would save lives. In 2014 a patient died after an ABO-incompatible transfusion where the wrong unit was collected and administered. The experienced nurse has since been convicted of manslaughter. In this current report for 2016 there is a mirror image case where the patient suffered major morbidity (Case 10.5). The wrong unit was collected then administered by a registered nurse who did not complete the bedside check. In both cases the patients had similar names to another patient on the ward. Let this be a warning. Long experience and seniority are no substitute for correct checking every time as every highly trained pilot (junior or senior) knows. We recommended a checklist last year and also in the Annual Report for 2011. There are different ways of doing this such as having it on the prescription, or on the reverse of the blood unit tag; it needs local champions and commitment from leaders (Anthes 2015). An audit of the London lanyard version noted that the checklist was effective but less likely to be used where staff were experienced in transfusion. There is no place for this complacency. A two-person dependent check by challenge and response (Winters et al. 2009) may be safer and should be piloted (see Chapter 10, Incorrect Blood Component Transfused).

### Key recommendations (revised and updated from the Annual SHOT Report 2015)

- A checklist must be used at the patient's side as a final administration check prior to transfusion as standard of care. The checklist must include positive patient identification (forename, surname, date of birth and hospital number or other unique identifier). It should also confirm that the component is correct, ensure that it includes any specific requirements and that it has been prescribed for transfusion to this patient at this time. Errors are made with both one-person and two-person checks. Use of a verification process (two people working together, with challenge and response) may be more effective.

Whatever bedside system is in place (including electronic systems) it should be assessed and include a validation step where someone has to sign to say that all steps have been followed.

- Patients should be formally assessed for their risk of transfusion-associated circulatory overload (TACO) whenever possible since TACO is the most commonly reported cause of death and major morbidity. A revised checklist is shown in Chapter 18b (TACO) Figure 18b.1

**Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff**

Additional topic-related recommendations can be found in the following chapters: Chapter 10, Incorrect Blood Component Transfused n=1; Chapter 13, Information Technology Incidents n=1; Chapter 14, Adverse Events Related to Anti-D immunoglobulin n=3; Chapter 15, Immune Anti-D in Pregnancy n=1; Chapter 16, Acute Transfusion Reactions n=2; Chapter 21, Cell Salvage n=5; Chapter 22, Paediatric Summary n=1 and there is further explanation of Key Recommendation 2 in Chapter 18b, Transfusion-Associated Circulatory Overload.

## References

Anthes E (2015) **The trouble with checklists**. Nature 523, 516-518

Winters BD, Gurses AP et al. (2009) **Clinical review: checklists – translating evidence into practice**. Crit Care 13, 210 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2811937/pdf/cc7792.pdf> [accessed 14 April 2017]

# Donor Haemovigilance

# 5

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## **With contributions from:**

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*Dr. Stephen Field, Medical Director; Welsh Blood Service (WBS)*

## **Key SHOT messages**

- Serious adverse events of donation (SAED) are rare but do occur and may not always be preventable. These adverse events can be immediate or delayed and need to be recognised and managed promptly
- Vasovagal events resulting in donor hospitalisation or injury as well as nerve injuries post venepuncture continue to be the most frequently reported SAED
- Donor education, vigorous donor selection processes, good clinical governance, effective staff training and competency assessments, clinical audits, robust data capture and analysis of donor adverse events with regular review of trends and management of adverse events and corrective actions taken along with benchmarking will all help in promoting donor safety
- Further research into interventions designed to prevent or reduce donor adverse events especially vasovagal events in blood donors is needed to enhance donor safety and ensure sustainability of blood supply

## **Background**

Voluntary non-remunerated donors, donating regularly, are vital for the provision of safe and sufficient blood for transfusion. While blood donation is generally very safe, donor complications sometimes occur either during or after blood donation. Donor haemovigilance refers to the systematic monitoring of all adverse reactions, complications and incidents related to the care of the blood donor, with a view to improving quality and safety for all blood donors. The current European Blood Directives, issued and enforced between 2003 and 2005 (2002/98/EC and 2005/61/EC), provide the regulatory base of haemovigilance requirements for traceability and notification of serious adverse reactions and events (EU Directives). The EU Directives were transposed into UK law through the Blood Safety and Quality Regulations (BSQR) 2005. These regulations ensure that all transfusion services have a system for receiving and registering reports of serious adverse reactions and serious adverse events related to quality and/or safety of blood or components for transfusion.

## Data

The following table summarises the whole blood and apheresis donations collected in the 4 UK Blood Services last year with a total of 2,004,650 donations (whole blood and components) collected.

**Table 5.1:**  
Donation data  
from the UK Blood  
Services 2016

Donations made in 2016		NHSBT	SNBTS	NIBTS	WBS
<b>Whole blood</b>	Donations from male donors	760,085	77,162	26,441	43,798
	Donations from female donors	844,252	85,877	22,353	41,523
	Donations from new donors	210,346	15,260	5,568	9,268
	Donations from repeat donors	1,393,991	147,779	43,226	76,053
<b>Apheresis</b>	Donations from male donors	77,166	9,657	4,594	2,662
	Donations from female donors	6,944	969	718	449
	Donations from new donors	9,753	0	18	120
	Donations from repeat donors	74,357	10,626	5,294	2,991
<b>Total number of donations in 2016</b>		<b>1,688,447</b>	<b>173,665</b>	<b>54,106</b>	<b>88,432</b>

Donor adverse events are recorded in the UK according to the revised 2014 'Standards for Surveillance of Complications Related to Blood Donation' drafted by the working group on donor vigilance of the International Society of Blood Transfusion (ISBT) working party on haemovigilance in collaboration with the International Haemovigilance Network (IHN) and the American Association of Blood Banks (AABB) Donor Haemovigilance Working Group (Goldman et al. 2016, ISBT 2014). These have helped harmonise reporting of donor adverse events in all the Blood Services. Serious adverse events of donation (SAED) are those which either result in donor hospitalisation, interventions or significant disability/incapacity persisting for >1-year post donation or rarely death. These are reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) and investigated in a timely manner. The donor SAED are reportable if definitely, probably or possibly linked to donation.

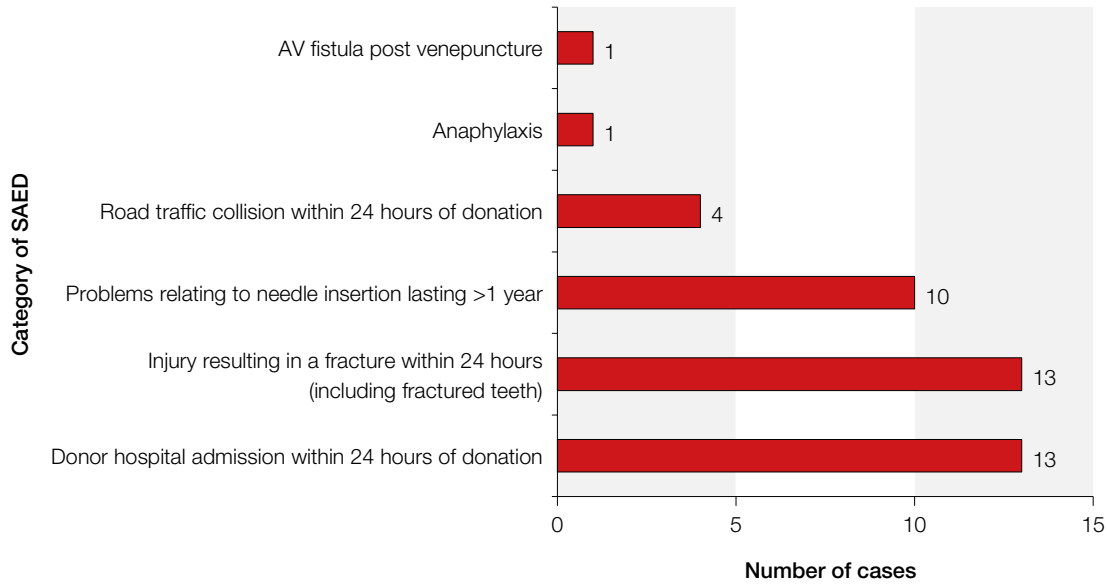
Table 5.2 provides information related to the total number of donations, number of whole blood donations, component donations and total number of SAED reported by each of the UK Blood Services for the calendar year 2016.

**Table 5.2:**  
Summary of SAED  
from the 4 UK  
Blood Services for  
the calendar year  
2016 (January to  
December)

	NHSBT	SNBTS	NIBTS	WBS
Whole blood donations	1,604,337	163,039	48,794	85,321
Apheresis/component donations	84,110	10,626	5,312	3,111
Total donations	1,688,447	173,665	54,106	88,432
Total number of donor SAED in the calendar year 2016	40	2	0	0
<b>Rate of SAED per 10,000 donations in the UK</b>	<b>This equates to a rate of 0.21 SAED per 10,000 donations or 1 SAED per 47,730 donations in the UK</b>			

Overall 42 SAED were reported from the 4 UK Blood Services for 2016. The two most common events were donors who required hospital admission and who experienced injury post donation resulting in fracture or broken teeth (n=13 in each category at a rate of 0.06 per 10,000 donations). Ten donors reported problems related to needle insertion persisting for more than a year (rate of 0.05 per 10,000 donations) with the majority being reported in male donors (n=8/10, 80.0%).

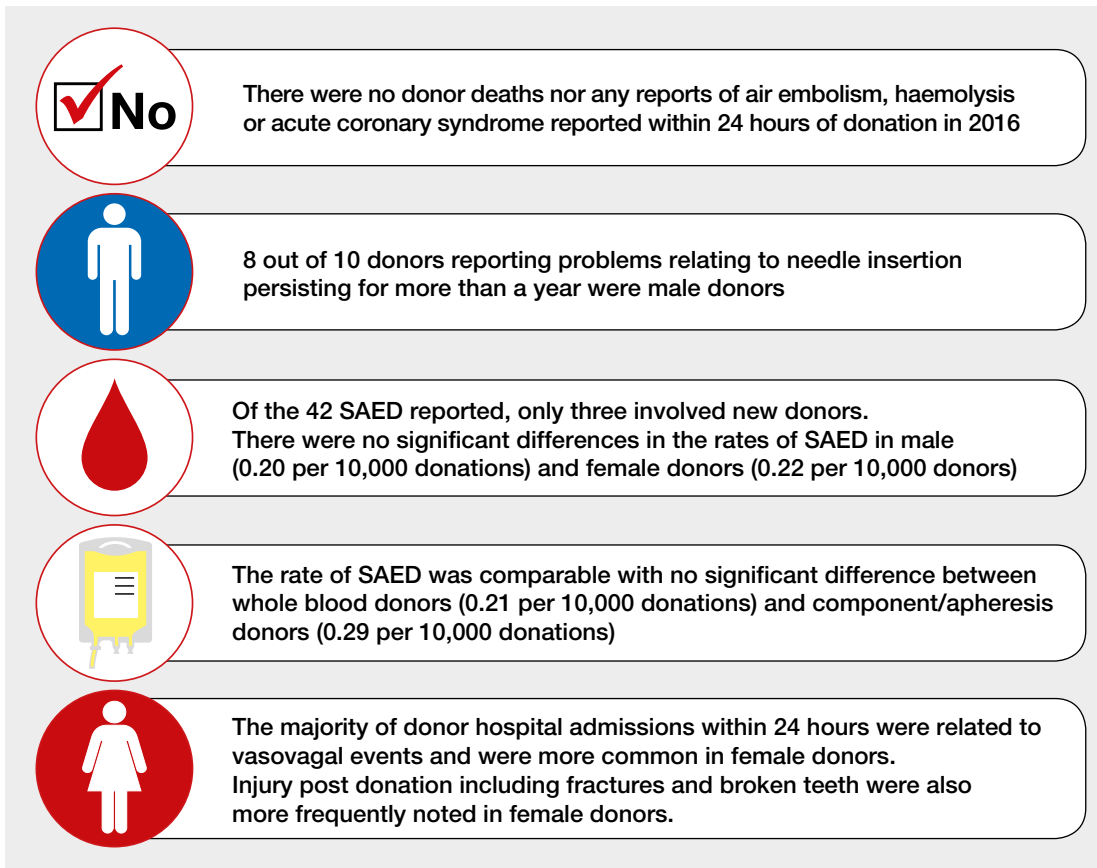




**Figure 5.1**  
Reporting categories for the SAED reported from the 4 UK Blood Services in 2016 n=42

AV=arteriovenous

Note: One donor who sustained a fracture within 24 hours of donation also needed hospital admission and is reflected in the number of donors who sustained injury within 24 hours of donation



**Figure 5.2:**  
Summary with further details regarding the SAED reported in UK

There were no donation-related deaths. There were no reports of haemolysis or air embolism related to component donation nor any acute coronary syndrome within 24 hours of donation. It is also useful to note that of the 42 SAED reported, only three involved new donors. The majority, 39/42 (92.9%), were reported in whole blood donors while only 3 SAED occurred in component donors; however there was no significant difference in the rate of SAED in whole blood donors (0.21 per 10,000 donations) versus component donors (0.29 per 10,000 donations). There were no significant differences in the rate of SAED in male (0.20 per 10,000 donations) and female donors (0.22 per 10,000 donations).

The majority (n=10/13, 76.9%) of donor hospital admissions within 24 hours were related to vasovagal events and were more common in female donors (n=8). Of these, 7/10 (70.0%) donors suffered a delayed vasovagal event which is a well-recognised complication post donation. Injury post donation including fractures and broken teeth were also more frequently noted in female donors (n=9/13, 69.2%).

#### **Case 5.1: Rare complication of AV fistula post venepuncture in a blood donor**

*A regular male donor fainted 4 minutes after venepuncture. The donation was stopped and the donor recovered uneventfully. He was contacted for follow up on the next day, when he reported that venepuncture had been more painful than usual and queried whether it had been an arterial puncture. Review of his session record showed that blood flow had not been faster than usual and he described no bruising, pain or swelling in his arm. Arterial puncture was therefore considered unlikely.*

*The donor called back the next day to report a 'buzzing' sensation in his arm, which he could also feel if he palpated the venepuncture site. He had no other symptoms, but described his arm as 'feeling funny'. He was advised to attend the emergency department (ED) where an AV fistula was diagnosed. The donor subsequently required surgery to close the fistula. The vascular surgeon who conducted the procedure reported that the brachial artery lay close behind the brachial vein and that during venepuncture the needle had passed through the back of the vein and into the artery. Retraction of the needle during venepuncture may have pulled the damaged arterial wall into the vein, allowing the fistula to develop. The arterial puncture was not recognised because the normal effects (fast flow, bruising post-donation) did not occur. The donor made an uneventful recovery from surgery. He has been advised not to donate in future.*

The development of an AV fistula is an extremely rare complication of arterial puncture during blood donation, with only a handful of cases reported in the literature (Newman 2013). An AV fistula usually presents as an elongated pulsatile mass in the arm, associated with a palpable thrill and bruit. Phlebotomy-related AV fistulae are initially small but will generally increase in size over time and may only become symptomatic some time after venepuncture. Surgical repair is required, but is usually uncomplicated, with no long-term consequences.

In documented cases, donors have reported symptoms to the Blood Service days or weeks after venepuncture. Donors should be encouraged to make early contact with the Blood Service if they experience any arm complications, even if symptoms develop some time after the donation. Careful attention should also be given if a donor reports unusual or atypical symptoms, whether or not the donor has more obvious complications such as pain, bruising or paraesthesia.

#### **Case 5.2: Donor with delayed faint requiring hospital admission within 24 hours post donation**

*A regular female whole blood donor had an uneventful donation and sustained a delayed faint 6-8 hours post donation and banged her head. She was admitted via the ED at the local hospital where blood tests, X-rays and a brain scan were all normal. The donor had a swollen jaw but recovered slowly. The donor had taken her pre- and post-donation drinks and had followed the advice regarding applied muscle tension (AMT) exercises. No bruise was recorded and the donor felt well before leaving the session venue. A root cause analysis confirmed that all standard NHSBT procedures were followed and nothing could be identified that needed to be addressed to be able to prevent this SAED.*

Adverse events related to blood donation can occur during or after donation. Delayed complications are defined as complications which occur after the donor has left the donation venue. Delayed vasovagal reactions are a well-recognised but poorly understood complication of blood donation. They are thought to occur because of failure of the donor's normal compensatory reflexes to respond to the volume loss associated with donation. Inadequate fluid intake post donation, prolonged standing, and high environmental

temperature are recognised factors increasing the risk of a delayed vasovagal reaction. Delayed reactions occur more frequently in female than male donors. Unlike immediate vasovagal reactions, the risk of a delayed reaction is not significantly higher in new and inexperienced donors compared to experienced and older donors. It is possible that experienced donors become less attentive about following advice to increase their fluid intake following donation, thereby increasing their risk of a delayed reaction.

Post-donation information must be provided to all donors. This should include the risk of delayed reactions and advice on prevention, in particular, advice on maintaining post-donation fluid intake, and avoidance of known precipitating factors such as overheating and prolonged standing.

### **Case 5.3: Venepuncture-related persistent arm pain more than one year post donation**

*A regular male whole blood donor who had donated multiple times in the past without any adverse event, reported persistent problems with his donation arm >1 year post donation. He remembered the donation being uncomfortable but had no pain on needle insertion or removal. The donation was stopped midway as a swelling was noted at the venepuncture site. The swelling and local bruising resolved fully over the next couple of weeks. However, the donor was left with a constant 'niggle' at the venepuncture site with pins and needles sensation and intermittent numbness along his inner forearm. His range of movement was fully preserved. He was investigated locally and informed that he had median nerve damage and received regular physiotherapy with some improvement in symptoms. The haematoma following needle insertion contributed to the initial nerve irritation and had been managed promptly and appropriately at the donation session. Traumatic venepunctures are known to be associated with nerve injury.*

Needle-related complications include haematoma, arterial puncture and painful arm, which may result from nerve irritation through a haematoma or from direct injury to a nerve or other structure. It is recognised that arm symptoms from needle-related complications may take several weeks or longer to resolve, and these complications are usually over-represented among reported cases where there is long-term morbidity following a blood donation. Despite adequate staff training and competency-assessment, nerve injuries may not be completely avoidable because nerve anatomy is variable and nerves cannot be palpated. Most nerve injuries resolve, but in a few cases, it may take months, and in rare instances there may be permanent injury. Nerve injuries are the most common cause of disability among donors. Nerve injury is usually immediately apparent with donors reporting a sharp, burning or electrical pain radiating to the lower arm or into the hand/fingers and in some cases also proximally. Donors may also experience paraesthesias. This must be recognised by staff who insert needles and when donors report severe pain, the needle should be removed immediately.

## **References**

BSQR (2005) **The Blood Safety and Quality Regulations**. ISBN 0110990412.

<http://www.legislation.gov.uk/ukxi/2005/50/contents/made> [accessed 10 March 2017]

EU Directives: [http://ec.europa.eu/health/blood\\_tissues\\_organs/key\\_documents/index\\_en.htm#anchor0\\_more](http://ec.europa.eu/health/blood_tissues_organs/key_documents/index_en.htm#anchor0_more)

[accessed 10 March 2017] Then click Blood-Legislation and Guidelines to expand list and select each option below:

Commission Directive 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards **Traceability requirements and notification of serious adverse reactions and events** [2005] OJ L 256/32

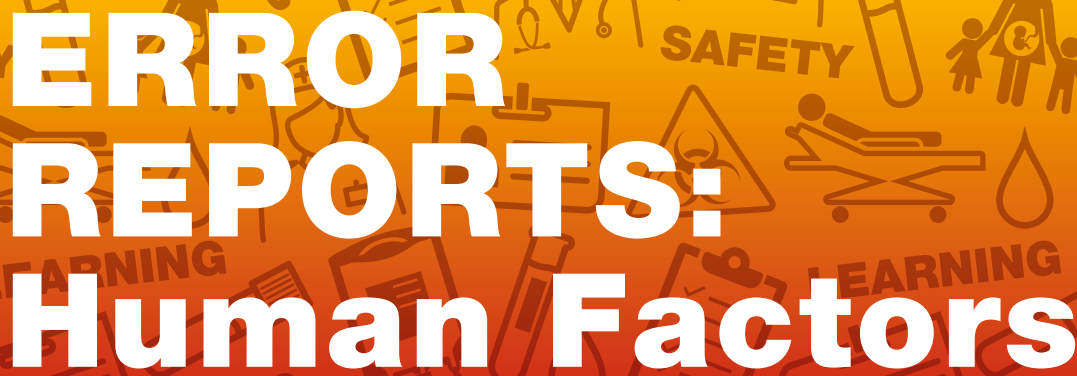
Directive 2002/98/EC of The European Parliament and of the Council of 27 January 2003 **Setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components** and amending Directive 2001/83/EC [2003] OJ L33/30

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# ERROR REPORTS: Human Factors

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# 6 Human Factors in SHOT Error Incidents n=2677

Author: Alison Watt

Over the last few years SHOT has highlighted the importance of considering human factors when investigating transfusion incidents. As noted in every Annual SHOT Report over the past two decades, most incidents are caused by errors in the transfusion process. Therefore a recommendation was made in the 2013 Annual SHOT Report (Bolton-Maggs et al. 2014) that in line with human factors research it may be better to review the transfusion process to design out the errors.

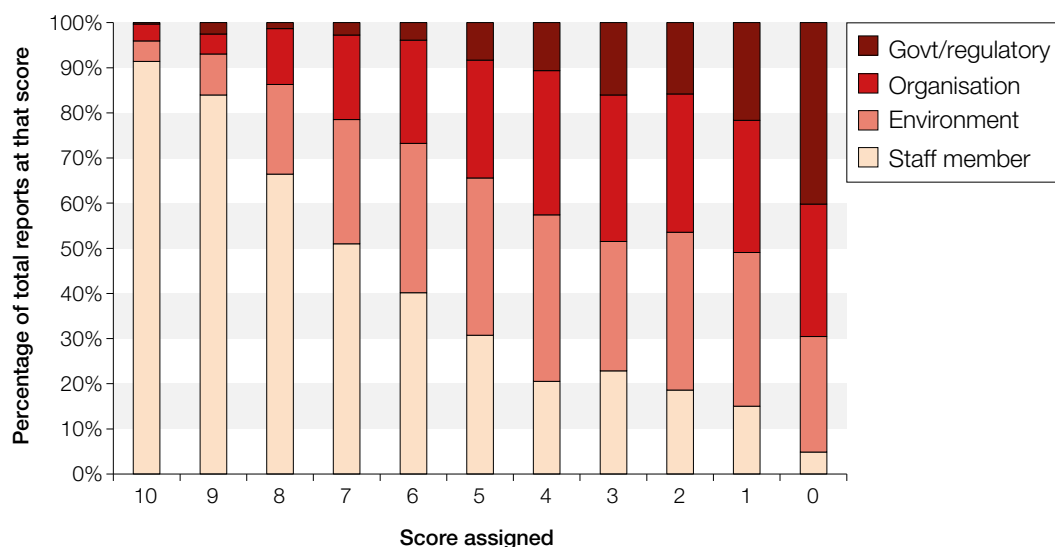
In January 2016 a human factors investigation tool (HFIT) was added to the SHOT database (Dendrite). Human factors questions were added in all error categories to examine which of four human factors was estimated to be implicated in each incident:

To what extent is the cause of this incident attributable to:

- Unsafe practice by individual staff member(s)
- Unsafe conditions associated with the local environment or workspace
- Unsafe conditions associated with organisational or management issues in your Trust/Health Board (e.g. staffing levels)
- Conditions associated with the government, Department of Health or high level regulatory issues (i.e. the error was caused by regulatory issues, not reportable as a regulatory failure)

Reporters were asked to score each question from 0, no contribution, to 10, fully responsible. Data have been analysed from all error reports completed in the SHOT database in 2016 (n=2677) where the HFIT questions were available (in 11 instances not available where cases were transferred from reaction categories or where incidents involving several patients were duplicated by SHOT staff). The error categories included incorrect blood component transfused (IBCT), avoidable, delayed or undertransfusion (ADU), handling and storage errors (HSE), right blood right patient (RBRP) and errors with anti-D immunoglobulin (Ig) administration. There was considerable variability in the scores allocated and the percentages of each score attributed to each of the four human factors is shown in Figure 6.1.

Figure 6.1:  
Estimation of  
different human  
factors contribution  
to errors, score out  
of 10





Incident reporters seem to consider the cause of errors to be predominantly attributable to unsafe practice by individual staff member(s). At the simplest level, a total of the scores attributed to each of the human factors (Table 6.1) shows 62.6% of the cause was attributed to staff members, with the percentages diminishing as the human factors get farther removed from the individual.

	Staff member	Environment	Organisation	Government/ regulatory
<b>Total sum of scores assigned to each</b>	16,891	5,087	3,862	1,141
<b>Percentage assigned to each</b>	62.6%	18.9%	14.3%	4.2%

**Table 6.1:**  
Total scores (0-10) for each of the human factors

Studies using James Reason’s decision tree for determining the culpability of unsafe acts (Reason 1997) have shown that 90% of quality lapses are defined as blameless (Karl 2012). If culpability by the individual is about 10%, then there may have been an overestimation of the liability of individuals (62.6%) in the answers to the SHOT HFIT questions, and an underestimate of the impact of environmental, organisational or high level government or regulatory factors.

### Discussion of results

These data show that the HFIT added to the SHOT database is a reasonable method of elucidating at a high level which human factors are considered most likely to be the cause of blood transfusion errors. However, the scores given may not always reflect the reality if there is too much focus on individual error. We reviewed these data by taking a selection of cases to assess whether the details of the incident as reported matched the scores allocated. As an example, Case 6.1 was scored as 10 for unsafe practice by the individual, with no scores for any of the other human factors.

#### Case 6.1: Total cause of incident attributed to individual

*Patient 1 had a pre-transfusion sample taken by a nurse in a side room of the ward. The nurse was also coordinating the ward beds and labelled the sample away from the bedside, while dealing with a query from another member of staff about Patient 2. The nurse labelled the sample and request form with Patient 2’s details instead of Patient 1. Patient 2 had a historical blood group result, so the ABO mismatch was detected by laboratory testing. The nurse then realised her error and repeated the sampling of Patient 1. There was a slight delay in ordering blood for Patient 1, but no major harm was caused.*

The following observations can be made from the information provided in this case:

- The local environment or workspace was not ideal, because the nurse was working in a side room, while also being responsible for coordination of all ward beds. This observation suggests that a score should have been given for local environment or workspace
- The member of staff involved in the critical task of taking pre-transfusion samples should not be disturbed by another staff member
- A patient’s request form should be written in advance of taking a sample, so the details can be cross-checked during the sampling process, but on this occasion that was not done, because ‘the nurse labelled the sample and request form with Patient 2’s details instead of Patient 1’

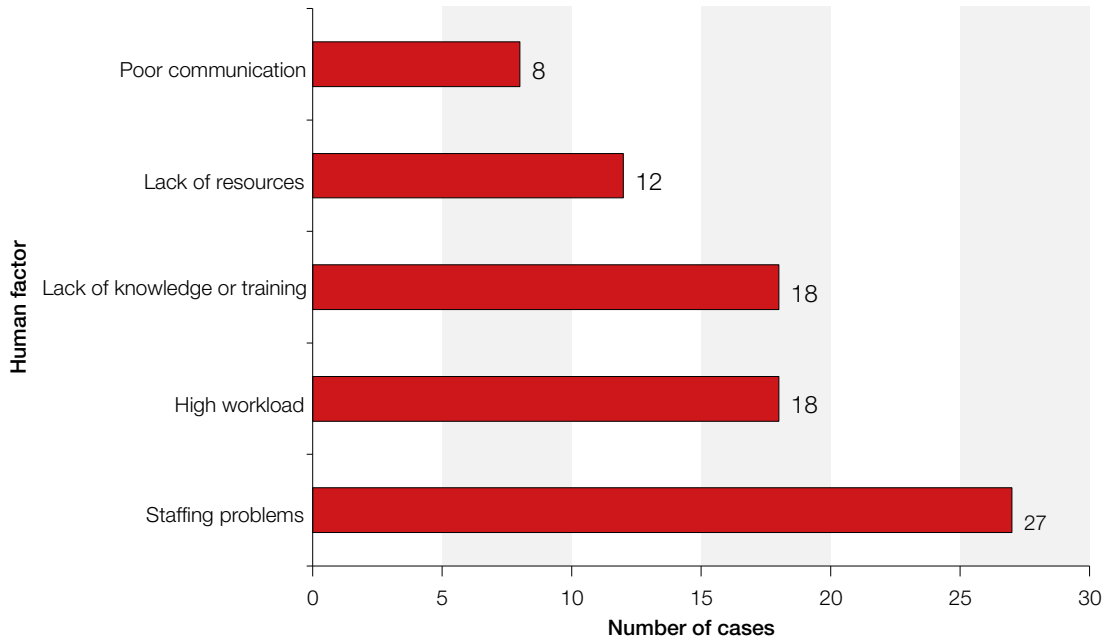
These latter factors could have been caused by a lack of appropriate policies, which is an organisational factor. Alternatively, staff may have failed to comply with policies, because of an excessive workload, also an organisational factor. If the excessive workload was caused by poor staffing levels, that could be as a result of government-level factors affecting the health service. The recent Care Quality Commission (CQC) report (CQC 2017) states ‘The scale of the challenge that hospitals are now facing is unprecedented’. Therefore, in this case it might be more accurate to have an even spread of scores across all four of the human factors identified for this study.

Concern has been expressed about staff shortages, particularly in transfusion laboratories, with dependence on locum and agency staff. The United Kingdom transfusion laboratory collaborative (UKTLC) survey in 2015 (UKTLC 2015; Bark et al. 2016) showed that 90/204 (44.1%) transfusion laboratories

were carrying vacancies and 43 of these laboratories were using agency staff. Reorganisations often lead to staff vacancies and 100/178 (56.2%) laboratories were involved in reorganisation processes.

An analysis was made of the comments given in responses to the HFIT questions in the most serious categories of errors made, such as ADU or cases of IBCT. There were 96 serious incident reports where comments were given. In 83/96 (86.5%) cases the human factors responsible for the incident could be identified and these are summarised in Figure 6.2.

**Figure 6.2:**  
Human factors identified from comments in HFIT n=83



These data corroborate concerns that staff shortages in all departments might be contributing to errors. Staffing problems were mentioned in 27/83 (32.5%) cases and a high workload or being busy was mentioned in a further 18/83 (21.7%).

**Figure 6.3:**  
Example of a comment about staffing in a transfusion laboratory

*The BMS was sick and should not have been at work, but there was no one else available to cover the night shift so he came in. Staffing levels are critically low and there is no give in the system to allow for sickness. All band 6 staff are locums, because the pay is better.*

BMS=biomedical scientist

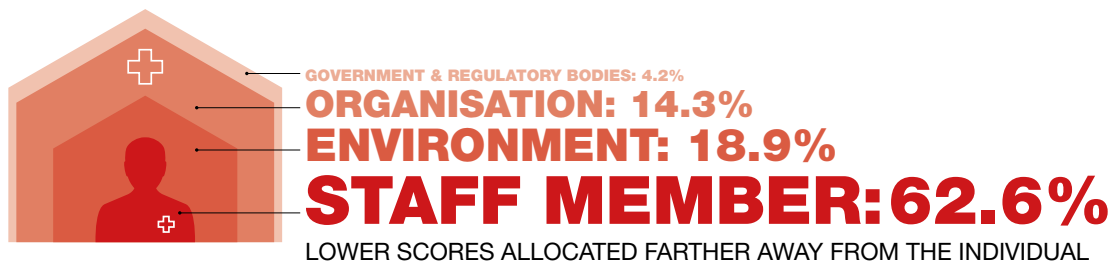


Figure 6.4:  
Scores for factors other than the staff member decrease the farther away they are from the individual

## Commentary

After one year of data collection it is apparent that higher scores have been attributed to staff members as a cause of error than to other potential human factors. From January 2017 a self-learning package has been made available to help reporters consider the human factors aspects of adverse incidents. This package includes real case studies and examines how best to categorise and score the human factors aspects of these cases. The tuition package is published on the SHOT website:

<http://www.shotuk.org/reporting/human-factors-tuition-package/>.

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# Laboratory Errors

# 7

SHOT laboratory errors n=678 (378 laboratory and 300 laboratory near miss)

Medicines and Healthcare Products Regulatory Agency (MHRA) serious adverse events (SAE) n=1027

Authors: Hema Mistry, Chris Robbie, Peter Baker

## Key SHOT messages

- Understaffing and poor knowledge and skills featured in many reports in 2016: 10.0% (103/1027) of SAE reported to the MHRA result from errors made when the workload was considered to be too high or staffing too low. This was also reflected in SHOT reports. This confirms the findings in the UK transfusion laboratory collaborative (UKTLC) survey 2015 (UKTLC 2015). Staffing gaps may be filled with staff who are not transfusion-competent and lacking knowledge in transfusion. Laboratories should always have adequate staffing at the appropriate grade to support those that require training (Chaffe et al. 2014)
- Appropriate use and management of laboratory information management systems (LIMS) are essential for patient safety
- Gap analyses should be performed against national transfusion guidelines (e.g. BSH Harris et al. 2017, BSH Milkins et al. 2013, BSH Jones et al. 2014) and standard operating procedures (SOP) amended to correct deficiencies and to identify any necessary alterations to laboratory procedures

## Introduction

From October 2015 all errors and near misses have been reported without the need to specify to which organisation the incident should be reported. Both SHOT and the MHRA can now review all haemovigilance incidents. The MHRA has been able to select SAE that meet the Blood Safety and Quality Regulations 2005 (BSQR) reporting requirements.

When comparing the number of SAE and reports to SHOT there are significant recognised differences, therefore the incidents are classified here under 3 main headings:

- Both SHOT- and MHRA-reportable
- Reportable to SHOT only
- Reportable to MHRA only

These **differences** in reporting between the 2 haemovigilance organisations include, but are not limited to the following issues:

### MHRA reporting:

- Includes all SAE reports where a confirmation report was submitted in 2016 and reports where the notification report may have been submitted in a different year prior to 2016. Any report where a confirmation report has not been submitted is not included. Therefore SHOT may have a completed report that the MHRA cannot include in its 2016 assessment and vice versa
- Is based on reports made strictly under the BSQR. Excluded reports may include laboratory errors that were not reportable under BSQR (e.g. not related to the potential issue of a component, or related to other laboratories such as haematology, etc). Incidents may not involve the laboratory, but would still be reportable under the BSQR (e.g. storage errors in a clinical area)

- Does not include errors in clinical practice and administration of blood, e.g. wrong blood in tube (WBIT), inappropriate or wrong transfusions where there is no serious reaction in the patient and errors in anti-D immunoglobulin (Ig) issue and administration
- Does not include reactions to blood products which are classified as medicines rather than blood components such as Octaplas® (solvent-detergent fresh frozen plasma (SD-FFP)) and immunoglobulins (both anti-D Ig and intravenous Ig). The MHRA issue data also do not include these products
- Excludes some incidents reported to the MHRA as serious adverse reactions (SAR) where the reaction may have resulted from a SAE that originated in the laboratory. These are counted in the SHOT reports as incorrect blood component transfused (IBCT) because SHOT categorises these as errors whether or not they lead to a reaction

**SHOT reporting:**

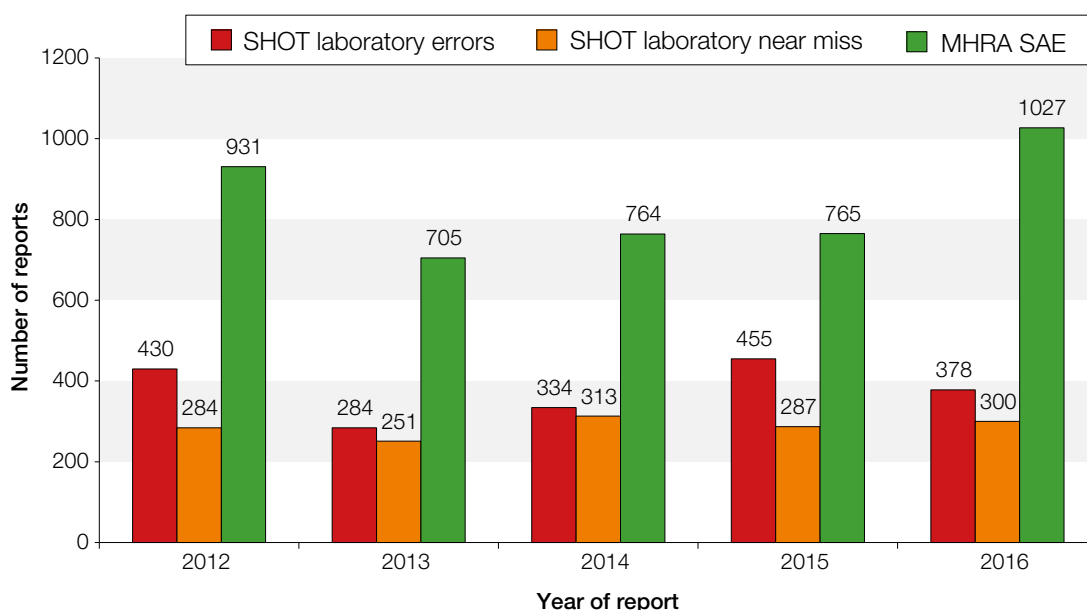
- Does not include cases where the component does not leave the laboratory, e.g. expired components left in the refrigerator, unless these were missed during a routine stock check
- Does not include cases where there was failed recall of a blood component, unless this resulted in a transfusion reaction, which would be reported as a SAR
- Each report is linked to a specific patient, therefore if an incident has multiple patients associated with it SHOT will duplicate the incident for each patient but it will remain a single case for the MHRA

Laboratory staff are encouraged to focus on the key messages and learning points that are highlighted by both organisations.

**Serious adverse events (SAE)**

**Definition:**

**Any untoward occurrence associated with the collection, testing, processing, storage and distribution, of blood or blood components that might lead to death or life-threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity.**



**Figure 7.1:**  
A comparison of the numbers of laboratory-related reports to SHOT and the MHRA over a 5-year period

There were 300 near miss laboratory cases reported to SHOT which are also reportable to the MHRA as there was potential for harm. These are included in Table 7.2.

**Table 7.1:**  
Categories of SHOT laboratory errors

Laboratory categories			Outcome					
	Total	%	IBCT	SRNM	HSE	RBRP	Anti-D Ig	ADU
Sample receipt and registration	94	24.9%	9	40	0	35	4	6
Testing	99	26.2%	11	53	0	0	16	19
Component selection	50	13.2%	18	23	2	0	3	4
Component labelling, availability, handling and storage	116	30.7%	3	5	44	55	1	8
Miscellaneous	19	5.0%	4	4	0	0	4	7
<b>Total</b>	<b>378</b>	<b>100%</b>	<b>45</b>	<b>125</b>	<b>46</b>	<b>90</b>	<b>28</b>	<b>44</b>

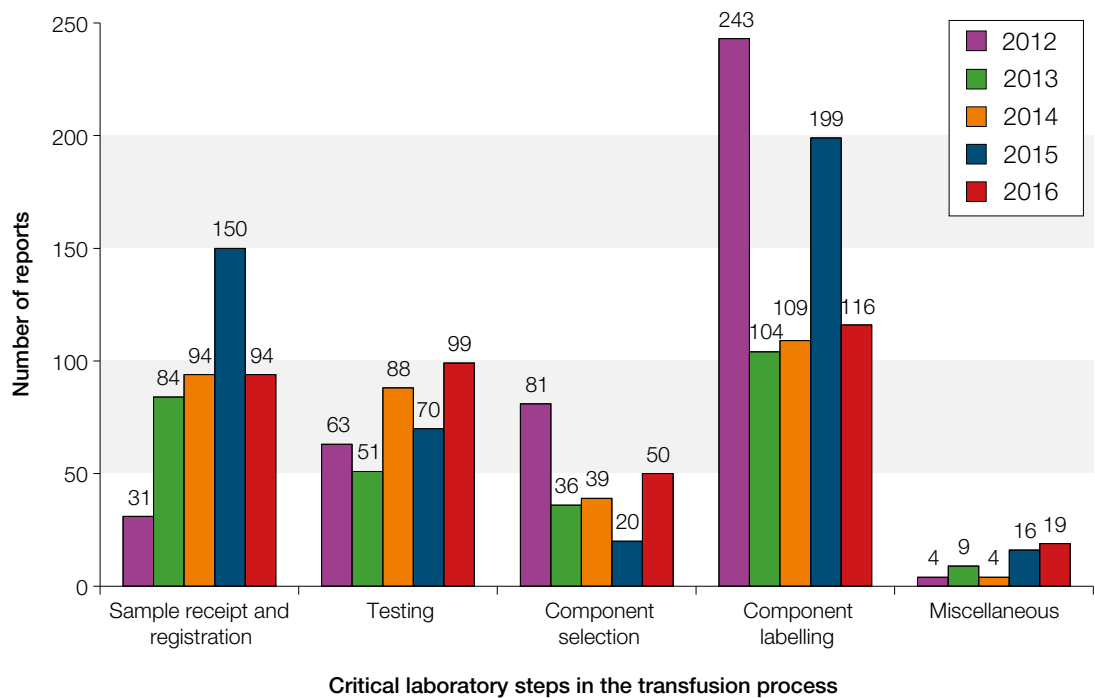
*\*IBCT=incorrect blood component transfused; SRNM=specific requirements not met; HSE=handling and storage errors; RBRP=right blood right patient; Anti-D Ig=anti-D immunoglobulin (Ig) errors; ADU=avoidable, delayed and undertransfused*

**Table 7.2:**  
Categories of SHOT laboratory near miss errors

Near miss laboratory categories			Near miss would have resulted in:					
	Total	%	IBCT	SRNM	HSE	RBRP	Anti-D Ig	ADU
Sample receipt and registration	44	14.7%	2	23	0	18	1	0
Testing	46	15.3%	19	20	0	0	7	0
Component selection	66	22.0%	13	42	7	0	4	0
Component labelling, availability, handling and storage	144	48.0%	11	0	55	73	5	0
<b>Total</b>	<b>300</b>	<b>100%</b>	<b>45</b>	<b>85</b>	<b>62</b>	<b>91</b>	<b>17</b>	<b>0</b>

In 2016 there was an increase in near miss SRNM reports. Failures to notice requests for specific requirements at sample receipt were n=23 in 2016; n=7 in 2015.

**Figure 7.2:**  
SHOT laboratory errors 5-year trend



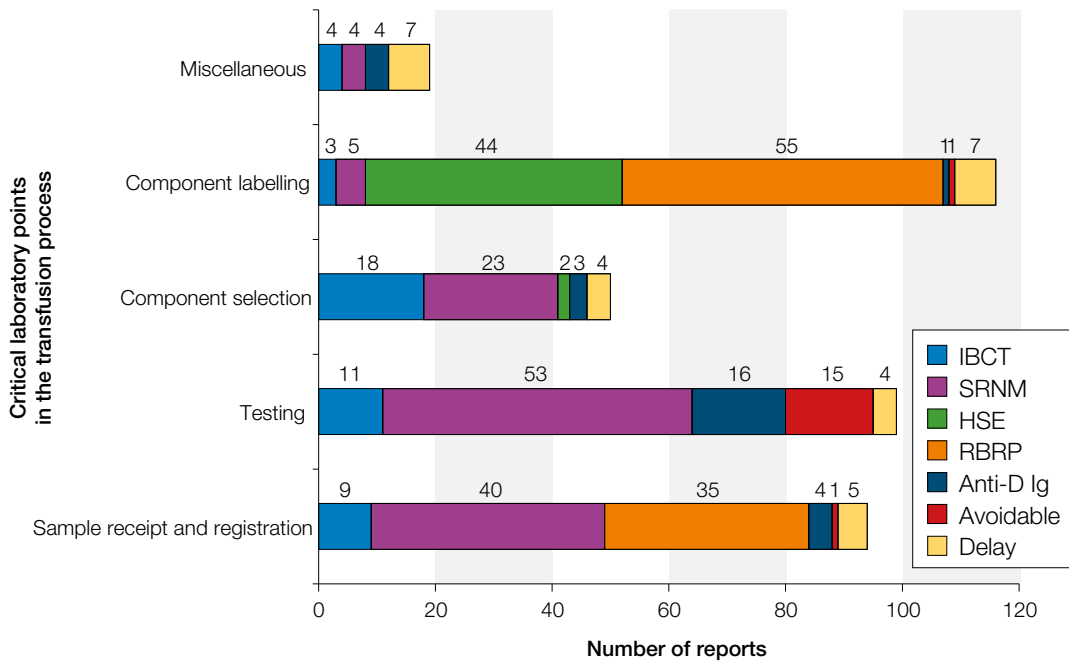


Figure 7.3a: 2016 SHOT data (n=378) including cases that were not reported/reportable to the MHRA showing outcome

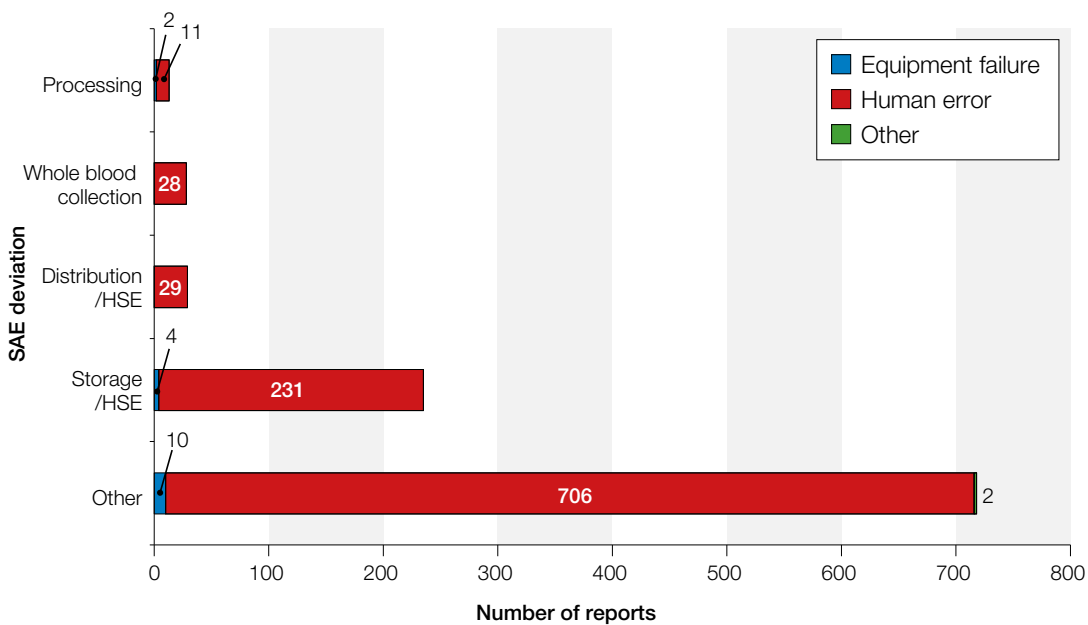


Figure 7.3b: 2016 MHRA SAE data (n=1027) including cases that were not reportable to SHOT

4 additional reports excluded from Figure 7.3b above due to small numbers: 3 testing of donations (human error) and 1 apheresis collection (product defect)

### Discussion of incidents reported to both SHOT and the MHRA n=252

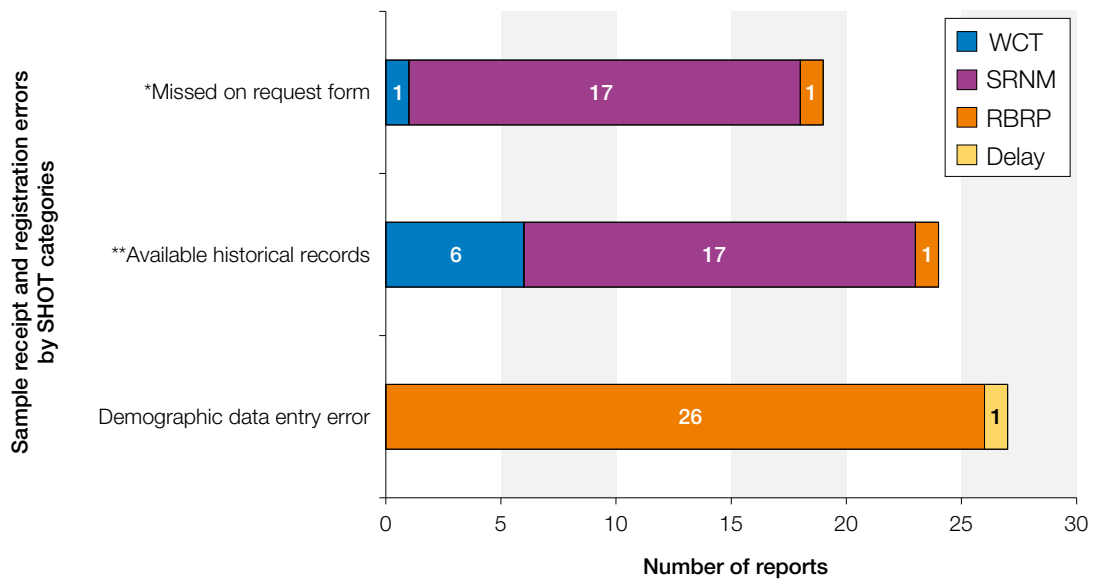
Cases reported to both organisations during 2016 are analysed in this section. The numbers differ from the numbers in the graphs shown in Figures 7.1-7.3 because not all incidents were analysed by both organisations. This could be because they were not reportable to the other organisation, or that they were not completed in time to be included in the analysis for that organisation (and may be included in the 2017 dataset). Incidents that were not analysed by both organisations have been included under the SHOT-only or MHRA-only headings.

### Sample receipt and registration n=70

Correct sample receipt and registration are essential to ensure that the right investigation is performed for the right patient on the right sample at the right time (depending on the patient’s transfusion history). The SOP for sample acceptance by the laboratory must define locally agreed and minimum acceptable identification criteria and the course of action to be followed when these criteria are not met, and should comply with the British Society for Haematology (BSH) guidelines on administration of blood components (BSH Harris et al. 2017).

This is a complex step, much more than just ‘booking in’ of a sample, as staff need to ensure that the request and sample match up and then accurately transcribe that into the LIMS, including noting any specific requirements on the request form or in the LIMS patient history.

**Figure 7.4a:**  
Sample receipt and registration errors by SHOT categories n=70



\*Cases where specific requirements were indicated on the request form but missed by laboratory staff

\*\*Cases where patient history was not heeded that would have indicated specific requirements e.g. antibody history, or information if a patient had received a HSCT

Figure 7.4b shows the same 70 cases by MHRA classification.

**Figure 7.4b:**  
Sample receipt and registration errors by MHRA categories n=70

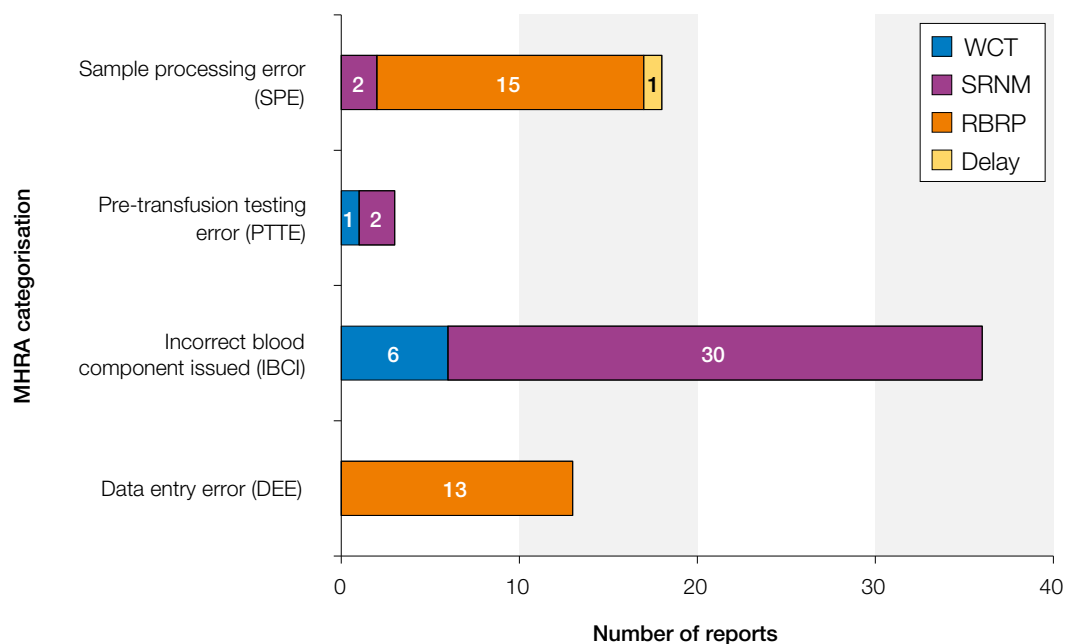




Figure 7.4b demonstrates the subtle differences between SHOT and MHRA classifications. The MHRA recorded 134 sample processing errors (SPE), but since these may be identified prior to any components being issued, these will not be included in the SHOT 'sample receipt and registration' category, but are categorised in SHOT as near misses, see Chapter 12, Near Miss Reporting (NM). SPE refer to errors where discrepancies between sample, forms and LIMS are not identified when the sample is booked in. Data entry errors (DEE) refer to those which are correctly labelled, but for first time patients are booked into the LIMS with errors, creating an inaccurate LIMS entry. Incorrect blood component issued (IBCI) are incidents where specific requirements may not have been entered onto the LIMS at the sample registration stage, but this information was otherwise available to laboratory staff, e.g. on the request form. Pre-transfusion testing errors (PTTE) are those where there was an error in the testing process or in the interpretation of test results.

### **Case 7.1: Failure to use correct documentation leads to IBCT and formation of an antibody in a female of childbearing potential**

*A 15-year-old female patient presented to the emergency department (ED) at 22:30 in sickle cell crisis. At 01:30 two units of red cells were requested, the HbSS diagnosis was recorded on the request form but missed. The group and screen was converted to crossmatch, the biomedical scientist (BMS) printed a screen shot of the patient record that did not include the requirement for HbS-negative units instead of using the original request form that identified the patient's requirements and the diagnosis of sickle cell disease. The patient, subsequently known to be phenotype R2R2 (cDE/cDE), developed anti-e as a result of the transfusion of emergency blood (i.e. negative for C, E, and K, and HbS-negative). The patient record was updated incorrectly to recommend transfusion of C-, E- and K-negative units following the initial transfusion. The correct units should be e-negative.*

It is important to always use all information available (LIMS record and request form) to make the correct choice of components. Updates to patient records should be carefully noted especially if there are specific requirements. The patient record should have been reviewed more thoroughly to identify previous history including pre-transfusion extended red cell typing for this sickle patient if available.

**MHRA regulatory view:** The SOP was not followed and staff used a number of ways of performing the procedure contrary to the written SOP. The SOP was reviewed, improved and re-written. Staff should be trained to follow the SOP without deviating from it.

### **Case 7.2: Incorrect patient record association fortuitously resulted in the right blood to the right patient**

*A male patient who had been stabbed was transfused with two units of emergency O D-negative red cells on admission to the ED. Samples were sent to the laboratory labelled: 'Surname: unknown, Forename: unknown, Hospital number 479628, date of birth (DOB) 01/01/1902' and a further six units were requested. Instead of creating a new patient record the BMS pulled up a previous record of 'Surname: unknown, Forename: unknown' and appended the group O D-negative to this new patient as they thought this would be quicker and that they could retrospectively edit the result. Labels were printed out and read: 'unknown, unknown, 415735, 11/02/1895' and red cells issued (so with wrong number and wrong DOB). Due to the urgency the red cell units were not placed into the electronic tracking system and were collected by a porter and signed for manually. The porter failed to notice the discrepancy in the patient identification number and DOB. In the ED the red cells were noted as O D-negative and only 'unknown, unknown' was checked. There was no check of the patient identification number or DOB. The patient was transfused three of the four units and the discrepancy was detected when the fourth unit was returned to the laboratory and could not be returned to stock.*

This case shows three major errors. The clinical area was contacted following the discovery of the error. They stated that staff only checked the name and group and as the patient was in a very unstable condition they would have transfused the O D-negative units anyway as it was 'a matter of life and death'.

Even in emergency or high pressure situations short cuts in processes must not be undertaken as failure to follow procedure can lead to errors. The identifiers for all patients, including emergency patients should include the gender. The use of 'unknown/unknown' is an unsatisfactory naming system for unidentified patient. LIMS training and competency-assessments need to include the correct procedure for entering unknown patients' details onto LIMS. Full bedside identification checks should be undertaken at all times to include DOB.

**Testing n=56**

The correct tests/analyses are required to ensure the safe provision of blood components and should be undertaken in full compliance with local and national guidelines for pre-transfusion testing (BSH Milkins et al. 2013).

Pre-transfusion testing for ABO/D grouping is the most important serological test. With the introduction of electronic issue (EI) the antibody screen is now also very important as it is the only test, in addition to the blood group, which can ensure compatibility. There is no other opportunity to detect incompatibility in the absence of a serological crossmatch. Ten cases in 2016 demonstrated inappropriate use of EI. EI is increasingly used: data collected in surveys by the UK national external quality assessment scheme (NEQAS) for blood transfusion laboratory practice show an increase in use of EI from 140/392 (35.7%) in 2008 to 153/253 (60.5%) in 2016. See the 2015 Annual SHOT Report (Bolton-Maggs et al. 2016) chapter on haemolytic transfusion reactions (HTR) for more information about the risks/benefits associated with electronic issue.

**Figure 7.5a:**  
Testing errors by SHOT categories n=56

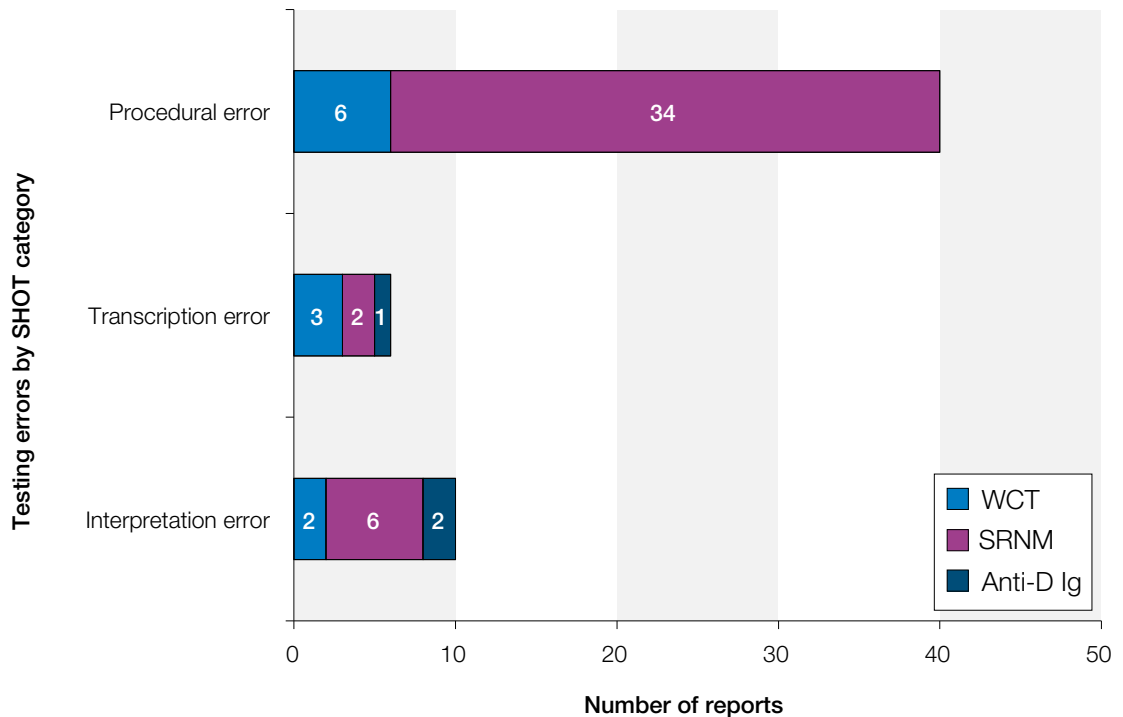


Figure 7.5b shows the same 56 cases by MHRA classification.

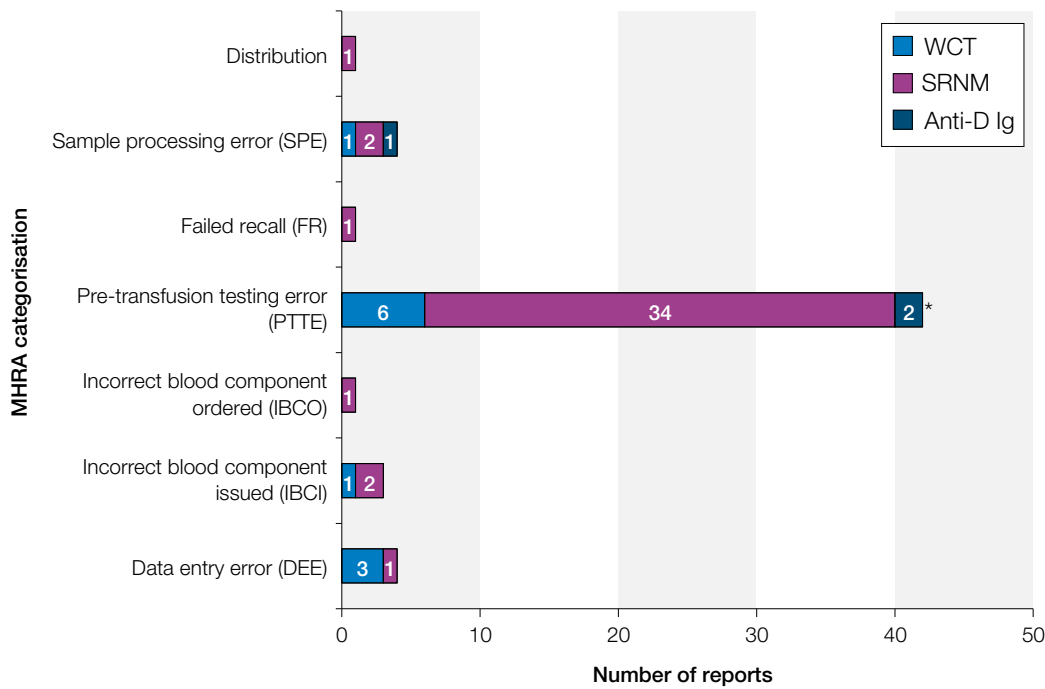


Figure 7.5b: Testing errors by MHRA categories n=56

\*These were 2 errors where anti-D Ig was administered late/omitted

The majority of testing errors that are reported to both haemovigilance organisations are recorded in the MHRA category pre-transfusion testing errors (PTTE). There were 110/1027 (10.7%) PTTE SAE reported to the MHRA of which 108/110 were caused by human factors. Analysis of these data demonstrates no common root cause. However these errors fall evenly into four of the MHRA root cause subcategories:

- **Inadequate processes** - where the process does not always ensure the correct outcome, even when followed correctly. Often a process might not include relevant steps that ensure a consistent and safe outcome, or has not even been designed and established and relies on staff performing tasks which have not been standardised
- **Incorrect procedure** - the correct process has not been properly described in the SOP. Key steps have been omitted, or do not describe what to do, e.g. if unexpected results are obtained
- **Procedural steps omitted/wrong procedure performed** - staff have either missed out key steps in a procedure or followed the wrong procedure from the start, such as a failure to perform the required antibody investigations following a positive antibody screen
- **Procedure performed incorrectly** - where the correct steps have been taken, but incorrect decision-making has resulted in the error being made, such as misinterpreting manual testing results

In these cases laboratory staff have been trained and should know what to do and be able to perform these tasks correctly and competently, but for some reason a slip or lapse of concentration results in mistakes.

Although each member of staff has a responsibility to work safely and accurately, slips or lapses may occur. There are steps that can be taken by both laboratory management and individuals to reduce the chances of these:

- Review process design and use of equipment to ensure they are robust
- Review the SOP ensuring the process is described in logical order and staff can perform the steps as written, including what to do if the task goes wrong
- Ensure that critical points are covered during training and that competency-assessment challenges them

- Minimise all distractions and ensure the layout of the laboratory is logical
- Allow staff to work safely at their own pace without rushing
- Have contingency plans in place for when staffing levels are below minimum or there are spikes in workload and ensure these contingency plans are activated when required
- Follow the SOP. Staffing pressures should never be an excuse to cut corners or deviate from a SOP
- Never improvise. Consult the SOP for the correct procedure rather than asking colleagues or working contrary to the defined process

The NEQAS for blood transfusion laboratory practice (BTLP) paragraph below describes additional testing errors identified from their annual pre-transfusion testing questionnaire. Laboratory-related errors in children are described in Chapter 22, Paediatric Summary.

### **Case 7.3: Inappropriate use of EI excludes essential crossmatch**

*Two units of group A red cells were electronically issued for a group A solid organ transplant patient. Prior to transfusion a full blood count (FBC) sample showed evidence of haemolysis on a blood film and was direct antiglobulin test (DAT)-positive. A recall of blood components issued to the patient was initiated. One unit already being transfused was stopped. Further group A red cell units were crossmatched by indirect antiglobulin test (IAT) and were found to be predominantly incompatible. The Blood Centre reference laboratory testing found no alloantibodies but the patient's eluate demonstrated anti-A as a result of passenger lymphocytes from the group O lung transplant. The SOP was not compliant with the BSH guidelines on pre-transfusion compatibility procedures in blood transfusion laboratories (BSH Milkins et al. 2013). This patient should have been excluded from EI. A serological IAT crossmatch would have demonstrated the incompatibility and then group O red cells selected as the alternative.*



### **Learning point**

- BSH guidelines (BSH Milkins et al. 2013) state that patients who have received solid organ transplants should be excluded from electronic issue for 3 months to enable the detection of IgG isoagglutinins produced by passenger lymphocytes

### **Component selection n=32**

Component selection should ensure that the correct components (together with the correct specific requirements) are selected to comply with the patient's requirements and the clinical request. One serious selection error resulted in a 4-day-old baby with haemolytic disease of the fetus and newborn receiving incompatible red cells (group O D-positive cells to a baby with haemolysis due to anti-D). This is described in Chapter 10, Incorrect Blood Components Transfused (IBCT), Case 10.1.

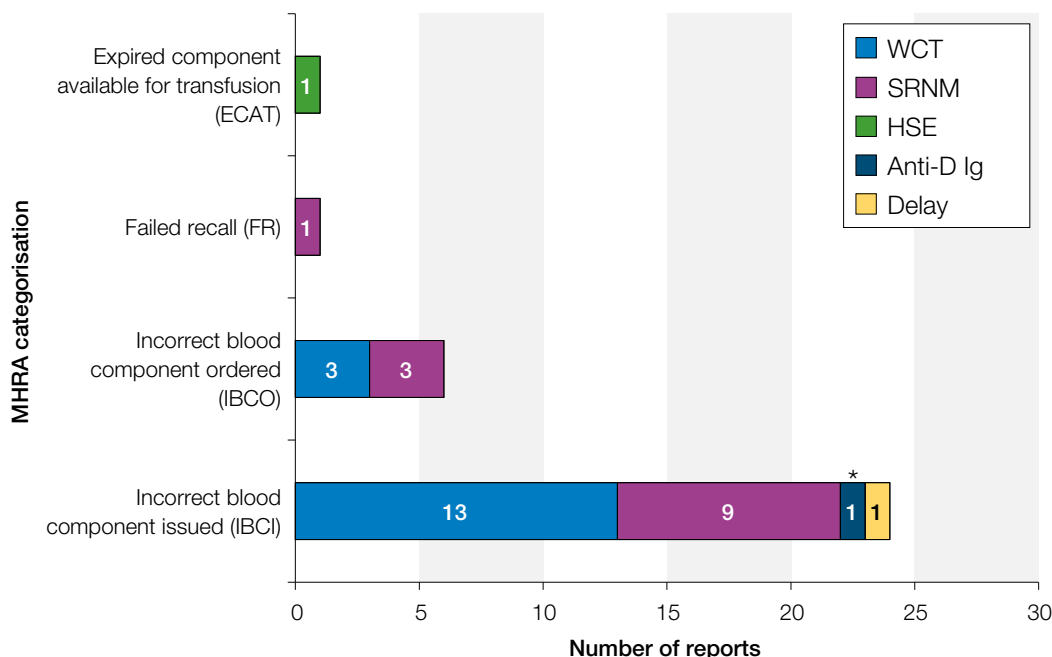


Figure 7.6: Selection errors by MHRA categories n=32

\* Anti-D Ig was not given following a selection error (D-positive platelets selected)

Incorrect selection of components can be assessed a number of different ways by the MHRA, and not just based on missing specific requirements on the request form (IBCI). Expired component available for transfusion (ECAT) refers to a case where an otherwise suitable unit was selected, but without reference to the planned transfusion date. The component was short-dated and issued before midnight when the planned transfusion was the next day. The incorrect component assessed by the MHRA as a failed recall (FR) refers to a case where the incorrect issue was identified in the laboratory, but was not recalled from the supply chain in a timely manner. Incorrect blood component ordered (IBCO) refers to those cases where the laboratory orders incorrect blood from the Blood Establishment and does not identify this prior to issuing the component to the patient.

Many of these reports relate to allogeneic haemopoetic stem cell transplant (HSCT) or solid organ transplant where the appropriate ABO and/or D group for transfusion has changed from the patient’s original group (n=18), see Chapter 23, Summary of Incidents Related to Transplant Cases. The introduction of new guidelines for the use of hepatitis E virus (HEV)-screened components (SaBTO 2016) has had some impact on the number of incidents reported, see Chapter 10, Incorrect Blood Components Transfused (IBCT) Figures 10.4 and 10.5. Reasons for failure to provide HEV-screened components include not having a robust process for flagging these requirements, or the new guidance was not communicated to laboratory staff by means of a robust SOP and training.

**Case 7.4: Inappropriate red cells issued by BMS unfamiliar with the LIMS**

*A 62-year-old female with newly diagnosed acute myeloid leukaemia (AML) required two units of red cells, the request noted these should be cytomegalovirus (CMV)-negative. This request was not urgent. The patient grouped as A D-negative. There was no historical record of the blood group on the LIMS. A group-check sample was not obtained. The BMS (working out-of-hours) selected and issued two units of group O D-positive red cells. The error was detected 6 days later when a mixed field blood group pattern was displayed. The BMS undertaking the selection had more than 15 years’ experience overseas and was undergoing competency-assessment and had not been signed off to work autonomously. The BMS stated that they must have ignored the warning message on the LIMS as they were used to coloured (red) warnings using their former LIMS. The BMS was being indirectly supervised during component issue, by a BMS2 who was supervising two trainees at the same time, but failed to spot the D-positive selection error.*

Irrespective of the error made in selection of D-positive red cells, there is no clear reason given why group O was selected and not group A (the patient's group). If this was because there was no group-check sample, the correct action would have been to request a second sample to confirm the patient's group, as this was not an urgent request. Group O may have been selected to meet the requirement for CMV-negative, but CMV-screened components are not required for this group of patients (SaBTO 2012).

LIMS technology can only support safe transfusion practice provided it is used according to a robust local SOP and by competent staff. BSH guidelines (BSH Milkins et al. 2013) state that in the absence of a robust electronic patient identification system a second sample is recommended to confirm the blood group. Laboratory staff did not consider the patient's historical information. This led to the issue of components to a patient who was known to have both antibodies and other specific requirements.



### Learning point

- Compatibility labels should display the patient's blood group. This will help to alert the biomedical scientist (BMS) when labelling, and nursing staff when performing the final bedside check. Any discrepancies should be discussed with the laboratory immediately

**MHRA regulatory view:** New members of staff, even if they are experienced having worked elsewhere, must be trained and competency-assessed as they may be used to different procedures and equipment. They must be actively supervised prior to being signed off as competent and not expected to work unsupervised.

#### Case 7.5: Red cells reserved for multiple patients stored together leads to labelling error

*A BMS selected two units of red cells for serological crossmatching and returned them to the refrigerator. When testing was complete, the two units were removed from the refrigerator and the printed compatibility labels attached. One of these units was not one of the crossmatched units, but fortuitously of the correct blood group. The label check was not completed correctly as the BMS was rushing to go home. While putting these units into the electronic blood tracking system, the second unit gave an error message that highlighted that this was an unknown unit for the patient. The BMS did not read the error message and thought the system had a fault. The BMS decided to release them manually. A porter collected one unit from the laboratory at 23:48 but did not perform the visual check properly or notice the label and the unit had different unit numbers. This may have been because the unit was collected face to face with a BMS. Nurse 1 receipting the blood did not notice the discrepancy and had not completed a competency-assessment for receipting blood components. Nurse 2 who ordered the red cells accompanied Nurse 1 to complete the bedside check. Neither of the nurses recollects any problems with numbers not matching nor were they competency-assessed for the bedside check. The red cell unit was administered to the patient without any adverse consequences.*

Red cells allocated to a patient for crossmatching should be quarantined from stock units. If red cell units for more than one patient are being stored in the same location then they must be kept in a discrete area of the refrigerator and not together. Information technology (IT) systems are designed to support processes and any warning/error notification should be carefully noted and acted on appropriately. When two people are completing checks together, care must be taken as there can be complacency with neither person taking responsibility to complete the check properly. A better check may be to use a challenge and response method with two people as described in Chapter 10, Incorrect Blood Components Transfused (IBCT).

**MHRA regulatory view:** This report highlights the need for having a robust process in place when storing components during a serological crossmatch. No part of the quality check should be abbreviated due to time constraints. If staff do not have time to perform a task, they should leave it for another member of staff or take the extra time to complete it adequately rather than rushing through the process.

### Component labelling, availability and HSE n=86

The correct component needs to be labelled with the correct four (or five) key patient identifiers; these are the first name, surname, DOB, unique patient ID identifier and first line of address if in Wales (Milkins et al. 2013). Components need to be accessible and available for the time required, if this is not attainable then the clinical area need to be informed. The components need to be handled and stored in the correct method as defined in the guidelines (JPAC 2013).

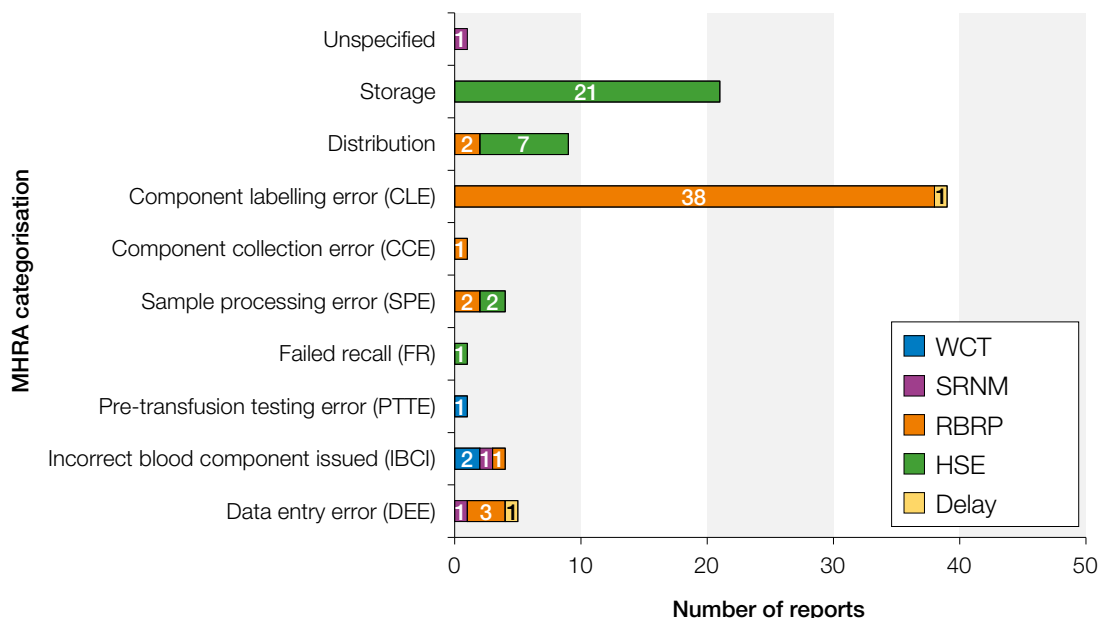


Figure 7.7: Component labelling, availability and HSE by MHRa categories n=86

There were 31 HSE laboratory cases reported to both SHOT and the MHRa (Table 7.3).

HSE subcategory	Number of incidents reported to both haemovigilance organisations
Failure to clear refrigerator/sample expiry	10
Stored inappropriately in laboratory area including cases where the transport and delivery was not adequate	8
Return to stock error/30 minute rule	7
Expired unit issued and transfused due to laboratory error	2
Equipment failure (alarm-related/not alarm-related)	2
Incomplete cold chain documentation	2
<b>Total</b>	<b>31</b>

Table 7.3: Handling and storage errors reported to both haemovigilance organisations

Last year the MHRa highlighted the need for improved processes regarding storage in general (The 2015 Annual SHOT Report - Web Edition, Chapter 18, 2016). While the total number of SAE reports has increased, the number of reports related to failure to respond to the alarm has decreased. This may suggest that laboratories have heeded this advice and as a result of improved process design, improved SOP, training and understanding, laboratory staff are acting on alarms from storage locations. As a result blood components are less likely to be wasted, or removed from the supply chain.

Incorrect storage of components is one of the most common errors. Typically storage of a component is at the wrong temperature or in an unmonitored storage device. Eighty five SAE were reported to the MHRa involving the incorrect storage of components. Only eight of these errors occurred in laboratories, which suggests that the remaining 77 occurred in the clinical area. Platelets are often reported to have been placed in refrigerators, and granulocytes have been reported to have been placed in agitators. Components have not been removed from transport containers and stored correctly, or have been left out by the bedside or elsewhere. The most common cause of components being stored incorrectly were:

- **Ineffective training** - of staff who had either not understood the process or had forgotten it due to infrequent update training for a rarely performed task
- **Inadequate processes** - where there was no defined process for what to do if blood was not administered immediately or where out-of-service storage equipment was not adequately prevented from being used

Staff in clinical and laboratory areas should be encouraged to ensure that procedures related to storage of components, temperature monitoring and removing unsuitable units from storage locations are robust and clear and that staff are trained in them and able to activate those procedures effectively, even when lone-working or during emergency situations.

#### **Case 7.6: Labelling of red cells for two different patients simultaneously leads to error**

*Two units of red cells for Patient 1 and one unit for Patient 2 were manually crossmatched at the same time. Upon completion all three compatibility labels were printed together. The numbers on two of the donor units were similar. The label check was not completed correctly and one unit for Patient 1 was labelled for Patient 2 and one unit for Patient 2 labelled for Patient 1. All three units were placed into the electronic blood-tracking system but at this stage the system only identifies the unit number and not the patient as well (this part of the system was not purchased due to the additional cost as it was deemed unnecessary at the time). The first unit was transfused to Patient 1 without incident (correct label). A healthcare assistant (HCA) collected the second unit for Patient 1 and the tracking system showed the identity of Patient 2 on the screen and asked for confirmation that this was the correct patient. This was confirmed as being correct by the HCA by pressing the green confirmation button, even though it was not. The error came to light when the clinical area found the second unit but the tracking system thought the unit was in the refrigerator.*

**Outcome:** Verbal instruction was given to a locum BMS following the incident that only one patient should be crossmatched at a time in line with the SOP. The investigation also indicated that the lack of an additional centrifuge to process the serological crossmatches, in addition to a time-pressured environment, makes it much less efficient and practical to process one serological crossmatch at a time. The hospital's policy required two people to do the pre-transfusion checks but in this incident the component was checked by only one nurse.

Component selection, crossmatching and labelling should only be undertaken for one patient at a time and should be stated in the SOP. All staff, including locum staff, must undertake full training and competency-assessment although there is no evidence to suggest this locum BMS was not sufficiently trained. No short cuts should be taken and regular staffing reviews should be performed to ensure there are sufficient staff in both laboratory and clinical areas.

**MHRA regulatory view:** The report highlights the necessity to perform all checks thoroughly and to act on any discrepant information and system warnings without making assumptions.

#### **Miscellaneous n=8**

The 8 miscellaneous cases were reported as IBCT-WCT (4) and SRNM (4), and all of these occurred as a result of inadequate processes. In 3 cases the error originated at the Blood Service, where the wrong component was sent and it was not detected or communicated to the laboratory staff. One of these caused serious harm (development of anti-D in a D-negative woman following transfusion of D-positive platelets), see Chapter 10, Incorrect Blood Components Transfused (IBCT).

### **Human factors**

**Inadequate quality management systems (QMS) – staffing and workload.** This category was introduced to gain insight in the extent of staffing and workload problems contributing to SAE. Evidence collected in previous years' serious adverse blood reactions and events (SABRE) reports, MHRA inspection reports, SHOT, UKTLC surveys and other sources suggest that resource issues are having a serious and detrimental effect on a laboratory's ability to function safely.



To qualify for this category, the SABRE team aimed to include SAE where staffing levels were below minimum levels as defined by the capacity plan or workload was high, either in the long term or short term. It is also important to consider the appropriate level of 'skill-mix' to ensure that the right level of suitably qualified and experienced members of staff are available. We have tried not to simply record every SAE where the report stated staff were busy. We assigned different subcategories where other human factors were more likely to have an impact, e.g. if a BMS has made errors by trying to perform more than one task at a time, this may be a result of poor work prioritisation as opposed to an unacceptably high workload. This first assessment of these types of error has demonstrated that several, (103/1027) 10.0%, of all SAE fall into this subcategory. Continued collection of these data with time will be informative. It is evident that these pressures are real and can affect the quality and safety of blood and the quality of service provided.

When resolving issues related to staffing and workload, laboratories have been successful in using QMS data as evidence to increase resource. However, not every laboratory will be successful. It may be the responsibility of laboratory managers and their staff to suggest novel and innovative solutions. Some solutions evident in SABRE reports include:

- Training laboratory support staff to perform some additional tasks to provide relief for BMS
- Changing shift patterns and reviewing break times to ensure greater numbers of staff are available at busier times
- Reviewing rules related to numbers of staff on leave at the same time
- Reviewing processes to ensure they are streamlined
- Reviewing workloads to spread the work out more effectively when staff are available

### Laboratory incidents included as SHOT-only n=126

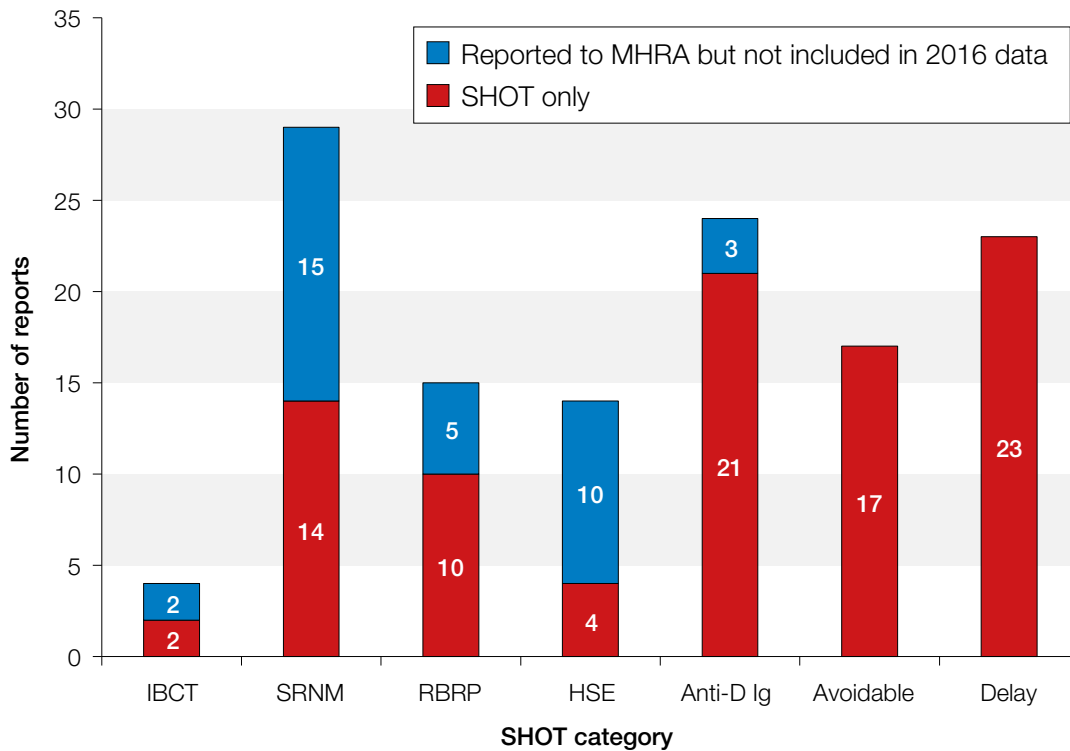


Figure 7.8: SHOT-only laboratory incidents n=126

A total of 91/126 cases were SHOT-only reportable excluding cases identified below because:

- 16/126 cases are at notification stage with the MHRA and will be included in the 2017 MHRA dataset
- 17/126 cases were duplicated by SHOT where the initial reports were submitted to both SHOT/ MHRA but do not need to be duplicated for each patient for the MHRA whereas SHOT requires each incident to relate to one patient
- 2/126 were reported as serious adverse reactions (SAR) to the MHRA, both cases involved patients that had a reaction due to the transfusion of an incorrect blood component. SHOT categorises these cases as IBCT, but they are reportable to the MHRA as SAR, not SAE

There were 28 anti-D Ig errors that originated in the laboratory where laboratory staff had an opportunity to prevent the issue of anti-D Ig requested inappropriately from the clinical areas. Fundamental errors in knowledge resulted in issue of anti-D Ig to women with allo-anti-D, women with D-negative infants and to D-positive women. Laboratory staff should have this basic knowledge and the LIMS should support this with appropriate warning alerts. Staff should also be aware of the requirement for administration of prophylactic anti-D Ig within a 72-hour window following a potentially sensitising event or delivery. The request from the clinical area should allow sufficient time for the issue and administration of this product. These errors are discussed in greater detail in Chapter 14, Adverse Events Related to Anti-D Immunoglobulin (Ig).

In 6 cases laboratory staff failed to follow major haemorrhage protocols (MHP) correctly, Case 7.7.

#### **Case 7.7: Contingency measures lead to delay and failure to follow MHP activation correctly**

*The ED activated the MHP at 03:00 for a gastrointestinal bleed in a 38-year-old patient. The refrigerator in the ED was not working and there was no emergency uncrossmatched red cell stock available. Despite the protocol being activated 15 minutes prior to the patient arriving no blood was available in the ED for 30 minutes or more after the patient arrived. Initially the transfusion laboratory staff refused to issue more than two uncrossmatched red cell units at a time for the first two occasions. The patient subsequently died in the intensive therapy unit (ITU), death unrelated to the delay.*

The local investigation identified:

- Concerns that there was a deviation from the MHP as four units of red cells should have been issued
- Concerns surrounding the laboratory escalation, resilience and contingency when the refrigerator broke down
- Although there was a delay they did not believe it had an impact on the final outcome

Laboratory staff should undertake regular competency-assessment in critical procedures, i.e. emergency drills should be practiced to ensure there are no delays due to a gap in knowledge. If emergency uncrossmatched red cells are part of the protocol, any inability to meet this provision, such as refrigerator failure, must have a backup plan clearly communicated to clinical areas to inform them to the change, however temporary, in procedure.



#### **Learning point**

- The major haemorrhage protocol (MHP) must be agreed by the hospital transfusion committee and all staff trained to deliver components in line with the protocol. Any deviation should only be authorised by a senior clinician

### **Incidents reportable only to the MHRA n=233**

There were 1027 MHRA SAE reports in 2016. However 233 were not reportable to SHOT. This section provides more detail to show why that is, and provides further analysis of those reports.

- 688/1027 reports were reported to SHOT but under various categories, i.e. a mixture of laboratory and clinical cases

- 47/1027 SAE were included in the 2015 Annual SHOT Report analysis but not the MHRA for that year because the confirmation report was not received by the MHRA until 2016
- 12/1027 SAE were submitted to SHOT but not completed by the SHOT deadline (31 December 2016), but received by the MHRA before 31 December 2016
- 47/1027 SAE were received by the MHRA but are still incomplete on the SHOT database (Dendrite)

Of the 233 reported to MHRA-only, 68 were from Blood Establishments and the remaining 165 were not SHOT-reportable.

The 233 MHRA-only SAE are displayed in Figure 7.9.

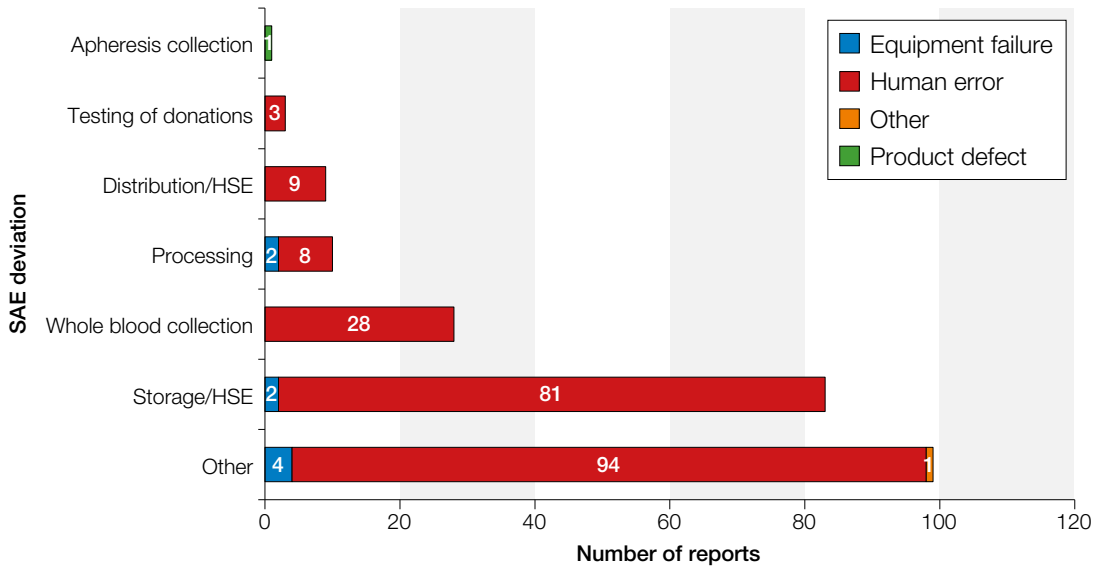


Figure 7.9: MHRA-only SAE by specification

The category **whole blood collection** refers only to the collection of donor blood by Blood Establishments and the majority of these refer to donors being accepted for donation who should have been deferred due to travel or lifestyle reasons. The largest category is 'other' and this is broken down by the MHRA 'other' subcategory in Figure 7.10.

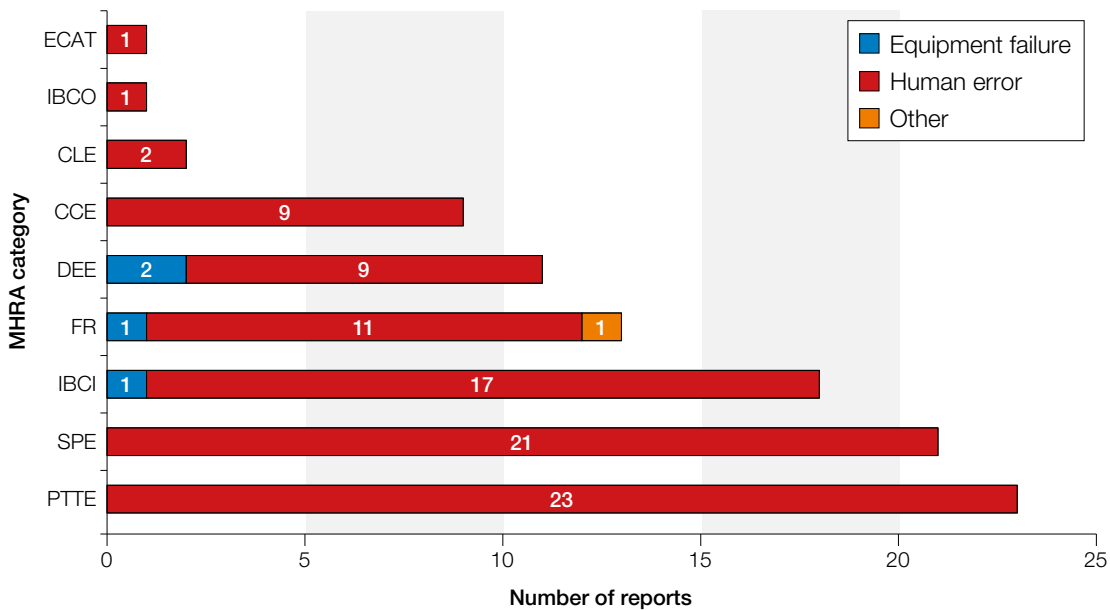
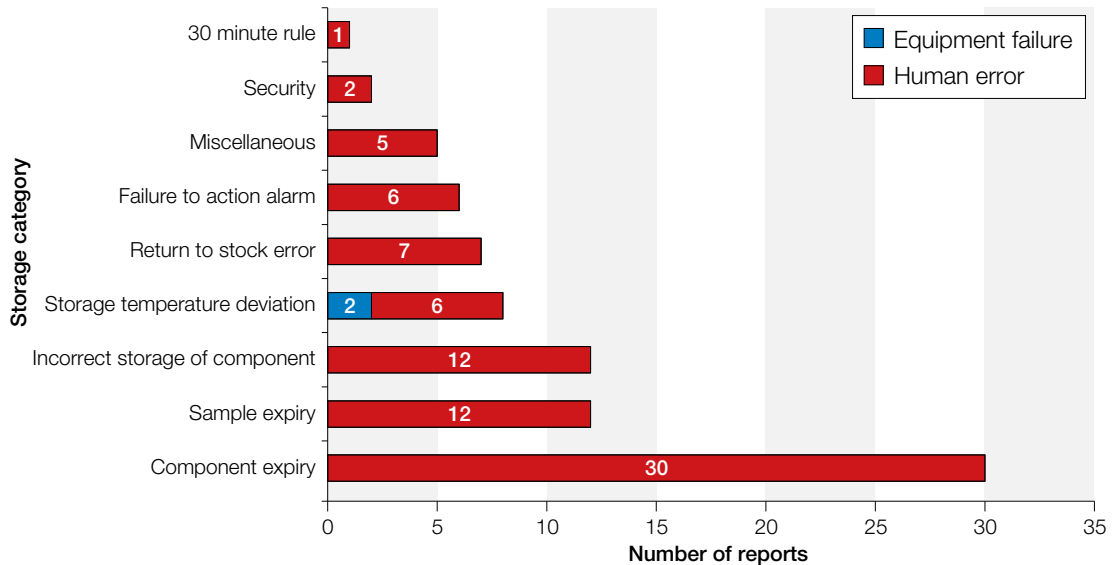


Figure 7.10. Subcategory 'other' by specification

The proportion of reports in each category is broadly similar to those where all MHRA SAE are analysed together. The only real difference is that these errors were detected prior to transfusion, often at the bedside, but demonstrate that the QMS did not detect the error at the point the error was made.

Figure 7.11 demonstrates further analysis of the storage SAE. These are a mixture of laboratory errors where components were not transfused, and errors by staff outside the laboratory which has affected the quality and safety of the component, such as incorrect storage of component where clinical staff have stored blood in unmonitored storage equipment, and security where access to storage equipment by untrained staff has occurred.

**Figure 7.11:**  
Storage error by  
specification



## MHRA inspection activity on hospital blood banks 2015–2016

This is a summary of the full report which is included in Chapter 25, MHRA (available on the SHOT website [www.shotuk.org](http://www.shotuk.org)).

A total of 303 blood compliance reports (BCR) were submitted for review for the reporting period 01 April 2015 to 31 March 2016. Following assessment, 17 hospital blood banks (HBB) including 1 control site were selected for inspection. One additional HBB was inspected following notification from the site that inaccurate information had been provided in the BCR.

### Inspection outcomes

A total of 19 inspections were performed and the numbers of deficiencies are as follows:

Critical	Major	Other
1	43	67

One HBB resulted in a critical deficiency finding and was referred to the Inspection Action Group (IAG).

The critical deficiency was as a result of the following:

- Senior management had not ensured that there were sufficient resources to support the quality system
- Management of deviations (incidents) was inadequate in several respects (detailed in the full report)

Three HBBs had serious deficiency findings related to their operations and were escalated to the Compliance Management Team (CMT).

An overview of the compliance management escalation processes used by the GMP Inspectorate, including information on the CMT referral process is available from the MHRA Inspectorate Blog <https://mhrainspectorate.blog.gov.uk/2017/02/06/overview-of-compliance-management-escalation-processes-used-by-the-gmp-inspectorate/>

Deficiencies classified as 'major' and 'other' were identified in the deficiency group and are shown in Figures 25.7 and 25.8 in Chapter 25, MHRA (available on the SHOT website [www.shotuk.org](http://www.shotuk.org)):

## Summary of significant issues identified at inspected sites

These can be found in more detail in the full report in Chapter 25 (available on the SHOT website [www.shotuk.org](http://www.shotuk.org)).

### CAPA implementation

The implementation of CAPA was generally found to be deficient with no system in place to track and monitor the progress of CAPA closure and no requirement to monitor and assess the effectiveness of implemented CAPA.

### Laboratory operations

Issues were identified from the sample receipt and acceptance process to suggest that the 'zero tolerance' approach could be bypassed.

Investigation of analyser quality control (QC) failure was in some cases inadequate. Little attention was given to establishing why the QC had failed before process re-runs were initiated. A single passing repeat could be used to invalidate a failed test. Investigation to identify potential causes of failure was not always evidenced.

### Document control and data integrity

Poor documentation practices were the most cited deficiency.

Records that had not been completed contemporaneously or staff signed for incorrect results, e.g. out of temperature limits for the temperature-controlled storage facilities or signed for other staff without explanation, had the potential to result in serious data integrity issues. It is important to apply the basic ALCOA principle to all data: Attribute, Legible, Contemporaneous, Original, Accurate.

### Personnel and training

A capacity plan should be put in place to demonstrate that the staffing level is sufficient to cover the workload including out-of-hours working and effective implementation of QMS. Where a shortfall is identified, senior management should ensure sufficient resource will be made available. Job descriptions and organisation diagrams should be consistent with respect to reporting lines and made available to all staff.

Evidence from inspection showed that staff were not being trained/updated following significant changes due to the lack of training policy and training matrix. Staff were not aware of, trained, and competent in the use of key quality system procedures, and this was especially an issue for staff working out-of-hours. Some training records did not reflect the correct competency assessment or the re-training was overdue. Training records were not always available for review including those for senior management.

Another area of concern related to nurses and porters who collect issued blood units from the issue refrigerator, as the re-training has not been performed in accordance with the training schedule. It was stated that the staff could not be released to complete the necessary training due to the demand on the wards. This is not acceptable practice and the senior management in the clinical area should also be made aware of the regulatory requirements.

### Computerised systems

With the innovation and development of computerised systems and software, it is more common to see the use of electronic quality and documentation management systems, automatic analysers, patient databases, automatic issuing system, blood tracking systems and temperature monitoring systems. Special attention should be given to the control of such computerised systems and the integrity of QC data.

Some common IT errors included:

- Data quality issues – merging errors and quality control of data entry and transfer between systems
- Level of availability of technical support/knowledge – amongst laboratory users and the organisations IT
- User requirements – not always met
- System security – appropriate access level, individual login and password
- Storage – backup
- Alternation of data – audit trail
- Contingency and failure – business continuity planning

### Summary of learning points from inspections

1. Define and review all system processes regularly to ensure that they are fit for purpose.
2. Improve root cause analysis procedures and applications ensuring that the whole process is looked at and areas of weakness identified (including internal and external QC) so that appropriate safeguards and corrective measures can be introduced.
3. Critically review all incidents so the severity of risk can be appropriately categorised and assessed and so that corrective and preventive actions can be introduced in an appropriate timeframe.
4. Senior management should ensure an effective quality system is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation.
5. Monitor system performance so that failures due to resource issues can be raised to the appropriate level.
6. Raise change controls in an effective and timely manner to ensure that process changes have an appropriate level of validation data.
7. Introduce measures that ensure effective laboratory housekeeping is undertaken and maintained. This applies particularly to the care and maintenance of storage facilities.
8. Design and implement an achievable and effective training plan for all routine and out-of-hours staff, and ensure that this includes the QMS procedures.
9. Attention and special care is required for the control of data in hard copy or in electronic format.
10. Good documentation practices must be followed.
11. Post-inspection actions must be completed as agreed or notify the inspector of slippage.

### Information and guidance

For further information on **MHRA and the Regulation of Blood** please refer to the MHRA website: <https://www.gov.uk/topic/medicines-medical-devices-blood/blood-regulation-safety>

The MHRA Blood forum was launched in June 2016 as a tool to help those involved in blood component collection, processing, testing and distribution to comply with the EU Blood Directives, UK Statutory Instruments and good practice requirements. It provides the ideal opportunity for extended communication between peers and allows users to put forward their comments and get 'real-life' examples of ways in which they can manage robust quality procedures that ensure compliance and which dovetail with their own business needs and resources.

<http://forums.mhra.gov.uk/forumdisplay.php?60-Blood-Forum>

## United Kingdom Transfusion Laboratory Collaborative (UKTLC)

Author: Rashmi Rook

The published UKTLC Standards (Chaffe et al. 2014), can be mapped across to the BSQR 2005 and European good manufacturing practice (EU GMP) and lay out in more detail the actual qualifications, training and knowledge that staff working in transfusion laboratories are required to have. It is essential that senior pathology managers support the standards with the aim to fully implement these as soon as possible. Where there is restructuring of teams and changes to working practices, this is especially pivotal in providing and maintaining a safe service. As the hospital chief executive officer (CEO) is deemed the 'responsible person' to ensure compliance with the regulations then senior pathology managers have the responsibility to inform them where there is a gap between the standards and actual working practices. The need to meet the requirements of the UKTLC standards (Chaffe et al. 2014) is due to the uniqueness of this pathology discipline in providing both a diagnostic and therapeutic service that works closely with clinical staff, and helps provide better patient care. BMS have to make real time decisions that may directly affect patient safety in a stressful and time-pressured environment, and they must be allowed to work safely and confidently. This department is additionally challenged by the necessity to comply with good practice guidelines for blood components, products and testing as defined within the industry. Increasing the knowledge of our staff is the key to future-proofing the service and maintaining patient and transfusion safety.

### Regulations:

*BSQR Regulation Section 9. (1) (a): The person responsible for the management of a hospital blood bank shall... ensure that personnel directly involved in the testing, storage and distribution of human blood and blood components for the hospital blood bank are qualified to perform those and are provided with timely, relevant and regularly updated training.*

*EU GMP 2.1: The manufacturer should have an adequate number of personnel with the necessary qualifications and practical experience. Senior management should determine and provide adequate and appropriate resources (human, financial, materials, facilities and equipment) to implement and maintain the quality management system and continually improve its effectiveness (EU regulations, see reference list)*

There are concerns that local transfusion meetings are not well attended by laboratory managers or their deputies, and reasons given are increasingly being cited as staffing difficulties. It is expected that this group plan educational leave well in advance to increase participation. The benefits of having a supportive professional network of colleagues and the sharing of ideas, and best practices can be of immense gain to the department, and can help to manage pressures that we all face from 'doing the job'. This should be reflected in adequate funding to attend meetings and courses.

- 'Drive out fear so that everyone may work effectively' (Deming 1982)
- 'Fear is toxic to safety and improvement' (Berwick 2013)

Despite the evidence from (Deming 1982) and (Berwick 2013) transfusion staff are nevertheless being penalised or censored for raising concerns within their hospitals. UKTLC stakeholders will be looking into this as it goes against the culture of encouraging candour, openness and honesty at all levels within an organisation. The culture of safety must become the overriding core principle within the department and throughout pathology. The impact of errors and mistakes not only affects the patient but also the staff (second victims). Regardless of the severity of an incident or error this may adversely affect performance of the team and overall department morale. Staff come to work wanting to do a good job, and it is faulty systems and processes that may let them down (see Chapter 6, Human Factors). In an open reporting and transparent culture, staff should be encouraged to easily record concerns, incidents, errors and mistakes to use as evidence to support resourcing without censor.

During 2017 the UKTLC is working on the following projects to support BMS to achieve delivery of the standards:

- Producing formal guidance on staff capacity planning
- Promote better communication, conversations and sharing of ideas and documents between laboratory staff, via the MHRA blood forum
- Continue monitoring changes through the 2017 UKTLC survey

The survey was distributed from NEQAS-BTLP on 15 March 2017 to 302 UK transfusion laboratories in order to give a snapshot of one day in line with previous UKTLC surveys.

**The 2017 UKTLC survey showed the following results:**

Response rate: 245/302 (81.1%). In 50.6% (124/245) the laboratories stated staffing levels have remained the same or decreased since the previous survey in March 2015, with many leaving the NHS for posts in other organisations at the same grade or taking early retirement. Vacancies have been present in some laboratories (particularly at Band 6 BMS) for 2 or more years.

The calibre and suitability of applicants to laboratory posts are unsatisfactory; 60.8% (149/245) of laboratories recorded that newly registered Health and Care Professions Council (HCPC) BMS do not have appropriate knowledge/skills to work in blood transfusion. There is increased dependence on locum and agency staff. There is an increase in multidisciplinary staff, and in those who do not work >75% in blood transfusion. Some laboratories 85/245 (34.7%) reported an increase in workload of >50%. Also, 62% (152/245) reported more difficulty in training/mentoring inexperienced staff with 42.0% (103/245) reporting no identified training and development budget.

UKTLC standards have been considered by many laboratories during ongoing changes especially in relation to staffing levels. However staffing shortages have still not been addressed. This together with increased workload contributes to lower morale and reduced job satisfaction, with many leaving for posts in other organisations or taking early retirement. This is resulting in a great deal of experience and a wealth of knowledge being lost from the organisations.



**Learning point**

- A gap analysis can be performed against the UKTLC standards and this can be used to demonstrate to senior management/executive teams where the laboratory is falling short of any standards that require resolution from senior levels

**UK NEQAS**

*Author: Claire Whitham*

In May 2016, UK NEQAS Blood Transfusion Laboratory Practice (BTLP) sent out the annual questionnaire about pre-transfusion testing to laboratories in the UK and overseas. Most of the data reported had not changed significantly from that collected in 2015. However, it is noted that:

- 65.7% (167/254) of laboratories (compared to 54.1% (151/279) in 2015) request two samples taken at separate times for a group check (one group could be historical), before group-specific blood is issued in a routine situation, and a further 23.2% (59/254) are in the process of implementing this policy (compared with 20.1% (56/279) in 2015)
- The numbers using automation and EI, and requiring a second sample, varies significantly by country

Results reported for BTLP external quality assessment (EQA) exercises have shown some issues with laboratories failing to either adhere to or understand recommendations made by the manufacturers of their chosen technology, e.g. during exercise 16R9, where Patient 2 red cells (AB D-positive) were coated with anti-D to give a 2-3+ positive DAT. This caused a positive reaction in the control well of BioVue grouping cassettes due to the presence of potentiators (polyethylene glycol) in the reagent and control columns, invalidating the ABO and D-typing results. The majority of laboratories using BioVue either reported that they were unable to interpret the blood group or undertook repeat testing with a



second technique enabling them to make an interpretation of AB D-positive. However, four laboratories made an interpretation of AB D-positive, a fifth reported group AB unable to interpret D and a sixth reported it as uninterpretable for ABO but D-positive, all using BioVue only. It is of course possible that these six laboratories undertook additional testing without recording it at data entry.

Data analysis of EQA exercises repeatedly shows transcription and transposition errors made either during testing or reporting of results (which is also evident in the SHOT testing errors reported in 2016). Some of these are caused or exacerbated by the fact that processing and reporting of EQA samples is not identical to that for clinical samples. Manual testing is vulnerable to transcription and interpretation errors and must include checks at critical points. Even laboratories with full automation will on occasion be required to undertake manual grouping and should have a back-up process in place that is useable 24/7.

EQA 'requests' are booked into the LIMS in 72.8% (185/254) laboratories (73.5% (205/279) in 2015), allowing the EQA samples to follow the same process as clinical samples, thus making the EQA results more relevant to clinical practice. Some laboratories cited sample format (i.e. not whole blood) as a reason for not booking EQA samples into the LIMS, and whilst it is appreciated that the sample format is not ideal, this does not seem to be a barrier to LIMS entry in the majority of laboratories. In some cases there are additional obstacles to overcome, e.g. where there is a shared database and/or problems with building up historical records for EQA 'patients'. It might be possible to overcome these issues with additional planning in allocating names and numbers to the EQA samples for entry to the LIMS. In 28 laboratories 'custom and practice' was cited as a reason not to book in EQA samples, with this being the only reason for 11 (4.3% (11/254)) of all respondents (compared with 6.5% (18/279) in 2015).

## Commentary for errors that originated in the laboratory

Many errors originating within the laboratory are reportable to both haemovigilance organisations and reporting is a key requirement of any QMS. Thorough investigation and identification of the root causes are vital to implementing good quality corrective and preventive action (CAPA). Addressing errors and understanding the human factors involved will provide benefits in the long term by preventing errors from occurring and ensuring safe laboratory practices and the provision of components of the correct quality and safety. Evidence from the reporting of errors can be used to ensure laboratories are provided with the correct resources, but laboratory managers and staff may need to identify innovative and novel ways of utilising their existing resources effectively.

The standard of transfusion knowledge and education within laboratories is becoming a prevalent source of error. There is anecdotal evidence that there is a national shortage of qualified BMS staff applying for vacant positions and vacancies are being filled with trainee staff that require Institute of Biomedical Science (IBMS) portfolio, HCPC registration and the IBMS specialist portfolio. This is compounded by a lack of suitably skilled BMS staff able to train these new staff due to the workloads within their laboratories. This issue of concern is, at the time of publication of this report, being discussed nationally at the National Blood Transfusion Committee.

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# Right Blood Right Patient (RBRP) n=227

# 8

Authors: Diane Sydney and Hema Mistry

## Definition:

Incidents where a patient was transfused correctly despite one or more serious errors that in other circumstances might have led to an incorrect blood component transfused (IBCT).

## Key SHOT message

- It is a professional responsibility for all laboratory and clinical staff to adhere to the correct identification practice in every part of the transfusion process (Bolton-Maggs et al. 2016)



In 2016 227 cases were reported compared to 187 in 2015 (Bolton-Maggs et al. 2016). Laboratory errors accounted for 90/227 (39.6%) and clinical errors for 137/227 (60.4%), Figure 8.1. It is interesting that last year's percentages for clinical and laboratory errors have reversed.

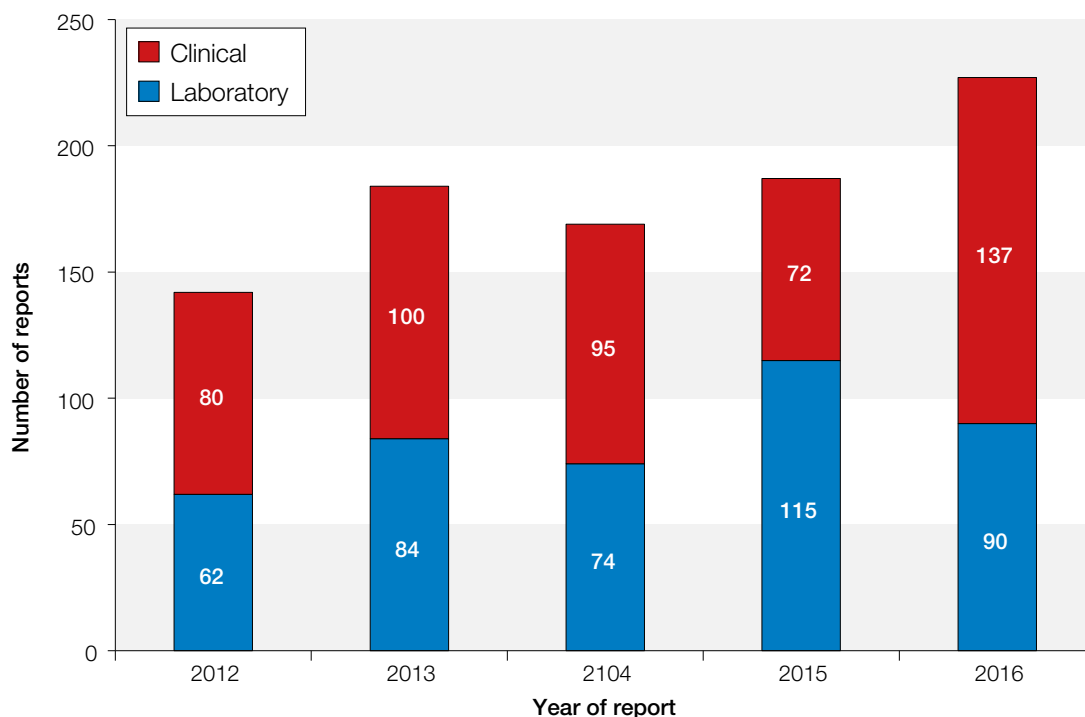


Figure 8.1:  
Breakdown  
of clinical and  
laboratory RBRP  
data 5-year trend

Figure 8.2:  
Overview of RBRP  
data n=227

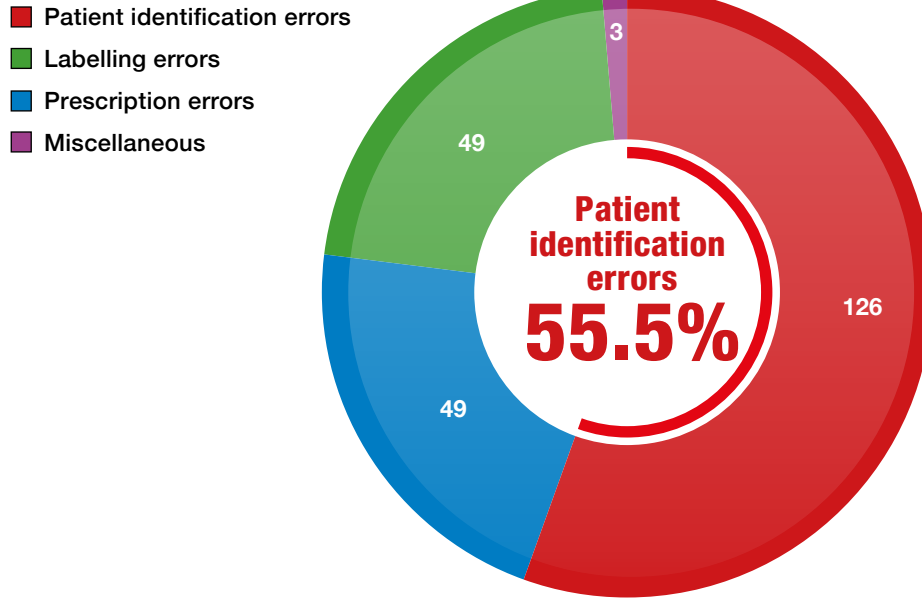
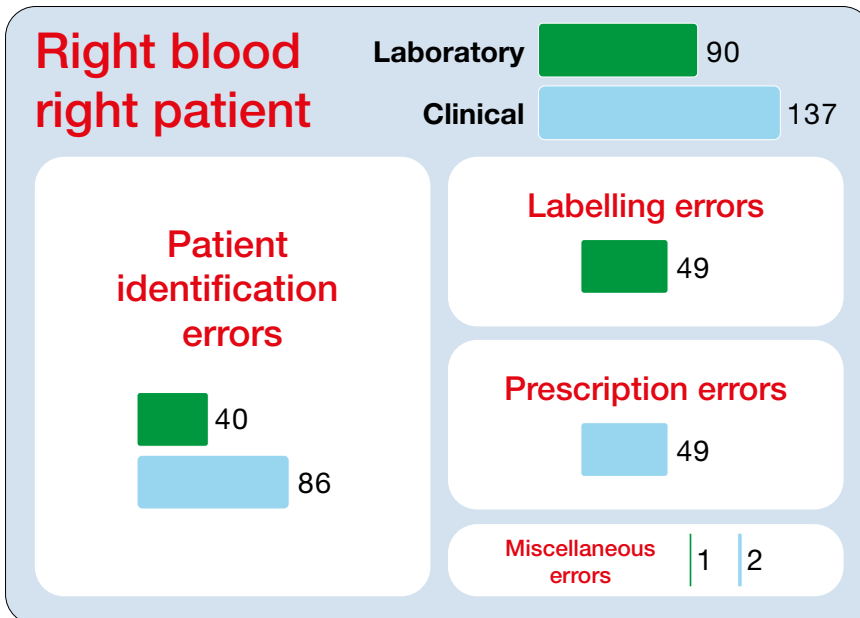


Figure 8.3:  
Breakdown  
of clinical and  
laboratory RBRP  
data n=227



### Patient identification (ID)

Failures in patient identification occurred in both laboratory and clinical settings:

- Laboratory
  - Demographic data entry errors during the booking-in of samples
  - Transpositions of labels
- Clinical
  - Incorrect patient ID on the request form/sample associated with the 4 key identification dataset (BSH Harris et al. 2017)
  - Absence of an ID band
  - Prescriptions were either completed incorrectly or had missing data

All staff supporting the transfusion process are reminded of the four key patient identification criteria; these consist of **first name, surname, date of birth** and a **unique patient ID number** (and **first line of the address** if in Wales) (BSH Milkins et al. 2013).

These patient ID errors occur at all stages of the transfusion process. Examples include clinical staff incorrectly transcribing or missing vital patient demographics during the completion of the request form and sample labelling, laboratory staff not transcribing and inputting data accurately into the laboratory information management system (LIMS) during booking-in of a sample.

There were 49 prescription errors; this is more errors than the total in the preceding four years (n=42). Analysis of these 49 errors highlights several areas of failure; clinical staff not completing the prescription correctly, for example providing inaccurate or incomplete identification criteria; the prescription not being signed, or no prescription being available.

**Case 8.1: Administration error**

*A unit of red cells was wrongly recorded in the electronic blood management system (BloodTrack) as transfused before the unit was connected to the patient. As a result of this, the secure electronic checking process was bypassed (no final bedside check was performed) by the clinical staff. Furthermore although two nurses checked the unit manually there was no documented evidence of this in the patient’s case records.*

**Case 8.2: Sample error**

*The laboratory received a request for crossmatch of four units of red cells. The crossmatched blood was made available. The following day a biomedical scientist (BMS) noticed that the sample tube appeared to have been pre-labelled as the staff signature had been crossed out and another signature added. The clinical area confirmed that the patient had been transfused two units, and the other two units were recalled by the laboratory. Investigation confirmed that one staff member had pre-labelled the sample tube and another member of staff took the sample then crossed this out and added their signature.*

Cases 8.1 and 8.2 demonstrate that even when there is a robust information technology (IT) vein-to-vein checking system and appropriate policies are in place, staff may not use these effectively or appropriately.

**Learning points**

All staff have a professional and personal responsibility to:

- Use information technology (IT) solutions which are available to enhance patient safety. In the absence of this a manual check is appropriate
- Ensure that they follow policy and procedures to ensure patient safety



Staff are accountable for ensuring that the relevant documentation is completed and the correct hospital policy is followed every time. **The administration identification check at the patient’s bedside is the final opportunity to ensure that the right blood is being given to the correct patient** (see main recommendation for a checklist in Chapter 4).

**Near miss RBRP cases n=121**

Point in the process	Type of error made	Number of cases	%
Sample labelling	Sample labelling error	29	24.0
Sample receipt	Wrong identifiers entered in LIMS	18	14.9
Component labelling	Transposition of labels for same patient	47	60.3
	Incorrect patient information on label	26	
Administration	Patient had wrong wristband	1	0.8
<b>Total</b>		<b>121</b>	<b>100</b>

**Table 8.1:**  
Near misses that could have led to RBRP n=121

## IT-related RBRP cases n=57

### Failure to consult historical record or link two records n=6

If there are incorrect details on the request form or sample, the historical computer record on the LIMS may not be accessible and this led to a situation where blood was transfused with incorrect demographic details in six cases.

### Discrepancy between LIMS and the patient administration system (PAS) n=28

In 12 cases blood should not have been given because there was a discrepancy in the demographic details between the LIMS and PAS and in a further 6 cases, the wrong record was selected on the LIMS or PAS. In 10 cases blood was issued against the wrong patient ID (sample or request form). These errors resulted in one or more core identifiers being different between the compatibility tag (printed from the LIMS) and the sample, request form or wristband (printed or hand-written from the PAS information).

### Incorrect result or data entered or accessed manually n=19

In these cases, at some stage an incorrect name or date of birth or address has been entered either onto the PAS or LIMS. On one occasion the wrong information from a reference laboratory was entered into the LIMS.

#### Case 8.3: Vigilant clinical staff query a laboratory error

*Blood was crossmatched for a patient by the reference laboratory and then issued by the hospital transfusion laboratory BMS via the LIMS as 'uncrossmatched' on the basis that they had not performed the crossmatching themselves. Prior to transfusion the ward staff queried why the paperwork said the blood was 'uncrossmatched' when they knew this was not an emergency and the patient had red cell antibodies. It was confirmed that the blood was fully suitable for the patient.*

#### Case 8.4: LIMS does not prevent issue of the wrong pack of apheresis platelets

*The transfusion laboratory held two units of apheresis platelets from the same donation - packs 1 and 3. Pack 3 was taken from the platelet incubator to issue but pack 1 was allocated to the patient who was transfused before the error was realised. Although this was a low harm incident it led to problems of reconciliation between stock and issued/transfused units. It was suggested that the LIMS system should be able to prompt whether the correct unit has been selected for components with multiple pack numbers i.e. paediatric blood bags, apheresis platelet donations e.g. 'You have selected pack 1, are you sure it is pack 1? Yes or No?'*

### IT systems and equipment failure n=3

There were three examples and two are presented in detail below. In the other case plasma was issued with a wrong number on the handwritten label when the IT system was down.

#### Case 8.5: Blood collected with patient details messaged to a handheld device

*Contrary to hospital policy, which requires full documentation containing patient ID to be brought to the refrigerator when collecting blood, a porter collected a unit of red cells using a handheld electronic device used to inform him about the job required, with the patient's name and unique identification number but not the details of the component.*

#### Case 8.6: Blood administered despite printing error

*A unit of platelets was issued, collected and administered without full details on both sides of the traceability label because it had been printed incorrectly. The patient's details only appeared on one half of the label and not in the section that includes the legal declaration that the blood has been transfused. The person administering the blood completed this part of the label by hand with the patient details, but not the details of the unit transfused so full traceability could not be recorded.*

## Incorrect use of an electronic blood management system n=1

### Case 8.7: Incorrect use of remote issue labelling

The transfusion laboratory received a completed traceability tag to confirm transfusion but in the LIMS it appeared that the unit had already been transfused to someone else on a different day. On investigation it was discovered that the patient had been transfused with a different but correct unit of blood and the correct donation number had been entered onto the prescription chart. This unit had been collected using remote issue from a satellite refrigerator where the remote issue label had been printed but not attached to the unit. At the bedside, an old duplicate label for a different unit had been completed and returned to the laboratory.

#### Learning point

- New ways of working may improve patient safety but if incorrectly implemented they may pose a risk. Electronic devices are increasingly used in healthcare and the example of collection of blood using a handheld device which receives and displays messages on the screen rather than a handwritten or printed form could be appropriate providing this is carefully planned, risk-assessed with a robust policy and associated training in place



### Commentary

There has been little change in the overall findings compared to previous years apart from an increase in prescription errors and an increase in the clinical errors with a corresponding reduction in laboratory errors. These errors indicate that ALL staff participating in the transfusion process must adhere to correct identification practice in all steps of transfusion.

For further laboratory-related errors please see Chapter 7, Laboratory Errors.

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# 9 Handling and Storage Errors (HSE) n=192

Authors: Diane Sydney and Hema Mistry

## Definition:

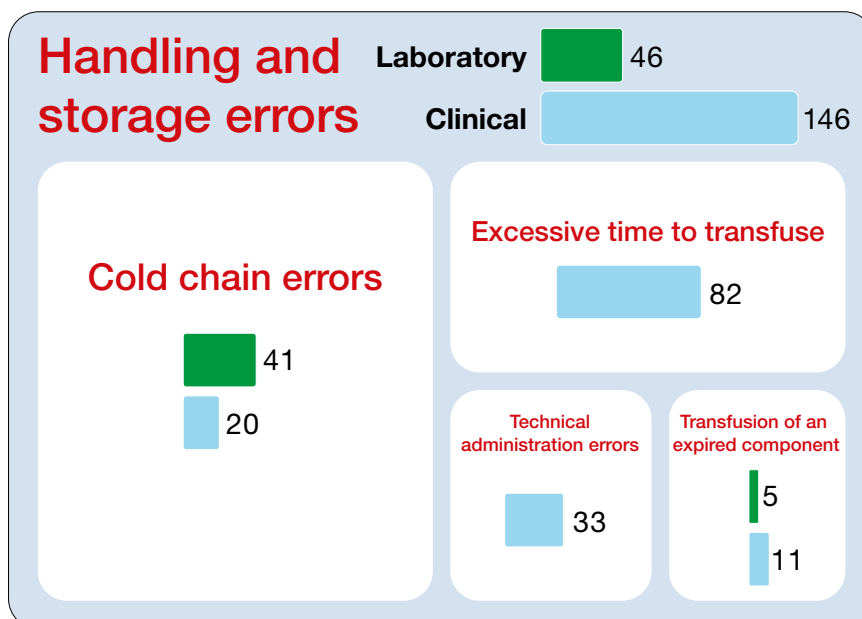
All reported episodes in which a patient was transfused with a blood component intended for that patient, but in which during the transfusion process, handling or storage errors may have rendered the component less safe for transfusion.

## Key SHOT message

- Return of blood components:** The British Society for Haematology (BSH) updated guideline for the administration of blood components notes changes to the 'Return of Blood Components' section. This guidance should be risk-assessed against local practice and agreement reached as to whether they are adopted in whole or in part (BSH Harris et al. 2017)

In 2016 there were 192 cases reported compared to 254 in 2015 (Bolton-Maggs et al. 2016). Clinical errors accounted for 146/192 (76.0%) and laboratory errors for 46/192 (24.0%). Laboratory errors have reduced from 122 to 46. There has been a noteworthy reduction in cold chain errors (CCE) from 134 in 2015 to 61 in 2016, Figure 9.1. This reduction in reports might be due to a number of factors, particularly that there were several multiple reports in 2015 due to refrigerator failures. The number in 2016 is more consistent with 2013 n=67 and 2014 n=79. All laboratory HSE-related errors are discussed in detail in Chapter 7, Laboratory Errors.

Figure 9.1:  
Breakdown  
of clinical and  
laboratory HSE  
data n=192





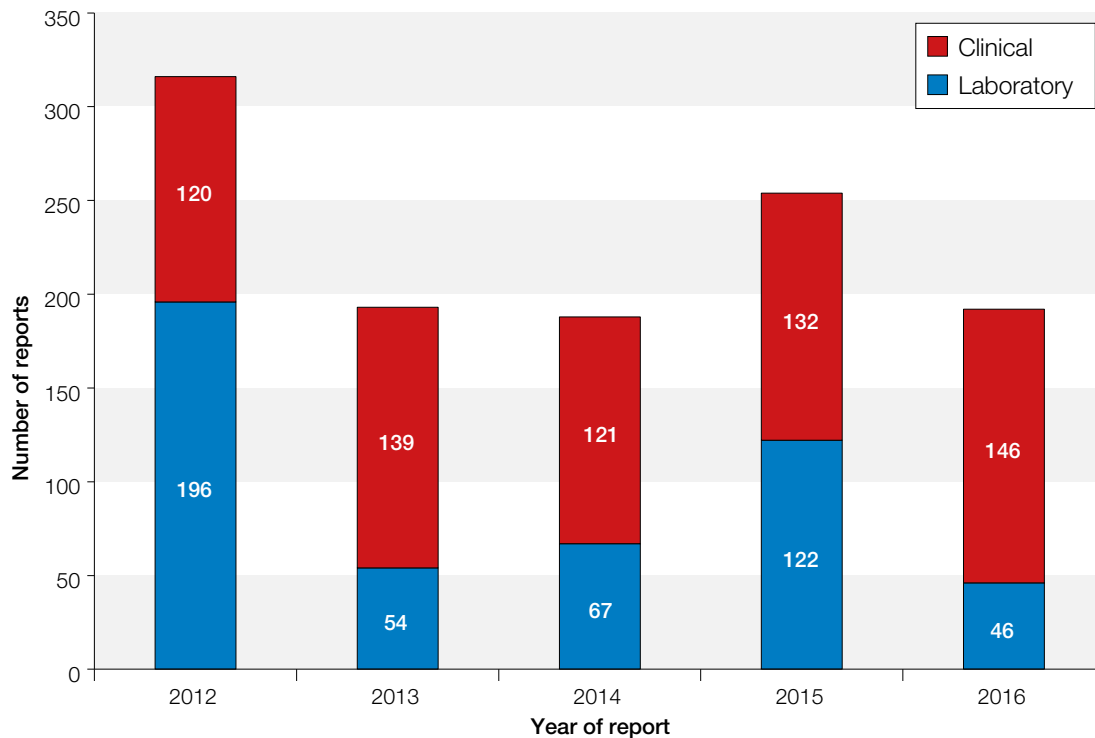


Figure 9.2: Breakdown of clinical and laboratory HSE data 5-year trend

**Case 9.1: An additional risk to an immunocompromised patient (technical administration error)**

*A haematology patient with sepsis related to neutropenia was admitted via the emergency department to a general ward before being transferred to the haematology ward the next day. The patient needed a blood transfusion but the nurse damaged the bag during spiking. The patient reported that the nurse then taped up the bag and continued with the transfusion. The bag was discarded when there was further leakage before the unit was completed.*

This case highlighted that a patient who was already immunocompromised and unwell was put at additional risk by this error. It has not been established if the staff member had undertaken this action as a result of not wanting to waste the unit. However staff should take the correct action and discard the punctured bag immediately.

**Case 9.2: Failure to transport components appropriately (cold chain error)**

*A patient was transferred to a ward out-of-hours as an emergency by a technician as there was no other escort with the patient. The patient had a platelet transfusion in progress and an additional component was found in a carrier bag with no record of when the red cell unit had been removed from controlled temperature storage.*

**Learning point**

- All staff (clinical and laboratory) should ensure that components are packaged appropriately in a validated transport box and that the correct documentation accompanies the components. Clinical staff should contact their local transfusion laboratory to seek advice and be aware of local policy before transferring patients



## Near miss HSE cases n=124

Table 9.1:  
Near misses that  
could have led to  
HSE n=124

Point in the process	Type of error made	Number of cases	%
Component selection	Time-expired unit selected	7	5.6
Collection	Time-expired component available	33	26.6
Administration	Inappropriate storage in clinical area	55	47.6
	Incorrect transport/packing of units	3	
	Wrong giving set used	1	
Other	Incorrect storage in the laboratory	17	20.2
	Component available outside sample suitability	7	
	Part-used unit returned to refrigerator	1	
<b>Total</b>		<b>124</b>	<b>100</b>

In 2016 there was an increase in near miss HSE cases, 124 compared to 97 in 2015. The main causes of this increase were:

- Laboratory errors causing time-expired components to remain available for clinical staff to collect, 33 in 2016; 12 in 2015
- Components being stored incorrectly in the clinical area 55 in 2016; 26 in 2015

## Information technology (IT)-related HSE cases n=3

All three cases related to refrigerator alarms. In one case the power to the refrigerator was cut and the temperature exceeded 6°C but the alarm did not work as intended so the blood was transfused. On another occasion a refrigerator was out of temperature control and temperature mapping was unsatisfactory but blood was still transfused because the alarms were not acted on correctly.

### Case 9.3: Blood-tracking system fails to prevent storage of platelets in the refrigerator

*The theatre porter collected platelets and fresh frozen plasma (FFP) required for surgery from the transfusion department. On arrival in theatre the FFP was scanned into the theatre refrigerator using the blood-tracking system. The blood-tracking kiosk tried to prevent the platelets being put in the refrigerator by issuing a storage alert when the unit was scanned. Ignoring this, the emergency button was pressed and the platelets were put in the refrigerator. On attempting to scan the platelets to remove them from the refrigerator an alert stating that the unit was not in the location (because they had not been scanned in) was also ignored and the platelets were taken to theatre and transfused to the patient.*



### Learning point

- Satellite refrigerators improve access to blood for patients but must be used correctly and staff must be trained to understand the action to take when an alarm or alert is noted

## Commentary

All staff should note the potential for error in relation to removing, returning, transferring and administering components; staff should adhere to the recommended infusion times and use the correct giving sets.

All laboratory-related HSE are discussed in further detail in Chapter 7, Laboratory Errors.

## References

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# Incorrect Blood Components Transfused (IBCT) n=331

# 10

**Laboratory errors n=170**

**Clinical errors n=161**

*Authors: Jayne Addison, Hema Mistry, Peter Baker, Chris Robbie and Paula Bolton-Maggs*

## **Definitions:**

### **Wrong component transfused (WCT)**

Where a patient was transfused with a blood component of an incorrect blood group, or which was intended for another patient and was incompatible with the recipient, which was intended for another recipient but happened to be compatible with the recipient, or which was other than that prescribed e.g. platelets instead of red cells.

### **Specific requirements not met (SRNM)**

Where a patient was transfused with a blood component that did not meet their specific requirements, for example irradiated components, human leucocyte antigen (HLA)-matched platelets when indicated, antigen-negative red cell units for a patient with known antibodies, red cells of extended phenotype for a patient with a specific clinical condition (e.g. haemoglobinopathy), or a component with a neonatal specification where indicated. (This does not include cases where a clinical decision was taken to knowingly transfuse components not meeting the specification in view of clinical urgency).

### **Key SHOT messages**

- Obtaining a second sample confirms the ABO group of a first time patient prior to transfusion and prevents wrong blood in tube (WBIT) incidents and ABO-incompatible blood components being transfused (BSH Milkins et al. 2013)
- Collecting more than one unit at a time or units for more than one patient can split the focus of the person collecting and leads to errors – collect one unit for one patient at a time where possible (BSH Harris et al. 2017)
- Good communication and teamwork is essential to aid patient safety and transfusion safety – all staff involved in the transfusion process should be encouraged to work cohesively as one team
- There has been a striking increase in laboratory errors over time resulting in specific requirements not met



Figure 10.1a:  
Overview of reports where an incorrect blood component was transfused in 2016

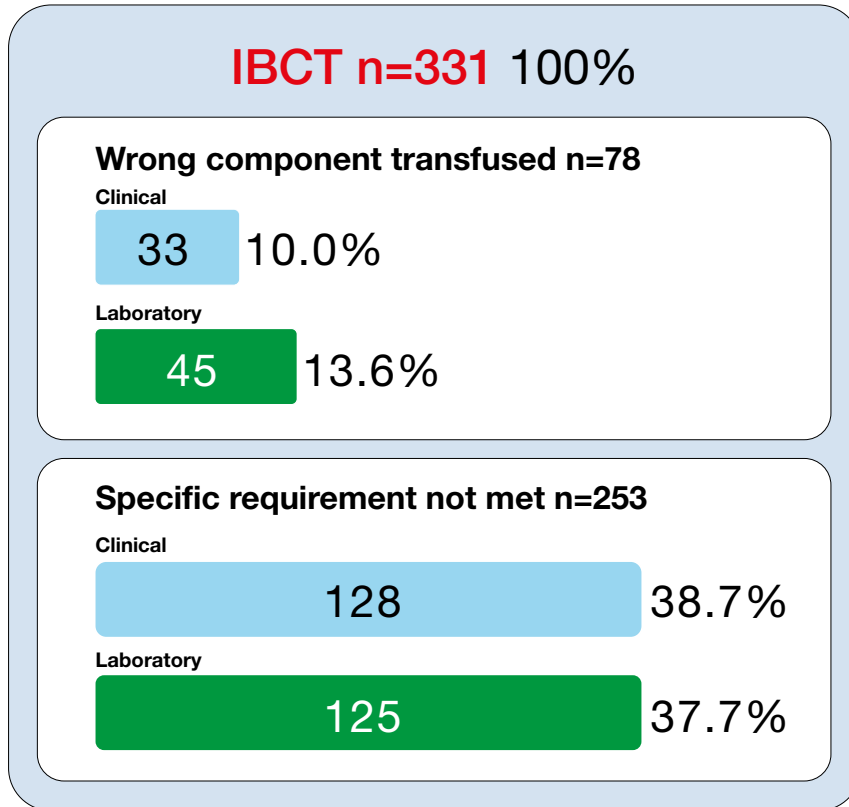
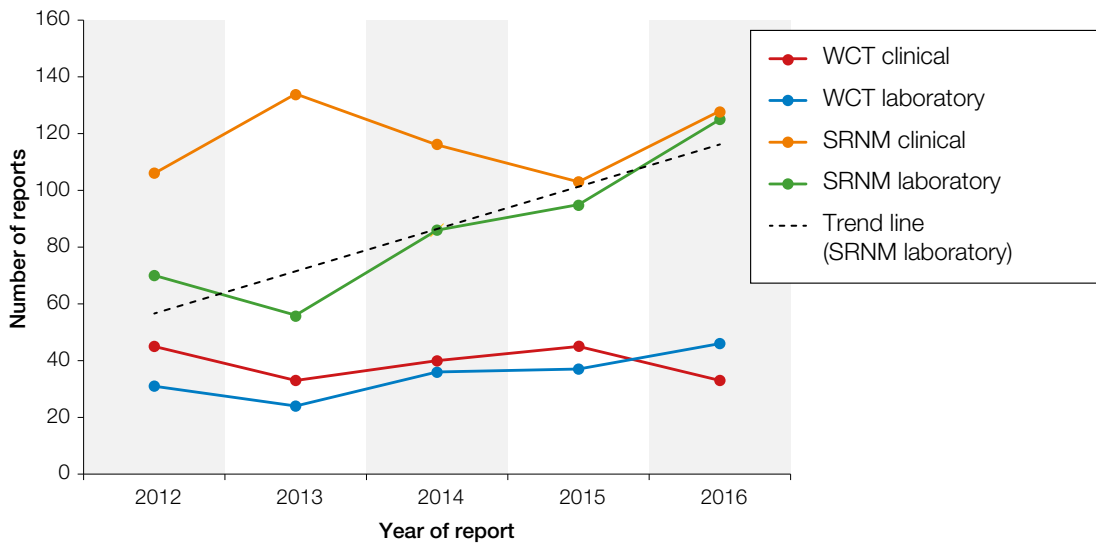


Figure 10.1b:  
Incorrect blood component transfused 2012 to 2016



The striking feature noted in Figure 10.1b is the increase over time of reports where specific requirements were not met. Review of data in Chapter 7, Laboratory Errors, shows that the most common cause of these in 2016 was failure to notice information on the request form, or failure to check available historical records (Figure 7.4a). There is also an upward trend in laboratory wrong component transfused reports whereas there is little change in the clinical reports.

## Deaths n=0

There were 22 deaths reported in the IBCT category. None of these were related to the transfusion (imputability 0: excluded or unlikely).

## Major morbidity n=8 (2 clinical, 6 laboratory)

### Clinical n=2

Two patients experienced serious harm as a result of transfusion of ABO-incompatible red cells. One incident was due to a sample error (WBIT) and the other due to collection and subsequent administration of the incorrect component. For further details, see Cases 10.3 and 10.5 in the ABO-incompatible red cell section below.

### Laboratory n=6

Two patients experienced haemolytic transfusion reactions, one a 4-day-old baby due to a component selection error, and the other resulted from a testing error, Cases 10.1 and 10.2 below.

Four women of childbearing potential developed anti-K or anti-D when transfused with K-positive/D-positive components:

- Two resulted from component selection errors where the biomedical scientist (BMS) ignored warning flags stating that the unit was not K-negative
- The Blood Service issued D-positive platelets for a D-negative woman without informing the laboratory; the laboratory staff did not check the group and therefore did not provide anti-D immunoglobulin for the patient
- A transcription error was made in D grouping when a BMS was working alone out-of-hours

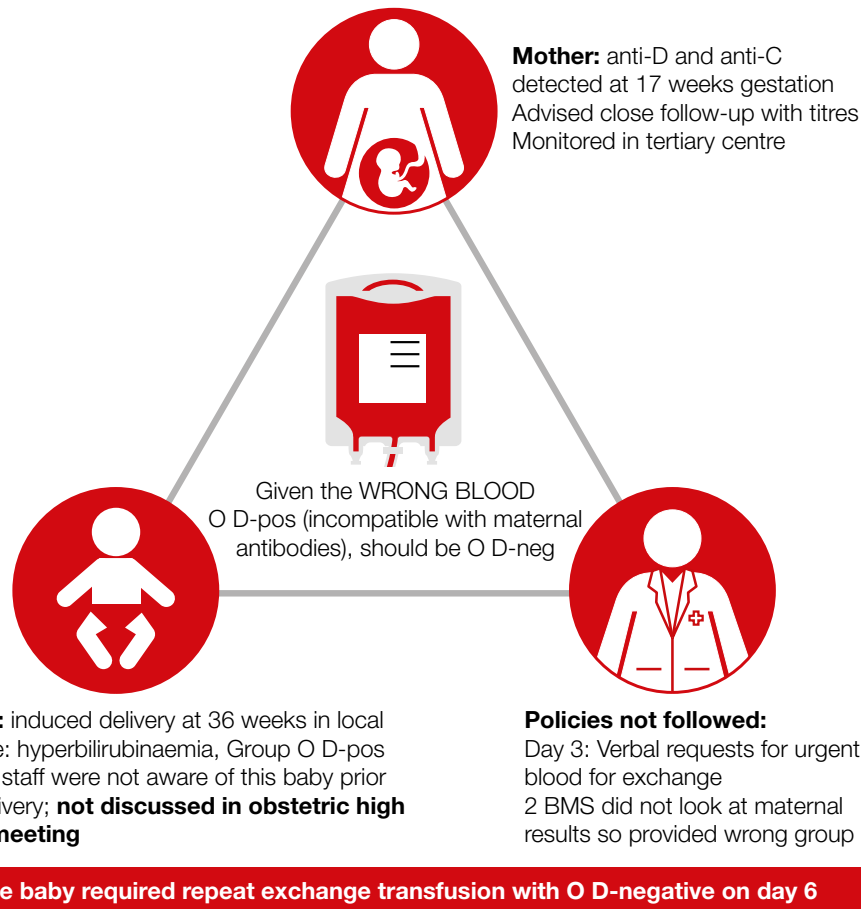
#### **Case 10.1: Selection error results in a 4-day-old baby with haemolytic disease of the fetus and newborn (HDFN) due to anti-D receiving incompatible red cells (O D-positive) and requiring further exchange (Figure 10.2)**

*A maternal antenatal sample (the second) taken at 16/40 was found to contain anti-D+C. The mother was monitored at a specialist fetomaternal centre throughout pregnancy. The baby was induced and born (at the local hospital) at 36<sup>+3</sup>/40 with hyperbilirubinaemia but levels were below the threshold for exchange transfusion, so the baby was treated with phototherapy and intravenous immunoglobulin. By the third day the serum bilirubin had risen so the clinician alerted the transfusion laboratory (verbally) that an exchange would be needed; the BMS stated he had O D-positive (the baby's group) neonatal red cells in stock. On the fourth day a request for two red cell units for exchange transfusion was made verbally. The BMS issued two units of O D-positive red cells without checking maternal group and antibody details, and without crossmatch against maternal plasma. Two registered nurses checked the units during the final bedside check. Three days after the exchange the baby's bilirubin continued to rise and a further two units were requested. A clinician reviewing the case realised that the wrong group red cells had been administered and requested a further exchange transfusion with two units of O D-negative red cells. The baby's bilirubin reduced and the baby was discharged 5 days later.*

*In addition, a Kleihauer test was wrongly requested on the mother, and she had inappropriate anti-D Ig administered.*

Figure 10.2:  
Combination of  
errors resulting in  
D-incompatible  
exchange  
transfusion

## Laboratory error and poor communication



### Root cause investigation

- On the 3rd day when the clinician alerted the transfusion laboratory, the BMS did not review the maternal details and issued O D-positive cells, the baby's group but incompatible with the antibody
- All requests were made by telephone, and the handover in the laboratory was not effective, although no follow up request form was received in the laboratory (several BMS were involved over the subsequent days)
- On several occasions (4<sup>th</sup> and 7<sup>th</sup> days) the BMS did not check the mother's blood group and antibody results and issued two O D-positive red cells units without crossmatching against the mother's sample. There were additional human factors during the initial transfusion episode: in the daytime there was a sole BMS dealing with haematology/coagulation/transfusion and an engineer on site. Subsequent transfusion episodes were dealt with at night by a lone worker

The Kleihauer test was inappropriate due to the mother's antibody status and the laboratory staff should not have issued the anti-D Ig. The nurses should have sufficient transfusion knowledge to question the group of the red cell units in this context. There need to be clear procedures in place and regular competency-assessment of all staff involved in the transfusion process. It is imperative that good communication links and updates are in place, especially during shared care.

Lone-working also appeared to be a factor in this event. The laboratory may need to produce or review their capacity plan to ensure that staffing levels are adequate for workload. Contingency plans must be written and implemented to cover periods when staffing levels are below minimum or workload is unacceptably high.

## Learning points

- Laboratories should always have sufficient staffing, correct staffing can support staff that require training (Chaffe et al. 2014)
- Telephoned requests should always be followed up with a request completed as described in British Society for Haematology (BSH) guidelines (BSH Milkins et al. 2013)



**MHRA regulatory reflection:** Standard operating procedures (SOP) should cover all tasks that staff might need to undertake, and they must be detailed enough to instruct the staff exactly what to do, even in rare or infrequent situations. Infrequently-performed tasks might require staff to be re-trained more frequently than daily tasks which are more familiar. Staff must recognise for themselves when they are unsure of the correct procedure and consult that SOP to ensure accuracy rather than asking other staff or improvising.

### Case 10.2: Elderly male patient given incorrect phenotype due to transcription error

*An 81-year-old male patient with myelodysplastic syndrome undergoing routine transfusion for anaemia required two units of red cells. The patient had a laboratory record of anti-S, a pan-reactive enzyme antibody and was direct antiglobulin test (DAT)-positive. Transfusion of the first unit was uneventful, however during the second unit the patient experienced a rise in temperature (35.5°C to 37.6°C) with rigors, hypotension (140/70 to 100/60mmHg) and tachycardia (70 to 104 beats per minute (bpm)), there was no change in respiratory rate. Haemoglobinuria was detected. Following the reaction the pre- and post-transfusion samples were sent to the Blood Centre and the second unit was found to be incompatible (S-positive). The symptoms were treated and the patient was discharged the same day.*

### Root cause investigation

- The second unit was S-positive and retrospective testing showed the unit was incompatible. The testing also confirmed haemolysis
- Further investigation identified that the laboratory staff:
  - Failed to select an antigen-negative component (the BMS mistook HbS-negative for S-negative)
  - Were unsure of the order of the units on the worksheet leading to a transcription error and failing to identify the incompatible unit
  - Failed to detect the unit was not S-negative during the second check

**Care is required** when selecting and checking components for patients with a specific requirement. Procedures must be robust, prescriptive and clear so as to avoid any confusion when using worklists.

**MHRA regulatory reflection:** The most significant error appears to surround the difference between HbS-negative and S-negative. It is vital that laboratory staff are aware of blood component labelling formats and where to find and how to use the information on labels and dispatch notes. Where possible, this information should be available on the laboratory information management system (LIMS) and used to prevent the issue of unsuitable components. Training in these procedures could be used to verify the laboratory staff's understanding of the component labelling information. This incident demonstrates that nothing should be taken for granted, even someone's understanding of component labelling.

One of the aspects of the corrective and preventive action (CAPA) relates to reinforcing the thoroughness of second checks. Checking work is vital to any quality management system (QMS) and laboratory managers need to ensure the benefit of additional checking steps and that they add value to the process. A second check may identify an error if performed correctly, but does not prevent the initial error from having occurred. Reliance on second checks alone as CAPA is to overlook the root causes of the error. Second checks may actually provide a false sense of security leading to inaccurate working practices, and even add distractions and increase workload for those expected to perform them.



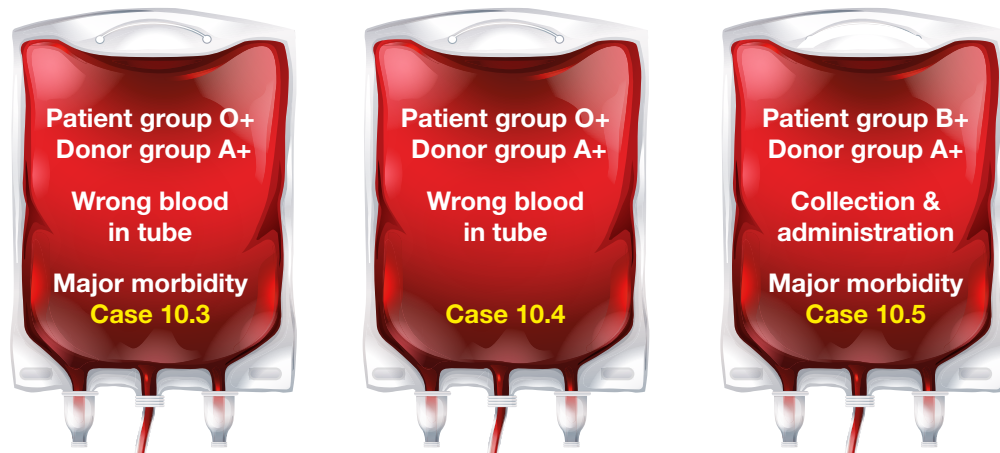
## ABO-incompatible blood component transfusions n=6 (3 clinical, and 3 laboratory)

Unintentional transfusion of ABO-incompatible blood components is a National Health Service (NHS) 'Never Event' (NHS England 2015). In Scotland these would be reported as 'red incidents' through the Scottish National Blood Transfusion Service clinical governance system and/or those of the Health Board.

These cases do not include a further 15 cases (12 laboratory errors, 3 clinical) where patients received incorrect ABO or D red cell transfusions related to haemopoietic stem cell transplants (HSCT) of which 6 could be classified as ABO never events (Table 23.4 in Chapter 23, Summary of Incidents Related to Transplant Cases).

## ABO-incompatible red cell transfusions n=3 clinical (2 resulting in major morbidity)

Figure 10.3:  
ABO-incompatible  
red cell  
transfusions



### Case 10.3: Wrong blood in tube leads to ABO-incompatible transfusion and major morbidity

A 61-year-old male (Patient 1) was admitted for coronary artery bypass graft. He received four units of group A D-positive red cells, had an uneventful stay in hospital and was discharged home. Fourteen days later he was admitted to critical care via the emergency department (ED) with renal impairment and a falling haemoglobin. On this second admission Patient 1 was grouped as O D-positive. The sample used for the crossmatch 14 days previous had been taken from the wrong patient (Patient 2) and labelled with Patient 1's details. A second sample was not obtained to confirm the ABO group although it was the hospital policy.

The haemolysis in this case must have been slow, probably because the anti-A was low titre and non-lytic. Red cell destruction in this setting usually starts much sooner, perhaps even immediately, but if the patient had no clinical symptoms, it would have gone unnoticed.

The investigation revealed that the trolley containing all patient request forms and labels was taken to the bedside. While the sample was being taken a colleague placed another set of labels on top of the current sets. The member of staff then labelled the sample using the incorrect labels and did not fully identify the patient. Positive identification of the patient and obtaining a second sample to confirm the ABO group at this critical step in the transfusion process could result in detection of the error and prevent serious harm.

### Case 10.4: Wrong blood in tube leads to ABO-incompatible transfusion

A sample was taken from a 66-year-old male with symptomatic iron deficiency anaemia and grouped as A D-positive. One unit of A D-positive blood was issued, a group-check (or second sample) was not obtained despite the hospital having a 2-sample policy in place. Three days later a further sample was sent to the laboratory which grouped as O D-positive; an additional check sample was sent on this occasion which confirmed the group as O D-positive. The patient experienced mild loin pain and mild 'haematuria' lasting 24 hours but made a full recovery.



## Learning points

- Both clinical and biomedical scientist (BMS) staff should adhere to a 2-sample policy/standard operating procedure (SOP) if this is the local arrangement. This process confirms the ABO group of a first time patient prior to transfusion (BSH Milkins et al. 2013)
- ABO-incompatibility does not necessarily cause immediate intravascular red cell destruction, but still potentially causes major morbidity



### Importance of a group-check policy, also known as the two-sample rule

The concept of a group-check policy was recommended in the 2013 BSH guidelines for pre-transfusion compatibility procedures in blood transfusion laboratories (BSH Milkins et al. 2013). Prior to a first transfusion, in the absence of a secure bedside electronic patient identification system, patients must have a blood sample grouped on two separate occasions where this does not impede the delivery of urgent red cells or other components. In practice, if the laboratory does not have a historical record for a patient, a second sample should be requested for all routine first time transfusions and components issued only if the results match. The importance of a group-check is also illustrated by Case 12.3, a near miss IT error where the LIMS auto-validation system assigned the wrong ABO group to a patient.

The second sample is a group check to confirm the sample was taken from the same intended patient on both occasions. The two sampling episodes must be separated and it is recommended that the samples are taken by different people. The time difference between episodes is not prescriptive in the guidelines but full and careful patient identification procedures must be followed on each occasion.

The 2012 Annual SHOT Report recommended strict adherence to the requirements for a group-check sample on patients without a historical group (Bolton-Maggs et al. 2013). It has been estimated that 1/2000 samples is from the wrong patient (Dzik 2003; Murphy 2004) i.e. wrong blood in tube (WBIT).

The practice of taking two samples from the patient at the same time is flawed. If the wrong patient is bled or the sample labelled with someone else's details, both samples will group identically but incorrectly. The patient could receive an ABO-incompatible blood transfusion. Analysis of SHOT data shows that about 33% of ABO-incompatible transfusions result in death or major morbidity (Bolton-Maggs et al. 2014).

#### **Case 10.5: Collection of the wrong component and subsequent failure of bedside check leads to ABO-incompatible transfusion and major morbidity**

*A 69-year-old male was admitted for an aortic valve replacement and coronary artery bypass surgery. A healthcare support worker (HCSW) was asked to collect two units of blood for this patient and one unit of blood for another. Both patients had the same forename. The two nurses who requested the collection were each unaware that the HCSW had been asked by the other nurse, however, it was not against hospital policy to collect more than one unit at a time. Communication between the HCSW and the laboratory staff was unclear but it seems this had an impact on failure to complete identification checks correctly when collecting the three units of blood. The three units were delivered to the correct clinical area. The registered nurse looking after the patient who required two units of blood failed to complete the identification checks for the first unit and consequently did not realise the wrong component was administered. When she commenced the second unit, there was a failure of checks again. Another nurse noted the error and the transfusion of the second unit was stopped. The patient suffered an acute transfusion reaction with haemolysis and respiratory distress. The patient was already on the intensive therapy unit (ITU) but required re-ventilation.*

## i

**Learning points**

- Collection of more than one unit at a time splits the focus of the person collecting and can contribute to the wrong component being collected
- If more than one blood component is required then patients should be prioritised and one unit collected at a time

The root cause investigation also revealed that the nurse was interrupted by a telephone call from a relative and at the same time distracted by the deteriorating condition of the patient requiring the transfusion. *This case is a mirror image of the case reported in 2015 where the patient died.*

## i

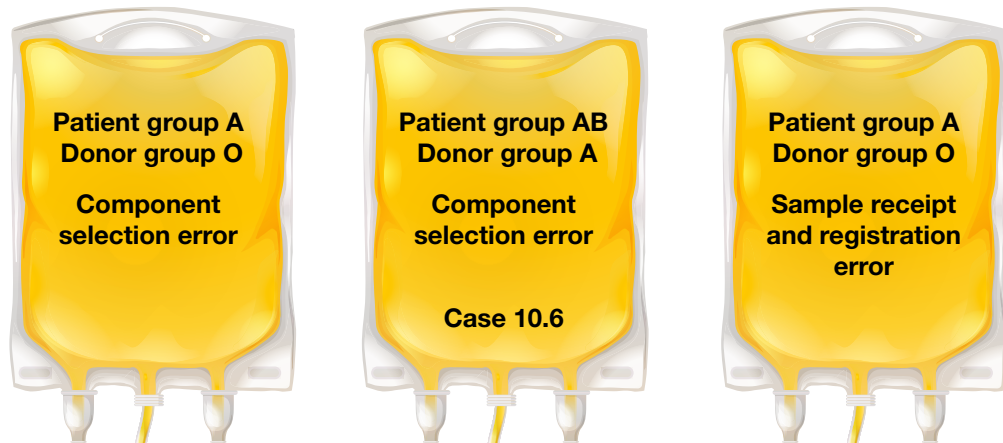
**Learning point**

- If staff are interrupted and/or distracted during the final bedside administration check, they should re-start the process from the beginning (BSH Harris et al. 2017)

### **ABO-mismatched or incompatible fresh frozen plasma (FFP) transfusions n=3 laboratory (these are also 'never events')**

In 2 cases the wrong component was selected. In one case the BMS followed the SOP for issuing platelets rather than FFP and there was no warning flag in the LIMS to alert the BMS to the selection of the ABO-incompatible plasma components. Case 10.6 describes the second selection error. In the third case the BMS failed to heed the patient history where the group of the 1-month-old baby was recorded.

Figure 10.4:  
Incompatible  
FFP transfusions  
n=2 (O to A) and  
mismatched n=1



#### **Case 10.6: Failure to heed warning flag results in group A FFP being given to a group AB patient despite group AB FFP being available**

*An 81-year-old male grouped as AB D-positive with anti-E and anti-K. The sample was also DAT-positive and further testing identified the patient phenotype to be C-E-c+e+ (Ro) and K-negative. Two units of red cells were requested and the consultant haematologist authorised group AB D-negative CDE-negative K-negative. A major haemorrhage pack (four units of red cells and four units of FFP) was later requested uncrossmatched. Only two group AB D-negative K-negative units were available so the consultant authorised and issued two group A D-negative (CDE-negative) K-negative units. A second BMS came to assist the first BMS and proceeded to thaw four group A FFP although group AB units were available. This BMS overrode the LIMS warning flag alerting them of the incompatibility. The second BMS was experienced in transfusion and had read the SOP and had been observed issuing components on several occasions, but had not been signed off as competent as there was an outstanding question surrounding lone working. This incident happened out-of-hours and was not detected until checking the work the following morning. It is thought the BMS may have been confused by the consultant authorising group A red cells and went on to issue group A FFP as well. The patient suffered no adverse reaction.*

Group A FFP may be given to AB recipients as long as it is high-titre negative. If not high-titre tested, group A FFP should only be used in an emergency.

### Learning points

- Laboratory and clinical staff should not undertake any procedure that they have not been fully trained and assessed to perform. It is the responsibility of both managers and staff to ensure this happens
- Warning flags on the laboratory information management system (LIMS) are there to alert and warn the user and require appropriate consideration before being overridden
- Always recheck the patient record on the LIMS before issuing any components



**MHRA regulatory reflection:** In this situation, the laboratory could have activated other contingency plans, or the BMS could have performed other activities they had been fully trained in to alleviate the pressures in the laboratory.

### Incompatible red cell unit transfused n=1

There was one laboratory labelling error, where the patient was transfused a serologically crossmatched but incompatible unit (not ABO-incompatible).

#### Case 10.7: Failure to check donation number against the compatibility label results in a serologically crossmatched but incompatible unit transfused to the patient

*A 21-year-old male in sickle cell crisis with anti-E, anti-Le<sup>a</sup>, a pan-reacting autoantibody and a positive DAT required transfusion. Two units that were CDE-negative, K-negative and HbS-negative were crossmatched and issued. A unit of compatible red cells was later identified as transfused but found in the stock refrigerator. A further unit associated with this crossmatch should have been returned to stock but could not be accounted for. Unfortunately a unit of blood deemed incompatible on the basis of a reaction with the patient's existing autoantibodies was selected in error and labelled with a compatibility label and transfused instead of being returned to stock.*

The compatibility label must always be cross-checked with the donor unit and preferably signed for an audit check. Any red cells identified as incompatible must be removed from temporary reservation and placed back into stock immediately. Electronic blood-tracking solutions can help identify any units incorrectly issued to a patient.

### Learning point

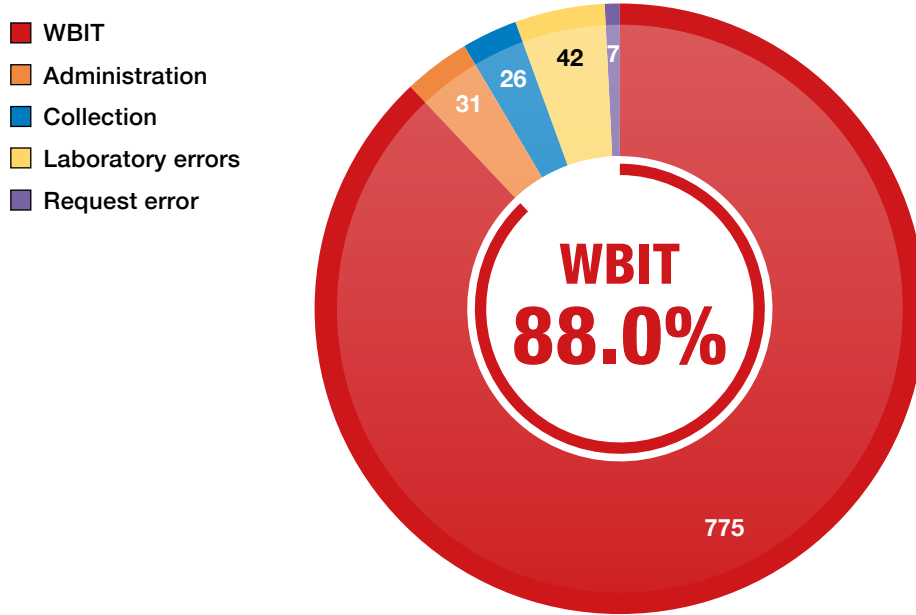
- Staff completing the final bedside checking process must check the compatibility label with the component donation number and document the donation number of the component pack and not the compatibility label into the patient notes



**MHRA regulatory reflection:** The investigation report identified a number of contributory factors. One of these was an increased workload at the time of the error as a result of a build-up of work which should have been completed overnight. Although staffing levels were adequate at the time of the error, the additional workload, due to the failure to complete the antenatal work from the previous night, is thought to have added additional pressures to the staff at the time. The lone-working BMS from the previous night was used to working in a different hospital and had not been trained in antenatal data entry procedures. It is essential that any member of staff working in the laboratory is fully trained to perform all of the duties expected of them.

### Near miss IBCT-WCT cases n=881

Figure 10.5:  
Most near misses  
were WBIT

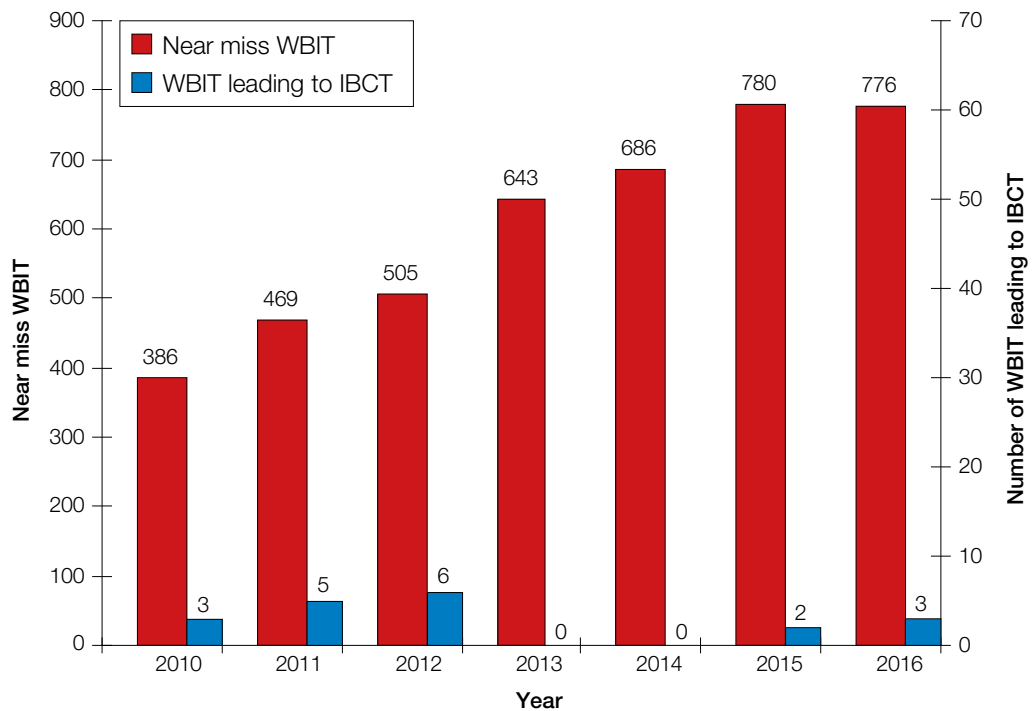


### WBIT potentially leading to IBCT n=775 (+1 avoidable n=776 WBIT in total)

#### Definition of WBIT incidents:

- Blood is taken from the wrong patient and is labelled with the intended patient's details
- Blood is taken from the intended patient, but labelled with another patient's details

Figure 10.6:  
Cumulative  
comparison of near  
miss WBIT and  
those leading to  
IBCT



### Detection of WBIT incidents

Quality processes in the laboratory are vital for detecting WBIT, but patient safety relies on vigilance and quality checking by all staff involved in transfusion. If processes were undertaken accurately at the time of sampling there would be many fewer potential WBIT.

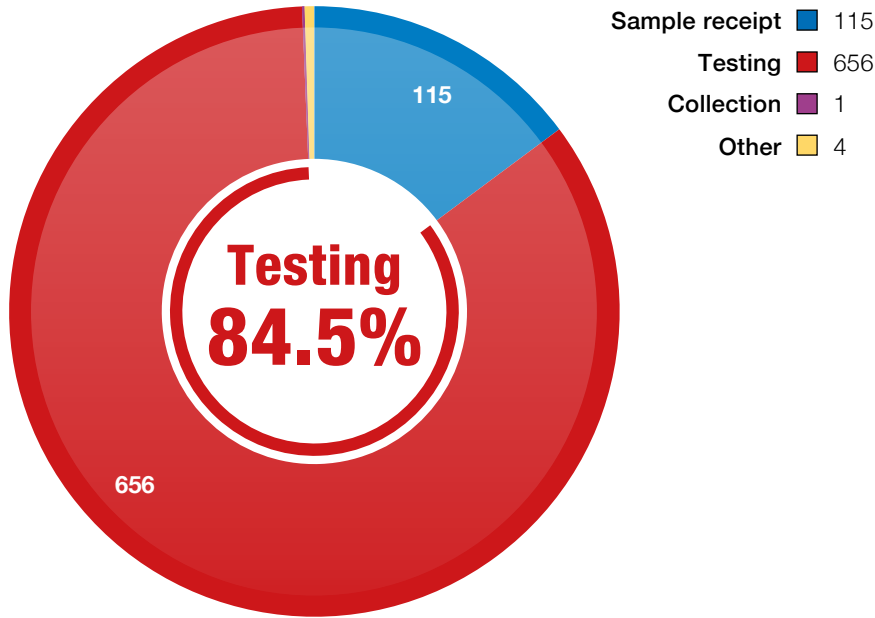


Figure 10.7: Point in the process where a wrong blood in tube incident was detected\*

\*includes 1 WBIT incident that could have led to avoidable transfusions and is included in Chapter 11b, Avoidable transfusion

Additional tables showing the subcategorisation of near miss errors consistent with those in previous Annual SHOT Reports (2010–2015) can be found in the supplementary information on the SHOT website [www.shotuk.org](http://www.shotuk.org).

### Information technology (IT)-related IBCT-WCT cases n=29

#### Laboratory n=26 and clinical n=3

#### Use of warning flags or alerts n=17 and failure to consult the historical record n=4

There were nine cases where a warning flag was in place but not heeded, one case where the flag was not updated and four where the historical record was not consulted.

There were a further seven cases where, had a flag been in place, the error might not have occurred.

11 of these ‘wrong blood’ incidents were in HSCT or solid organ transplant (SOT) patients.

Transfusion laboratories supporting allogeneic HSCT units need to use the LIMS to support complex specific requirements plus a change in blood group and hence a requirement for different blood components at different stages following the transplant. The LIMS does not replace laboratory expertise and knowledge about this specialised area and, of course, effective communication between the clinical area and the laboratory.

#### Incorrect result entered manually n=2

Both cases had anomalous groups that had to be interpreted and entered manually to allow issue of blood. One case with a weak D was transfused group A D-positive blood instead of AB D-positive blood during a postpartum haemorrhage because a lone worker had interpreted the group incorrectly and the blood was required urgently. A second case had an anomalous reverse group that was under investigation but a lone worker manually entered the interpretation O D-positive instead of O D-negative

on two successive samples and then issued blood for surgery to an elderly male patient. In the second case the LIMS incorrectly permitted electronic issue (EI) despite a manually edited result.

### Electronic blood management systems n=2 and online blood ordering system (OBOS) n=1

In one case an adult emergency O D-negative unit was removed from a satellite refrigerator and given to a neonate. There had already been a delay and the collector needed help logging onto the system to access the refrigerator, so when neither the paediatric nor the adult emergency units could be successfully scanned out of the refrigerator the adult unit was taken to prevent further delay.

In another case the kiosk alerted the collector that the wrong blood was being collected but an inexperienced BMS responding to the alarm thought it was a cold chain alert instead of a wrong blood alert and allowed the blood to be collected.

#### Case 10.8: Two electronic systems fail to prevent D-positive blood being transfused

*Blood was ordered for an exchange transfusion for a B D-negative patient with sickle cell disease using the OBOS and B D-positive blood was selected stating (in the comments box) that O D-negative blood could be substituted if necessary. Six units of O D-positive were provided, crossmatched and transfused. The LIMS did not prevent issue of D-mismatched blood and this error was not detected until the next transfusion was due when an unexplained mixed field was detected on the pre-transfusion sample (see Chapter 24 Haemoglobin Disorders: Update).*

### Computer downtime n=2

In one case D-positive blood was selected and given to a D-negative male surgical patient during planned computer downtime because the analyser result was misread. The reporter classified this transfusion as 'routine' which should ideally be avoided during planned computer downtime. Another series of errors occurred when selecting red cells and FFP because the computer screen froze and needed rebooting during a busy time when responding to an unexpected catastrophic haemorrhage during an invasive but routine procedure. IT failure can be extremely stressful for staff and very distracting when responding to an emergency.



#### Learning point

- In haemopoietic stem cell and solid organ transplant the elements requiring some IT control include the ability to
  - flag the date of the haemopoietic stem cell or solid organ transplant
  - store the recipient and donor blood groups as well as the current blood group
  - support the issue of each blood component of the correct group and specific requirements

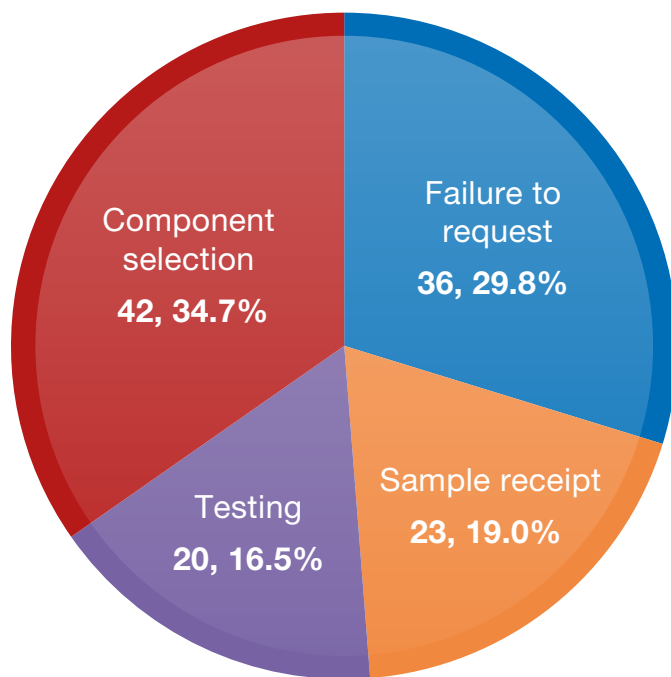
Some, but not all, IT systems can be configured to achieve this and it would be helpful to share good practice to improve the care of these patients and prevent errors

### Blood issued against wrong patient ID n=1

In this case, platelets were requested for the wrong patient with the same surname. The unit was transfused without a complete check of patient ID band.

### Near miss IBCT-SRNM cases n=121

The near miss incidents related to patients' specific requirements show similar learning points to the full incidents which led to a transfusion of components where specific requirements were not met.



**Figure 10.8:**  
Near misses that could have led to IBCT-SRNM n=121

In 2016 there was an increase in near miss SRNM cases, 121 compared to 97 in 2015. Failures to notice requests for specific requirements at sample receipt were 23 in 2016; 7 in 2015.

Additional tables showing the subcategorisation of near miss errors consistent with those in previous Annual SHOT Reports (2010–2015) can be found in the supplementary information on the SHOT website [www.shotuk.org](http://www.shotuk.org).

### **IT-related IBCT-SRNM cases n=161**

#### **Laboratory n=73 and clinical n=88**

#### **Use of the historical computer record: laboratory n=15 and clinical n=21**

There were 15 laboratory cases where the historical record was not consulted, or not linked to the current record, when selecting suitable blood components for transfusion. In 13 cases the blood selected was not of the correct phenotype either because the patient had historical antibodies but a negative antibody screen, or because there were other red cell antigens that should have been selected for. In one case non-irradiated blood components were issued because the historical record was not identified or merged and in another case non-CMV tested blood was issued to a pregnant woman.

There were 21 clinical cases where the historical record was not consulted or linked to the current record. On four occasions, non-phenotyped blood was selected for a patient in error. On 11 occasions non-irradiated blood components were issued in error. There were four clinical cases where a woman was being transfused electively in pregnancy and non-CMV-screened blood was transfused and two cases where HEV-unscreened blood was provided for a transplant patient.

#### **Warning flags not in place, not heeded or not used: laboratory n=45 and clinical n=67**

In 11 cases a warning flag was in place on the LIMS but was not heeded. This resulted in five patients not receiving irradiated components, one not receiving MB-FFP and two not receiving HEV-screened components as required. There were three cases who did not receive appropriate antigen-negative blood.



In a further 19 cases a warning flag was not activated, or updated with current information. This resulted in 11 non-irradiated components, four patients did not get HEV-screened components and four antigen-negative requirements were not met.

In 82 cases flags were not used but might have prevented errors had they been in place. The largest category here includes 40 clinical cases and a further five laboratory cases where flags could have been used to prevent the issue of non-irradiated components. There were 15 cases where a flag had not been used to highlight the need for HEV-screened components and no laboratory flag in seven cases to alert the requirement for MB-FFP or SD-FFP for those born after 1 January 1996. In three cases the need for HLA-matched platelets or red cells was missed and in 11 cases there was no flag to highlight the need for phenotyped blood. The final case was an unsuitable sample that the LIMS did not flag up as it was not working.

#### **Case 10.9: Flags can only be set correctly if clinicians can agree**

*A patient with chronic lymphatic leukaemia (CLL) and anaemia had bendamustine treatment 3 years ago. The transfusion was organised by the FY1 doctor and when the request arrived in the laboratory the BMS noted that, although there was no flag on the LIMS, of two previous transfusions one had been irradiated and one had not. The BMS phoned to ask if irradiated blood was required and the ward staff stated 'no' but when the FY1 discussed the transfusion with the consultant haematologist it became clear that lifelong irradiated components were required. The LIMS was subsequently updated with a warning flag.*

#### **Electronic issue n=20**

Electronic issue should be entirely dependent on the LIMS algorithm and there were 20 cases this year where blood was issued electronically where the patient was not eligible. The majority of these cases (n=17) have already been included within the numbers in the subheadings above. Most of these resulted in blood of the wrong phenotype being issued to patients with current or historical antibodies.

#### **Case 10.10: No information in LIMS to identify non-eligibility for EI**

*A shared care patient with HbSC disease was transfused prior to routine surgery. The current antibody screen was negative so blood was crossmatched by EI and the patient had a preoperative exchange transfusion. After the transfusion, the details on the patient's condition and history of red cell antibodies detected in the past by another hospital was discovered so the patient should have had a serological crossmatch with antigen-negative blood.*

#### **Case 10.11: Computer algorithm does not control eligibility for EI: still need to set manual flag**

*A patient post HSCT was identified as having received blood by EI on three separate occasions. The laboratory policy is to crossmatch blood serologically for these patients. The error was detected during an audit of specific requirements. The flag relating to the HSCT had been correctly set to ensure the correct group and other specific requirements were met but the additional flag required to prevent EI had not been included.*



#### **Learning point**

- Electronic issue (EI) is a safe and efficient way of providing safe and timely blood for transfusion but the computer algorithm needs to have access to all the relevant information on which to base eligibility for EI. Any change to laboratory information management system (LIMS) or patient administration system (PAS) including upgrades, replacements, mergers or hospital number changes should include the historical information on blood groups, antibodies and specific requirements including conditions such as sickle cell disease, haemopoietic stem cell transplant and solid organ transplants so that those ineligible for EI or remote issue can be determined accurately



The remaining SRNM-related IT cases consisted of:

- Wrong record selected on LIMS/PAS n=1
- Other equipment failure n=1
- Incorrect result or data entered manually n=2
- Electronic blood ordering/OBOS n=6

### Recommendation

- There should be an industry standard based on the British Society for Haematology (BSH) and Medicines and Healthcare Products Regulatory Agency (MHRA) guidance for laboratory information management systems (LIMS) and electronic blood management systems (EBMS) to support electronic issue which should apply to blood components provided from the laboratory and from remote issue refrigerators and should, where possible, have limited manual intervention

**Action: Software/IT/equipment providers/manufacturers with the UK transfusion laboratory collaborative**



### Critical steps in the transfusion process

The emphasis this year is to highlight the errors occurring at each of the nine steps in the transfusion process to enable more efficient learning points to be made. Rather than focussing on the outcome, we can learn from the root cause of the error and ensure improvement is made in that area of practice.

Figure 10.9 shows the different steps undertaken by both clinical and laboratory staff, each step incorporates independent checks at every point that should, if carried out correctly, be able to identify any errors made earlier.

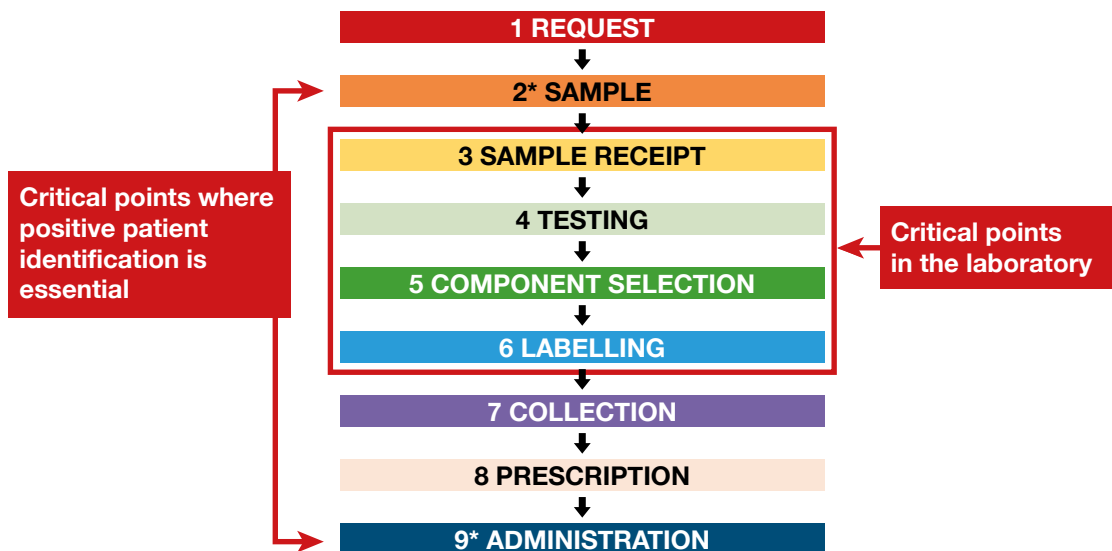
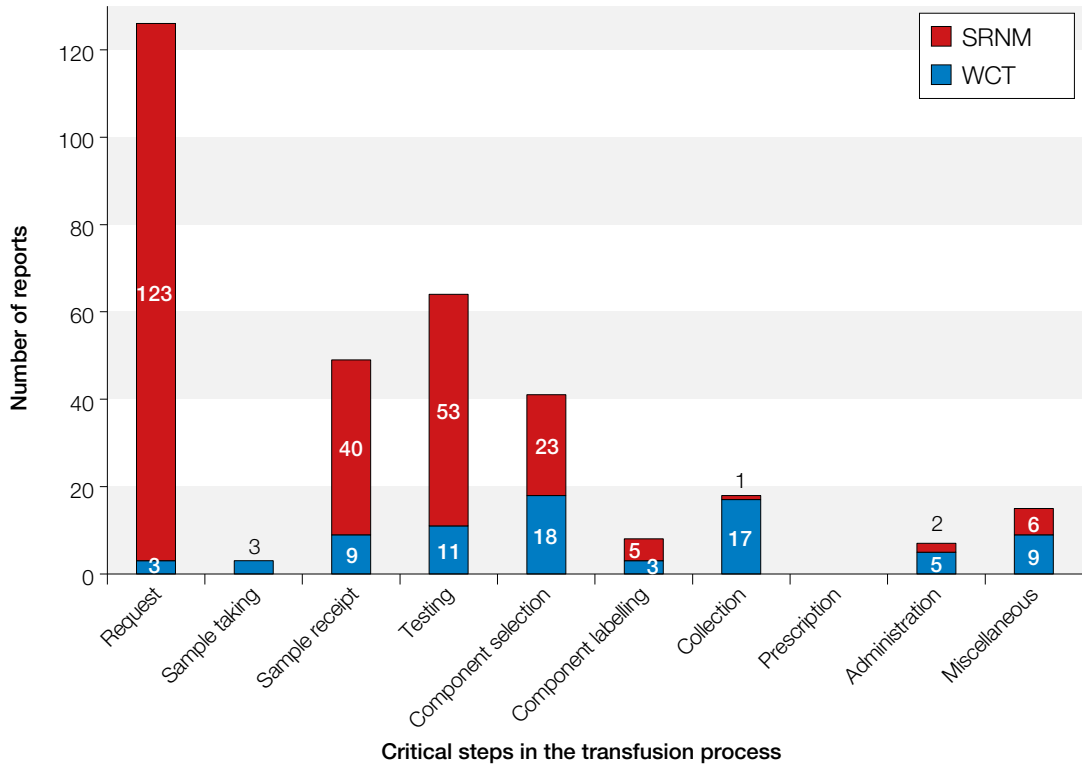


Figure 10.9: Transfusion process (nine steps)

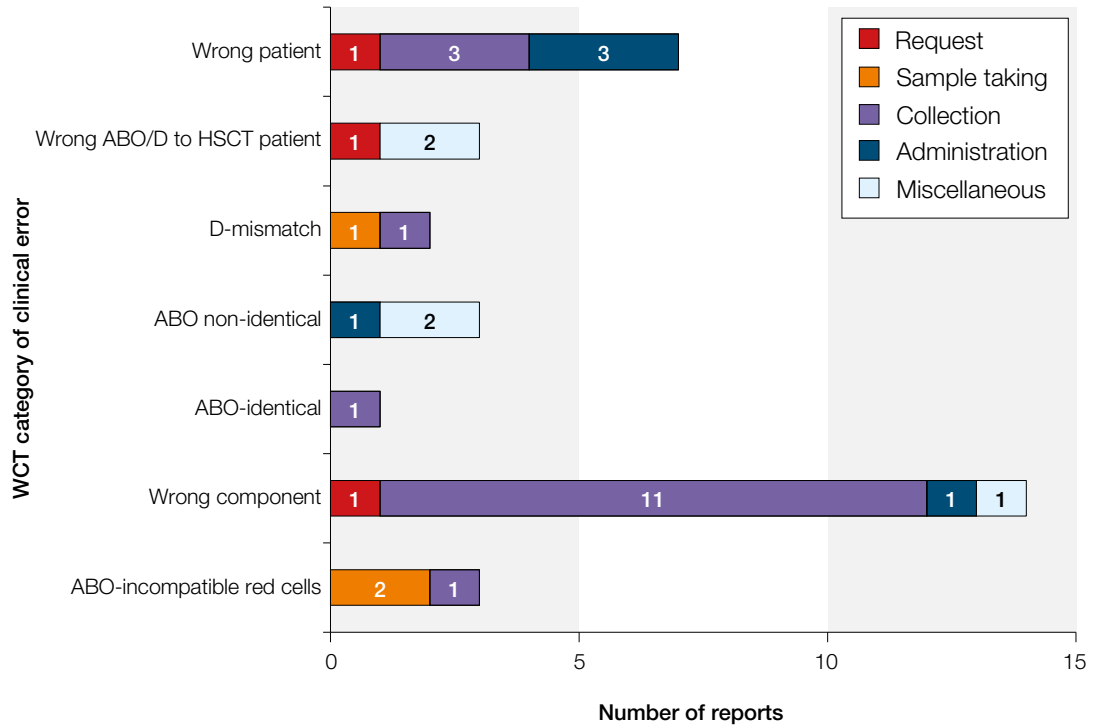
*Note: Once a decision to transfuse is made, the authorisation or prescription may be written at variable times during this sequence, but must be checked during the final stage*

**Figure 10.10:**  
Errors where the wrong component was transfused or specific requirements were not met in the transfusion process  
n=331



Figures 10.11 and 10.12 illustrate the step in the transfusion process where the primary error took place and the category for both clinical and laboratory steps.

**Figure 10.11a:**  
Clinical errors resulting in wrong component transfused n=33



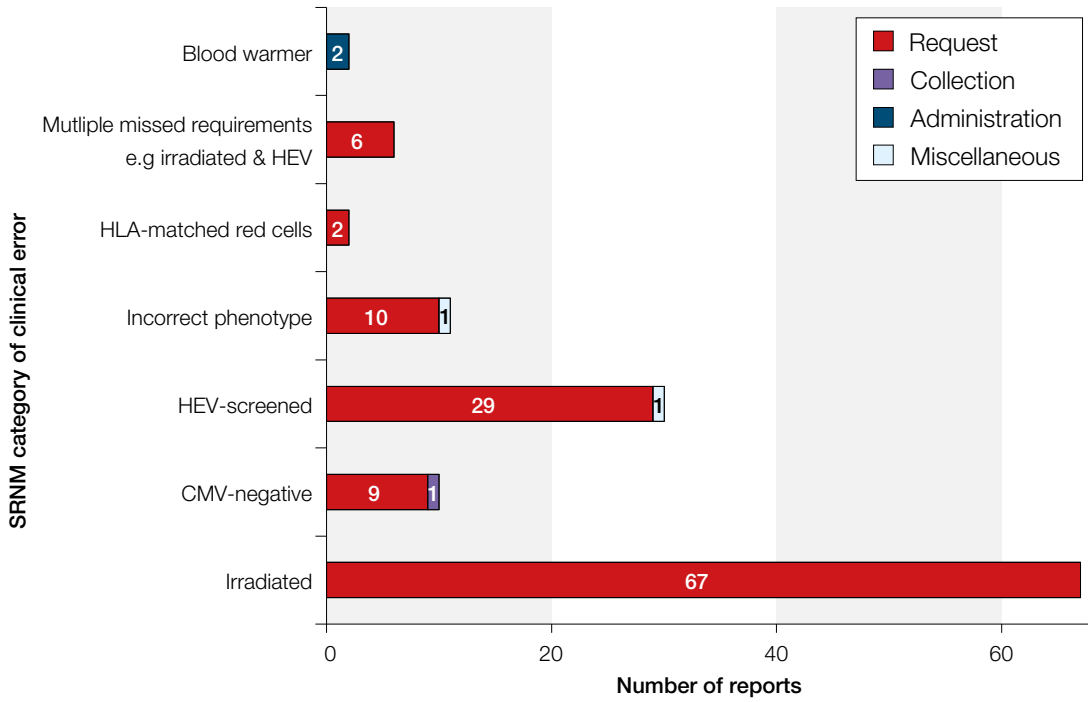


Figure 10.11b: Clinical errors leading to specific requirements not being met n=128

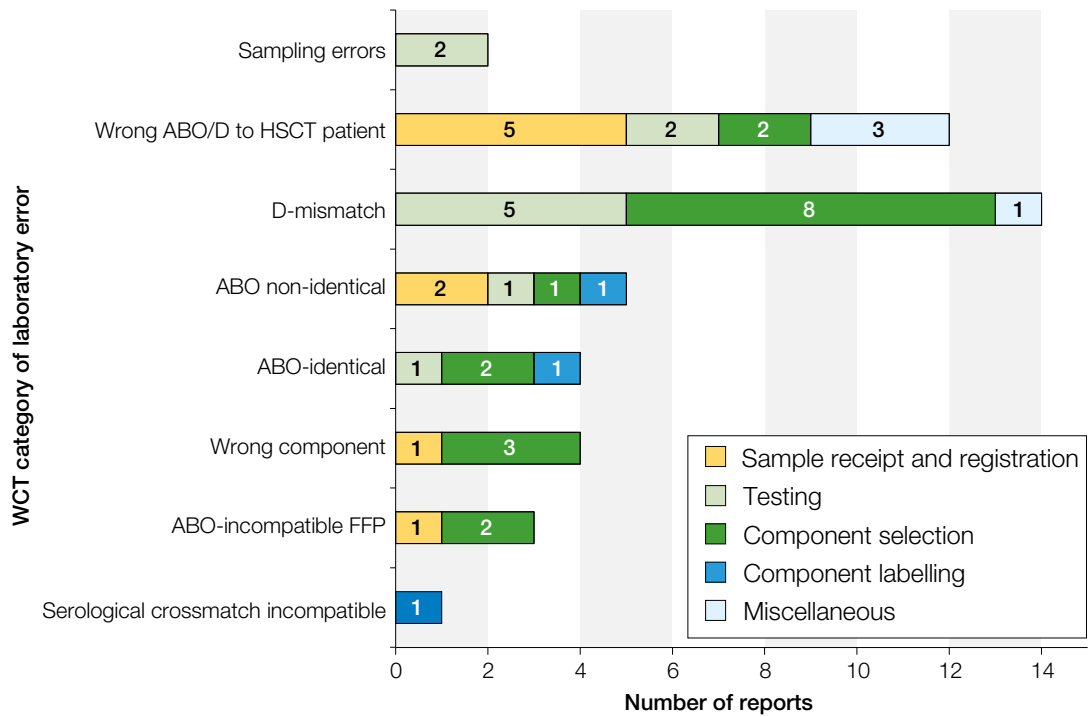
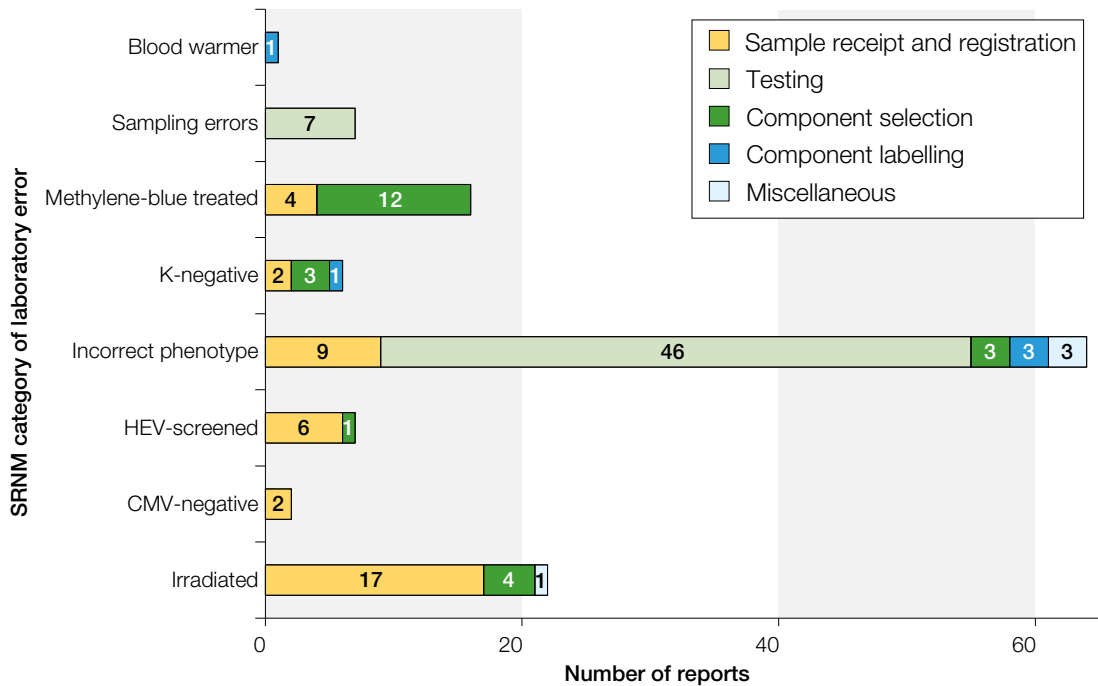


Figure 10.12a: Laboratory errors resulting in wrong component transfused n=45

\*Sampling errors associated with 2-sample rule or invalid sample when performing ABO/D grouping

**Figure 10.12b:**  
Laboratory errors  
resulting in specific  
requirements not  
being met n=125



### Step 1: Request errors n=128

The request is the first of the nine steps in the transfusion process following the decision to transfuse. It is essential that clinical staff ensure all necessary information is complete and correct according to national guidance and includes any relevant factors, where known, that influence transfusion requirements, including current diagnosis, any co-morbidities, pregnancy status and any clinical requirements (BSH Harris et al. 2017).

Despite several opportunities to identify the error at the remaining eight steps of the transfusion process 96.1% (123/128) specific requirements were missed.

Request errors can be further divided by method of requesting, where known:

- 16 verbal
- 17 computer-generated specific requirements request forms
- 56 written transfusion request forms
- 13 other including 5 by electronic request/prescription form
- 26 unknown

Wherever possible, communication should be in written or electronic format to minimise the risk of misinterpretation or transcription errors which may be associated with verbal communication (BSH Harris et al. 2017).

Common themes at step 1 include:

- Failure to complete and communicate that the patient was pregnant or had a known haemoglobinopathy. Often these patients are admitted through the ED where clinical staff may be unaware of the significance of the patient's underlying condition when requesting blood components
- Failure to identify a requirement for irradiated and/or HEV-screened components accounted for 79.7% (102/128) of SRNM. The recommendation for HEV-screened components for specific patients (SaBTO 2015) has proved difficult for hospitals to implement as captured by reports submitted to

SHOT. However, the reasons are similar to errors associated with failure to provide irradiated blood, with an initial failure to recognise the need for a specific requirement. Notably there may be a lack of awareness/knowledge, lack of information communicated from shared-care hospitals, or the patient has a historical diagnosis that requires a specific requirement

It is important to note that many patients are exposed to non-irradiated and/or non HEV-screened blood components on more than one occasion and in one case a patient received 486 non-irradiated blood components due to failure to recognise a historical diagnosis of Hodgkin lymphoma.


Clinical haematology teams should continue to ensure that patients at risk of transfusion-associated graft versus host disease (TA-GvHD) are made aware of their need for irradiated cellular components and provide written information and a specific alert card, but it is essential that adequate processes are also in place to educate/train both medical and nursing staff of all grades about specific requirements.

**Learning points**

- Clear communication channels should be developed with the local transfusion laboratory, pharmacy and shared-care hospitals to further minimise the risk of transfusion-associated graft versus host disease (TA-GvHD) to patients
- The use of an aide memoire for specific requirements on the reverse of written requests forms, prescription forms, on electronic request systems or at the final bedside check may help reduce the number of specific requirements not met (SRNM)



Figure 10.13a and 10.13b provide some examples of an aide memoire for specific requirements.



**Blood and Transplant**


**Before each unit is transfused, ensure you check if the patient requires:**


**Transfusion Special Requirements Checklist**

- ❖ **Irradiated Components** (Pre HSC donation or transplant- allo donor 14 days pre and during harvest, allo recipient from conditioning and post HSC transplant on GvHD prophylaxis, auto within 7 days harvest and from conditioning to 3 months post transplant or 6 months if TBI, HLA products, neonates post IUT, Hodgkin's Disease, Aplastic anaemia on ATG (rabbit) or for HSC, Live liver and renal donors 7 days pre and during transplant. Patients who have received: Fludarabine, cladribine, nelarabine, bendamustine, deoxycytosine, clofarabine, alemtuzumab, chlorodeoxyadenosin, ATG, ALG, alemtuzumab/campath, murmonab, SCID, DiGeorge syndrome and Wiskott Aldrich syndrome)
- ❖ **CMV Negative Components** (Neonate up to 28 days post delivery, pregnancy)
- ❖ **HbS Negative Components** (Sickle Cell Disease (SCD), Neonates )
- ❖ **Kell Negative Components** (Women of childbearing potential)
- ❖ **HEV Negative Components** (3 months pre planned SOT or date of listing, post SOT on immunosuppressants, acute leukaemia unless/until not for HSC, 3mths pre allo HSC to 6 mths post or while immunosuppressed, Extra corporeal procedures for above indications)
- ❖ **High Titre Negative Components** (A, B or AB patients receiving O component and AB receiving A or B)
- ❖ **Methylene Blue/ Solvent Detergent Components** (if born after 01/01/96)

Figure 10.13a: Indications for specific requirements included on an aide memoire card, the Therapeutic Apheresis Service, NHS Blood and Transplant

Figure 10.13b:  
Indications  
for specific  
requirements  
provided on  
the reverse of  
the transfusion  
prescription chart,  
The Christie,  
Manchester



The Christie   
NHS Foundation Trust

## DOES YOUR PATIENT NEED BLOOD PRODUCTS WITH SPECIAL REQUIREMENTS?

Patient Condition/Treatment	Irradiated Blood Products Required	Commence	Additional Information
Autologous Bone Marrow Transplant/ Peripheral Blood Stem Cells	<b>Yes</b> Continue for 6 months post BMT/PBSC Or lifelong if had purine analogue chemotherapy	7 days before stem cell harvest 7 days before transplant	It is not necessary to irradiate fresh frozen plasma or cryoprecipitate  <b>All patients requiring irradiated blood products must be given an information leaflet and card which they must carry at all times in case they require blood products at another hospital. These are available in your ward area, the transfusion lab or from the Transfusion Practitioner</b>  Discuss with attending Haematology consultant when required.
Allogenic Bone Marrow Transplant/ Peripheral Blood Stem Cells	<b>Yes</b>	7 days before conditioning for transplant	
Hodgkin's Disease	<b>Yes</b>	From diagnosis - indefinitely	
Has received Purine Analogue Chemotherapy i.e. Fludarabine, Cladribine, Bendamustine and Deoxycytosine, Clofarabine	<b>Yes</b>	From start of Chemotherapy - indefinitely	
Has received Alemtuzumab (MabCampath), Antithymocyte Globulin (ATG) and Antilymphocyte Globulin (ALG)	<b>Yes</b>	From start of Chemotherapy - indefinitely	
New Leukaemia Patients	<b>No</b> , unless fall into any of the above		<b>Pregnant patients must receive CMV - products</b>

Patient Condition/Treatment	Hepatitis E negative products required	Commence	Additional Information
New Leukaemia Patients	<b>Yes</b>	From diagnosis - until a decision is made not to transplant	<b>All patients requiring HEV negative blood products must be given an information leaflet. These are available in your ward area, the transfusion lab or from the Transfusion Practitioner.</b>
Allogenic Bone Marrow Transplant/ Peripheral Blood Stem Cells	<b>Yes</b>	3 months prior and 6 months post transplant - until patient is no longer immunosuppressed	
Patients awaiting solid organ transplant	<b>Yes</b>	3 months prior to transplant or the date listed for transplant	
Patients who have had solid organ transplant	<b>Yes</b>	Until stopping immunosuppressants	
Extra corporeal procedures	<b>Yes</b>	Dialysis, extra corporeal circulatory support is included if within above indications	

**Any questions contact: Consultant Haematologist  
Transfusion Laboratory 0161 446 3287    Transfusion Practitioner 0161 446 3055**

The Hospital Transfusion Team 2016

### Step 2: Taking the blood sample n=3

Positive patient identification is essential when taking a sample for pre-transfusion compatibility testing and is the first of the two critical patient identification steps in the transfusion process. Taking the correct blood from the correct patient and labelling the sample tube correctly at the patient's side at this step can prevent wrong components being transfused. A second sample should be taken if a historical group is not available complying with national guidelines (BSH Milkins et al. 2013). This is essential to confirm the blood in the labelled sample is from the correct patient.

Sample errors led to 2 ABO-incompatible red cell transfusions (Cases 10.3 and 10.4) and one D-mismatch.

### Step 3: Sample receipt n=49

As the first of the four critical laboratory steps, it is essential to ensure that the right investigation is performed on the right patient on the right sample at the right time (depending on the patient's transfusion history). The SOP for sample acceptance by the laboratory must define locally agreed and minimum acceptable identification criteria and the course of action to be followed when these criteria are not met and should comply with national guidelines (BSH Harris et al. 2017).

Sample receipt and registration errors are divided into three categories, demographic data entry errors, failure to heed available historical information and missed information on the request form. There were:

- 27 where laboratory staff did not heed available historical information
- 22 missed important information on request forms

Errors associated with sample receipt are discussed in more detail in Chapter 7, Laboratory Errors.

### Step 4: Testing n=64

The correct test/analysis is performed to ensure that the safe provision of blood components is undertaken in full compliance with local and national guidelines (BSH Milkins et al. 2013).

There were 2/64 testing errors that resulted in major morbidity, Case 10.2 and a transcription error in D-grouping resulting in development of anti-D in the patient.

Testing errors are divided into the following four categories of errors, technical, transcription, interpretation, and procedural. For IBCT there were:

- 6 transcription errors
- 12 interpretation errors
- 46 procedural errors

Errors associated with testing are discussed in more detail in Chapter 7, Laboratory Errors.

### Step 5: Component selection n=41

Component selection should ensure that the correct components (together with the correct specific requirements) are selected to comply with the patient's requirements and the clinical request.

There were 3/41 selection errors that resulted in serious harm. One selection error resulted in a 4-day-old baby with HDFN receiving incompatible red cells and requiring further exchange transfusion, Case 10.1.

Errors associated with component selection are discussed in more detail in Chapter 7, Laboratory Errors.

### Step 6: Labelling, availability and handling and storage errors (HSE) n=8

These are final laboratory steps before the components are available for collection by the clinical staff and so the last opportunity to ensure that the correct component leaves the laboratory. The correct component needs to be labelled with the correct four (or five) key patient identification criteria; i.e. first

name, surname, date of birth, unique patient identification (ID) identifier and address if in Wales (BSH Milkins et al. 2013). Components need to be accessible and available for the time required, if this is not possible then the clinical area needs to be informed. The components need to be handled and stored correctly as indicated in the guidelines for blood transfusion services in the UK (JPAC 2013).

In one case a patient was transfused serologically-crossmatched incompatible units (not ABO-incompatible) due to a labelling error, see Case 10.7 and Chapter 24, Haemoglobin Disorders: Update. Errors associated with component labelling, availability and HSE are discussed in more detail in Chapter 7, Laboratory Errors.

### **Step 7: Collection n=17**

This step requires that a trained and competent healthcare worker take authorised documentation containing the patient's core identifiers to the designated storage site. These documents should be checked with the laboratory-generated label attached to the blood component (BSH Harris et al. 2017).

Collection as the primary error is the most common cause for wrong components transfused 51.5% (17/33) and this step can be further divided to demonstrate some learning points.

Collection of blood components in these cases was carried out by a number of different healthcare workers

- 4 healthcare supporter workers
- 4 porters
- 7 registered nurses
- 2 unknown

In 13/17 staff were trained and competent but two stated their competency had expired. A further two had not received training or competency-assessment for collection and the remaining two were unknown.

In 7/17 the staff member did not formally check against paperwork and in 8/17 the formal check against paperwork was completed. In the remaining two cases it was unknown what checks had taken place.

In two cases more than one unit was collected at once for more than one patient. In cases where collection was carried out by non-registered staff, it was clear they were not aware of or did not remember the storage conditions or the visual difference between the different components.

### **Case 10.12: Unknown patient rushed to theatre with reliance that the final checks would be done at the patient's side**

*Four units were scanned out of the ED refrigerator to go to theatre with the patient and to be placed in the refrigerator in theatres. The need was urgent and the staff member scanned the units out without the necessary checks but relying on the fact that the blood would be checked at a subsequent step in the transfusion process prior to administration. In theatres a unit of blood was given that was incorrect, but colleagues assured the clinical team that the unit had already been checked and was ready to be administered.*

#### **The root cause investigation revealed:**

- Actions were performed based on a verbal assurance without confirmatory checking
- Actions were performed but incomplete as further checks should take place downstream in the patient pathway
- Communication breakdown during patient transit meant that staff members thought that a unit had been fully checked and was ready to use

***In addition to the above it was noted that the situation was extremely busy with conflicting attention required from the staff involved, and a lack of leadership during the trauma call.***



## Learning points

- Staff unfamiliar with blood components should be fully trained to recognise the difference in appearance of the different blood components and to know their storage conditions
- Where possible only one unit for one patient should be collected at a time (BSH Harris et al. 2017)
- Reliance on colleagues should not replace the checks required by each individual at each step of the transfusion process



### Step 8: Prescription n=0

This step is identified in Figure 10.9 as step 8, but the prescription may be written at different points in the transfusion process and should be completed and checked prior to the final administration step.

Prescription did not appear as the primary error in any cases, however it is possible errors made earlier in the transfusion process could have been detected at this stage or when making reference to the prescription.

### Step 9: Administration n=6

This is the final opportunity to prevent patients receiving the incorrect component or missing their specific requirement due to errors earlier in the transfusion process, therefore it is essential that the final administration check must always be conducted next to the patient by the healthcare professional who is going to administer the component (BSH Harris et al. 2017).

In six cases administration featured as the primary error: in 4/6 cases staff failed to notice that it was the wrong component during the checking procedure, one of which was checked away from the patient at the nurses' station. In 2/6 further cases staff failed to adhere to an instruction on the prescription for a blood warmer.

Two cases involved one nurse in the checking procedure and in the remaining 4 it was unknown, however, if local policy requires a two-person check, national guidance suggests each person should complete all the checks independently (double independent checking) (BSH Harris et al. 2017).

Double independent checking is resource-hungry by taking two nurses away from other tasks with a risk of being distracted in a busy environment or in the emergency situation when there is added pressure to rush. Double checking in this way can also provide a false sense of security, each believing the other person is checking everything correctly.

A clinical review of checklists (Winters et al. 2009) suggests that the use of **verification checklists** may be more helpful when time is short and competing priorities distract our attention. Thus a 'static sequential verification' checklist requires a **challenge and response** and is completed together rather than independently. This may be more effective than the current two-person independent or single person check. For example, the nurse responsible for administering the blood component performs the task and the second person challenges the completion of each step by reading them from the checklist, the nurse performing the task must respond to confirm completion of each step.

## Learning point

- The use of a five-point checklist at the patient's side immediately prior to connecting the transfusion as recommended (Bolton-Maggs et al. 2016) is an essential step. The two-person dependent check should be explored further



### Miscellaneous n=15 (7 clinical and 8 laboratory)

There were 15 cases where the primary error was not associated with the nine steps in the transfusion process.

### Clinical n=7

There were 2 cases where specific requirements were not met where blood was required urgently:

- A clinical decision made to give non-HEV-screened blood to an allogeneic HSCT patient
- A patient with a gastrointestinal haemorrhage admitted via ED; discovered post transfusion that the patient required HbS-negative components

There were 5 cases of wrong components transfused:

- 2 cases involved transcription of incorrect blood groups from one document to another
- 1 case involved shared care of a neonate (group B) who had received multiple group O units at a previous hospital. The receiving hospital was not informed of this multiple transfusion so the neonate grouped as O and received group O plasma inappropriately
- 1 case involved misidentification of an unknown patient who received blood labelled for another patient who had never even been in the ED. The error occurred when ambulance staff identified the unknown patient with the wrong details
- 1 case of lack of knowledge, a neonatal unit was used for an intrauterine transfusion see Chapter 22, Paediatric Summary

### Laboratory n=8

There were 4 cases where laboratory staff did not action notifications promptly, therefore patient records were not accurately maintained. In 3 cases this resulted in the wrong ABO/D group being given to HSCT patients and one where laboratory staff failed to provide irradiated units, see Chapter 23, Summary of Incidents Related to Transplant Cases.

There were a further 3 cases where the Blood Service issued incorrect/unsuitable components and did not inform the laboratory, one of these resulted in major morbidity.

A patient with sickle cell disease required 10 red cell units. A flag preventing release of red cells from the remote issue refrigerator was not applied to the patient record because the BMS did not have the right IT privilege access.

Additional miscellaneous cases are discussed in more detail in Chapter 7, Laboratory Errors.

### Importance of team work

The following demonstrate that multiple errors and missed opportunities to detect an earlier error could prevent incorrect blood components transfused.

- 21/170 (12.4%) cases where primary error originated in the laboratory could have been detected in the clinical area
- 72/331 (21.8%) errors could have been detected at administration, 30/72 where the primary error was in the laboratory and 42/72 where the primary error originated in the clinical area
- 710/818 (86.8%) cases of near miss where the primary errors in the clinical area associated with request or sample taking were detected by laboratory staff and prevented an IBCT, Chapter 12, Near Miss Reporting (NM)

#### **Case 10.13: A renal dialysis patient received two units of red cells that were crossmatched but were not intended for transfusion nor prescribed: four opportunities for detection (clinical)**

*A regular dialysis patient required two units of platelets prior to a minor surgical procedure to investigate haematuria. Two units of platelets were requested but the crossmatch box was ticked. Following a conversation between laboratory and clinical staff about the tick in the crossmatch box, red cells were crossmatched and issued. Platelets were prescribed before the procedure but not red cells. The healthcare assistant (HCA) was trained and competency-assessed to collect blood components, but red cells were collected instead of the prescribed platelets and then administered by the registered nurse.*

**Error 1: Request** – two units of platelets were requested correctly, but the crossmatch box was also ticked. Clinical staff were not aware that crossmatch was only required for red cells.

**Error 2: Component selection** – the BMS checked with the clinical staff, but failed to speak to an appropriately trained member of staff. Red cells were issued and made available for collection.

**Error 3: Collection** – the HCA was trained to collect blood components but there was a gap between theory and practice. She was not aware of the visual difference between red cells and platelets nor that platelets were only located in the laboratory and not in the remote refrigerator.

**Error 4: Prescription** – prescription of platelets clearly stated pre-procedure, red cells were not prescribed and therefore not indicated for transfusion.

**Error 5: Administration** – a failure to follow hospital policy. Nursing staff were also unfamiliar with the visual appearance of platelets because it was rare for them to be administered on the dialysis unit.

**Case 10.14: Primary error in laboratory: wrong component transfused, where there were five opportunities for detection (laboratory)**

*A unit of red cells was commenced in error instead of the prescribed plasma. The laboratory prepared the wrong component type following a telephone request. It was noted that laboratory staff were very busy and had inadequate staffing levels at the time of the incident. Two registered nurses checked the red cells but did not refer to the prescription so failed to notice it was the wrong component type, and should have been plasma. Verbal evidence from the ward manager confirms all patient details were checked correctly but the prescription form was not checked.*

This case demonstrated six errors:

**Error 1: Sample receipt and registration** – the laboratory prepared the wrong component type following a telephone request.

**Error 2: Component selection** – the laboratory staff selected the wrong component as they did not document the telephone request appropriately.

**Error 3: Component labelling** – while labelling, the laboratory staff did not detect that the wrong component had been selected.

**Error 4: Collection** – the prescription was not consulted before or during the component collection.

**Error 5: Prescription** – there was no documented evidence of these checks as the component was never prescribed therefore the prescription record was not completed.

**Error 6: Administration** – the transfusion policy was not adhered to by ward staff in terms of bedside checking procedure. Two registered nurses checked the component but did not refer to the prescription and failed to notice the wrong component during the final bedside check.

## Learning points

- Investigating, reviewing and reporting incidents from a team perspective including various disciplines, for example, consultant haematologists, nursing, laboratory, pharmacy, junior medical staff can encourage team work and help to identify specific areas of error in the transfusion process
- Consider the following:
  - Identify the step where the error occurred
  - Identify the first step where the error could be detected
  - Identify subsequent or previous steps (if present) where the error could be detected or prevented
  - Identify specific actions to prevent the same error occurring



## Commentary

Although the transfusion process is defined into separate clinical and laboratory steps (Figure 10.9) it is everyone's responsibility to ensure they complete their part of the process fully and with care. Each step incorporates independent checks and each staff member should ensure they complete the necessary checks at their step in the process as they can help to detect any errors that may have occurred earlier before the blood component reaches the patient.

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# Avoidable, Delayed, or Undertransfusion (ADU) n=246

# 11

*Authors: Paula Bolton-Maggs and Julie Ball*

Overall, 246 reports are included in the analysis. Eight of these were transferred in from other categories, one from handling and storage errors, three from wrong component transfused and four from the right blood right patient category.

- Avoidable transfusions n=114 (48.3%)
- Delayed transfusions n=101 (42.8%)
- Under or overtransfused n=21 (8.9%)

Ten cases relate to issues with prothrombin complex concentrate (PCC) alone (excluded from the percentages above), and in two further cases, a delay in PCC administration was in the context of other blood component delays, so are included in the numbers for the section on delays. These cases are analysed separately.

Note: one patient who was overtransfused was also a case of delay.

## **Deaths n=10**

There were 9 deaths related to delays, and 1 related to an avoidable transfusion. These are discussed in more detail in the relevant sections.

## **Major morbidity n=1**

There was 1 case of major morbidity related to a delayed transfusion (Case 11a.6).

# 11a Delayed Transfusions n=101 (an increase from 94 in 2015)

## Definition:

Where a transfusion of blood/blood component was clinically indicated but was not undertaken or was delayed with impact on patient care (not restricted to emergency transfusion).

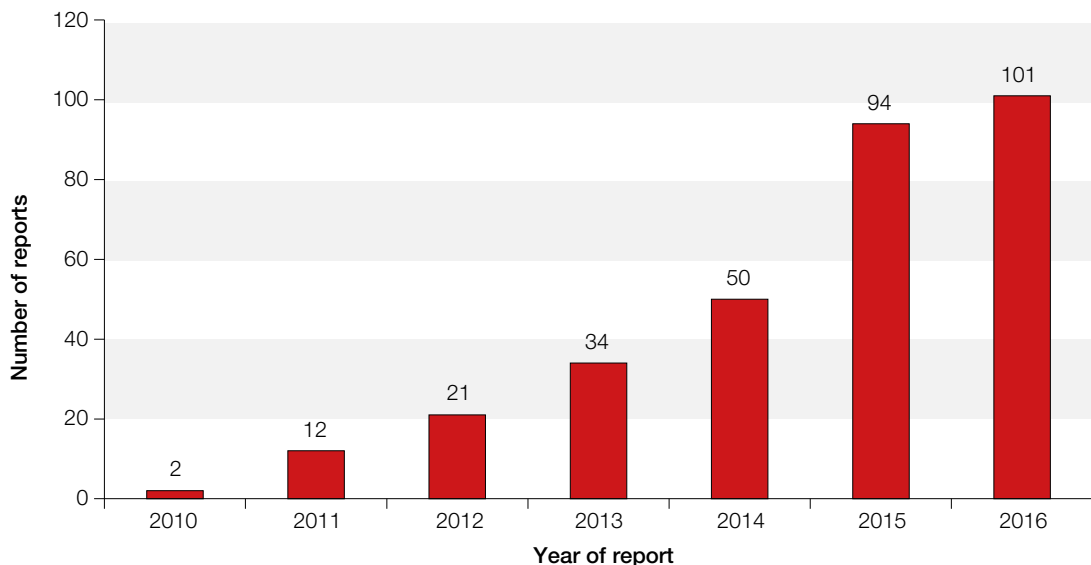
## Key SHOT message

- Delays most often result from failures in communication and poor handovers. Clinicians need to ensure the urgency of component requirements is clearly transmitted to laboratory staff, and to understand how rapidly red cells can be provided to their area (immediate, urgent group-specific or crossmatched). If a suitable sample is recorded in the laboratory red cell units may be immediately released electronically in organisations where the laboratory IT systems have the capability for electronic issue

## Learning points

- Ensure that staff know how rapidly components can be made available. Use a simple aide memoire as shown in Appendix 11.1 (page 97) which could be laminated and displayed in relevant clinical areas
- Communication failures occur when departments cannot contact each other. The transfusion laboratory should have a dedicated telephone for urgent requests and a fixed reciprocal contact point in the emergency department
- Transfusion education should ensure that clinical staff understand that fresh frozen plasma (FFP) will take about 30 minutes to thaw unless pre-thawed FFP is available (in some trauma centres)

Figure 11a.1:  
Delayed transfusion  
reports by year  
2010-2016



## Overview

The ages ranged from 2 days to 91 years; 32 were older than 70 years of age. In 57/101 (56.4%) reports the transfusions were emergency n=30, or urgent n=27 (Figure 11a.2). The location was theatres in 18, the emergency department in 15 and intensive therapy units in 10 (5 from neonatal intensive therapy units).

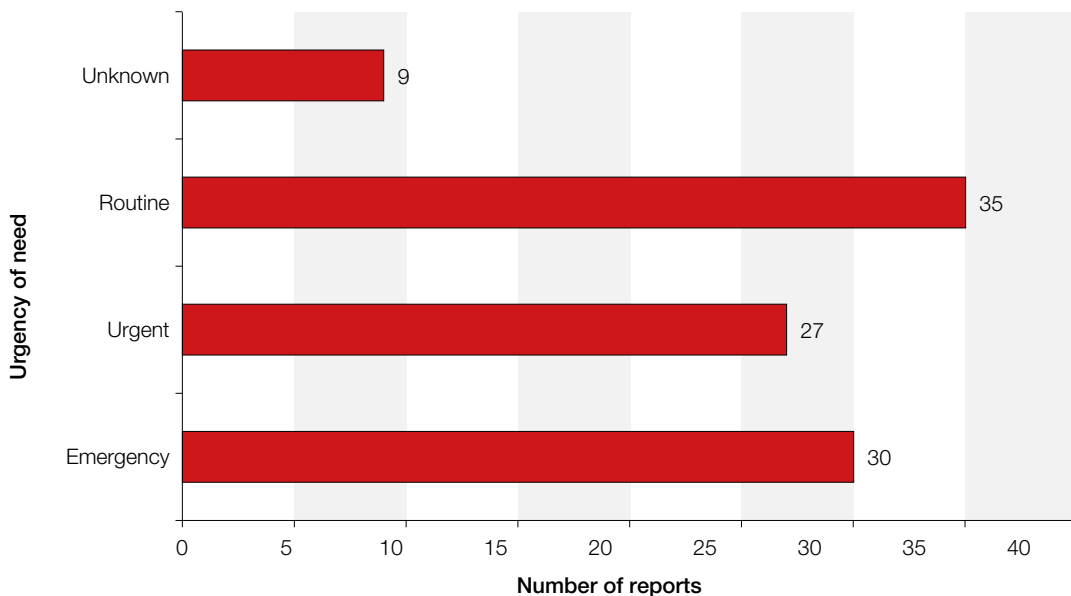


Figure 11a.2: Urgency of delayed transfusions

## Review of cases

Eighteen patients died with the following imputability (with or without major haemorrhage protocol (MHP) activation). The delay was implicated in 9/18 deaths. In the years 2010-2016, 25/115 deaths were due to delayed transfusion (21.7%).

There was one instance of major morbidity discussed below (Case 11a.6).

Imputability	Number	MHP activations
Definitely related	2	1
Probably related	2	
Possibly related	5	1
Unrelated	9	5*
<b>Totals</b>	<b>18</b>	<b>7</b>

Table 11a.1: Deaths showing imputability related to delay, and relationship to MHP activation

\*See Case 7.7 in Chapter 7, Laboratory Errors

## Deaths n=9

### Imputability: deaths definitely related to delay n=2

#### Case 11a.1: Death after haematemesis due to delay in transfusion

A 76-year-old man admitted with haematemesis and on anticoagulants for atrial fibrillation died associated with failure to activate the MHP and 5-hour delay in transfusion. His haemoglobin (Hb) was 69g/L at 00:15. The biomedical scientist (BMS) was lone working and had attempted to contact the emergency department (ED) to inform them of the abnormal blood result, but did not get an answer.

Several issues with poor communication were identified:

- The urgency of the situation was not communicated to the BMS in the laboratory
- The clinicians did not inform the BMS that the patient was on warfarin
- The medical registrar assumed that red cells had been ordered for the patient; however this was not the case. The red cells were ordered approximately 3 hours after the patient was admitted to the ED. When the red cells were ordered, the clinical staff did not request the blood urgently and therefore fully crossmatched blood was issued (rather than group O emergency or group-specific units)
- Policies were not followed: The MHP was not followed by the clinical staff in the ED, the BMS in the laboratory advised the doctor to obtain haematology consultant approval before requesting PCC for warfarin reversal, but this is not policy and further delayed the patient's care

Outcome of the review: Teaching in the ED has been revised to include:

- The need for accurate and comprehensive information on the request forms that are sent to the laboratory to ensure that BMS staff are fully informed of the clinical situation
- How to manage a major haemorrhage, clinically and strategically. Staff to be given training on the MHP
- Training to be given to all BMS staff to ensure they are familiar with correct procedure for issuing PCC

#### **Case 11a.2: Death in a patient with coagulopathy who failed to receive FFP**

*A 71-year-old man presented with a month-long history of constitutional symptoms and jaundice. Investigation raised the suspicion of pancreatic malignancy with blockage of bile drainage and he was admitted (day 1) for planned endoscopic retrograde cholangiopancreatography (ERCP). An initial attempt at ERCP failed on day 4 and he was then listed for a radiologically guided attempt at decompressing the biliary obstruction (percutaneous transhepatic cholangiogram - PTC). ERCP was attempted but failed again on days 5 and 6. A decision was made to perform PTC under general anaesthetic. In parallel the patient had deteriorated with hospital-acquired pneumonia, a fall, worsening liver function tests and the development of a coagulopathy. On day 7 a further ERCP failed and the PTC under general anaesthesia was organised. The complex coagulopathy was noted on the morning of day 7 which was not reversed by vitamin K. The consultant arranged for FFP to be administered to the patient prior or during the attempt at PTC under anaesthetic. Despite the FFP being ordered from the transfusion laboratory, (issued at 12:54) and being prescribed this was not administered prior to the PTC on the ward, during the procedure (in the radiology department) or in the immediate post-procedure period (in theatre recovery). The FFP was returned to stock at 16:17. The patient was transferred to the ward without having received blood components and deteriorated later that evening. He became moribund and despite attempts at fluid resuscitation and the administration of blood components he died. The coroner noted that the cause of death was intra-abdominal haemorrhage and that the failure to administer FFP was an important factor in the cause of death of the patient.*

The incident investigation noted that there had been multiple opportunities to hand over the need for blood and FFP transfusion and focussed on ways to improve handover. The electronic prescribing system does not include blood components which are prescribed on paper but the electronic system can be set with a prompt to flag the need to administer blood components which was not used in this case. The Bloodhound tracking system has been introduced which has a reminder function. The report suggested that failure to administer FFP ordered for a patient with a coagulopathy should lead to questions from the laboratory staff to the clinical area and a revised standard operating procedure will include this.



## **Imputability: deaths probably related to delay n=2**

### **Case 11a.3: Delayed transfusion contributes to death**

*An elderly man with shortness of breath was admitted to the ED at 11:45. He had a suspected posterior myocardial infarction. Blood samples were taken at 12:30. A low Hb was confirmed at 15:00, a tentative diagnosis of acute myeloid leukaemia was made, and decision to transfuse. At 16:00 blood tests were repeated and discussed with the haematology consultant. The patient was difficult to crossmatch and the laboratory staff did not advise the clinical team that they could have used emergency O D-negative units. The blood group was put on the analyser at 14:57 but suitable units were not issued until after 20:40 (a delay of more than 5 hours). The transfusion laboratory was contacted at 19:35 and 20:20. The patient suffered a cardiac arrest at 21:14. The first unit of blood was begun at 21:24 and the second at 21:45 but death occurred shortly afterwards at 22:15.*

The hospital review noted that clarity was required for transfusion requests where the need was urgent but not requiring trigger of the MHP. Verbal communication of transfusion requests to the general laboratory telephone was noted not to be a robust system. A transfusion laboratory emergency telephone number is to be used for all 'very urgent' requests with a log of calls kept in the ED. Staff were reminded how to access the emergency group O red cells. A named clinical leader should take responsibility for very sick patients in the resuscitation area until their transfer.

### **Case 11a.4: Death related to leaking abdominal aortic aneurysm (AAA) where transfusion was suspended during transit**

*An elderly man was transferred by ambulance from the ED to another hospital with a 9cm leaking AAA. Red cell transfusion stopped in transit as there was no nurse or doctor present on the transfer due to insufficient staffing levels. The patient arrived with systolic blood pressure (BP) of 47mm/Hg and a Glasgow coma score (GCS) of 10. The patient was taken immediately to theatres at the receiving hospital where he subsequently died. The reporter noted staffing issues which contributed to the need to suspend the transfusion during transfer.*

## **Imputability: deaths possibly related to delay n=5**

### **Case 11a.5: Delay in acting on abnormal blood results contributes to patient death**

*An elderly lady was admitted with Hb 33g/L at 13:30. There were several communication failures. The staff noted at 22:20 that no sample had been taken (9 hours from admission). The patient had a cardiac arrest and died at 00:31.*

The internal review noted that the ED was very busy on that day and stressed the importance of detailed handovers even when the unit is busy, and the importance of chasing up and acting on blood test results. A new dedicated telephone number was set up for results in the ED.

Another patient died related to delay in recognition of the severity of gastrointestinal bleeding. Her Hb was noted to be falling. Reaction was slow, and she died three hours following her deterioration, before emergency group O D-negative units were transfused. The most senior doctor on site was foundation year 2 and the escalation policy had not been effective.

## **Delay in release of emergency O D-negative units n=3**

In three cases staff in the ED refused to release O D-negative emergency units. These were from the same hospital, one in January, the second in September and the third in November.

### **Case 11a.6: Major morbidity in relation to delayed access to emergency O D-negative units**

*At 19:15 a porter attempted to collect a unit of emergency O D-negative blood from the ED blood refrigerator for a 39-year-old woman who was bleeding complicated by cardiac arrest but was informed that he was not allowed the blood as it was for ED patients only. The porter then proceeded to the main theatre blood refrigerator and collected an emergency unit there. This patient was admitted to intensive care and made a full recovery. She received five units of red cells and two of FFP.*

The staff member who refused to release emergency blood was not aware that the blood should be available to all patients in the hospital. Following this incident a communication was sent out to all ED staff informing them that the emergency O D-negative blood in their blood refrigerator should be available for all patients. Despite this, two further incidents were reported.

Several actions were taken by the consultant haematologist responsible for transfusion after the first event.

- Removal of some of the 15 emergency O D-negative units from the ED to the issue refrigerator in the transfusion laboratory
- Change activation of the MHP to go through the emergency switchboard number alerting the transfusion laboratory, porters (with a nominated porter) and clinical site team
- Update the training across the site as investigation revealed some senior staff did not know about the MHP or where the emergency O D-negative units were located

The reporter noted that delay in resolving these issues in this large hospital site (with 26,000 units of red cells issued per year) was hampered by having no dedicated transfusion practitioner. The issue of emergency provision of blood featured in the consultant's list of patient safety concerns presented to the medical director.

### Issues with major haemorrhage protocols resulting in delay n=16

In 16/101 cases the MHP was implicated in delay. Six of these were associated with obstetric haemorrhage. Delay in provision of FFP was noted in 10/16 cases. Some of these resulted from misunderstanding by clinical staff about the time taken to thaw FFP and others from poor communication between the clinical and laboratory staff.

#### Case 11a.7: Failure to follow MHP with misunderstandings and ambiguity in the protocol

*A 43-year-old trauma patient was admitted to the ED with major haemorrhage at 22:00. The BMS failed to respond to the MHP activation but the root cause analysis noted that several aspects of the MHP were unclear (including the role of the haematology registrar and the porter's role in collection and delivery), and this was the second incident within a month. The patient received 3L of red cells, 2750mL of FFP, two adult doses of platelets and 479mL of cryoprecipitate but died with delay in transfusion as a contributory factor. The MHP was revised and all BMS staff were reminded of their roles and responsibilities.*

### Cases associated with obstetric haemorrhage n=6

In one case of postpartum haemorrhage (PPH) staff were unable to release emergency O D-negative units from an information technology (IT)-controlled satellite blood refrigerator. In another case activation of the massive obstetric haemorrhage (MOH) protocol failed to trigger the porters to attend. A similar case is described below demonstrating the importance of logistics. In another instance the MOH was not followed correctly.

#### Case 11a.8: Blood components were delayed for 40 minutes from MOH activation

*A 27-year-old woman had a major PPH of 2.5L with ongoing bleeding. The MOH protocol was activated and she was transferred to obstetric theatre to obtain haemostasis. There was a 40-minute delay in receiving O D-negative blood from the transfusion laboratory. The patient was hypotensive and required vasopressors to maintain her blood pressure while waiting for blood transfusion. She quickly improved once the blood was transfused.*

There were misunderstandings and miscommunications. The obstetric staff should have sent someone straight away for pack 1 or the emergency O D-negative units. The porters were not contacted for 23 minutes to collect blood from the laboratory. The delay meant that electronic issue of compatible components could have taken place. The BMS was told that the clinical team were only interested in FFP and not the blood. However, the FFP was not used.

### **Case 11a.9: Communication failure and misunderstandings resulting in delayed supply of FFP - MOH activation did not result in the BMS in transfusion being informed**

*An obstetric patient delivered (forceps) at 02:06 but then developed a PPH with estimated blood loss 3.5L at around 03:15; an initial PPH call was made by the clinical team at 03:33 and escalated to MOH at 03:57. The theatre nurse contacted the transfusion laboratory to inform the BMS that two O D-negative units had been used but did not have the patient details or location. Activation of the MOH did not include contact with the laboratory and clinical staff were unaware they needed to contact the laboratory to inform them of requirements for transfusion support.*

*Two further O D-negative units were removed at 04:10; then the BMS telephoned the delivery suite to find out who the patient was. When the MOH pack A (six units of red cells and four FFP) was requested at 04:15 with the patient details the BMS had no transfusion sample for grouping. Once the group was established at 04:40, FFP could be thawed out. This was received 1 hour 15 minutes after the MOH call. The BMS was lone working and had not had time to process the full blood count (FBC) and coagulation samples. The patient developed a coagulopathy (results at 05:00) and received FFP, platelets and cryoprecipitate, and was transferred to the intensive care unit. She had evidence of acute kidney injury but recovered well and was discharged on the 5<sup>th</sup> day. The root cause analysis (RCA) noted that there were staff shortages.*

### **Case 11a.10: Delayed provision of FFP due to poor practice by BMS**

*A 41-year-old woman with a massive PPH had a delay of 20 minutes in provision of FFP during MHP due to poor communication between the BMS in the hospital transfusion laboratory. The BMS who put the FFP in the plasma thawer finished their work shift and did not handover to the next shift. When theatre staff came to collect the FFP for the emergency the units were not ready and were found to be in the plasma thawer and there was a delay until the FFP was labelled and issued.*

The BMS involved in this incident is under monitoring for poor practice and has been offered intensive mentoring and supervision. The BMS did not record any outstanding actions on the shift hand-over sheet as indicated by departmental policy.

## **Information technology (IT)-related delay cases n=19**

IT systems or equipment failure led to transfusion delays in 19 patients.

### **Electronic blood management systems (EBMS) n=4**

Four patients experienced delayed transfusions because of problems with EBMS. During normal working hours, no-one on the ward was trained to collect blood using the EBMS which resulted in a delayed red cell transfusion. On one occasion, when the EBMS was relatively new and not all staff trained, there was some confusion about collection using a pick-up slip and on another occasion despite using the correct log-on details and following instructions, staff could not access emergency blood in a satellite refrigerator because the default setting was 'locked'.

### **Case 11a.11: Providing a new but unnecessary sample causes delay**

*A large number of units of blood were issued electronically to a remote satellite refrigerator for a patient at high risk of bleeding intraoperatively. To be sure a current valid sample was available, a new sample was sent by the anaesthetist at the beginning of the list. The first unit was collected without any problems but on collecting the second unit, access was blocked and no other units could be removed from the refrigerator. This was because the unnecessary sample became the new 'valid sample' and remote electronic issue could not take place until a new result was available on the laboratory information management system (LIMS).*

Delays were caused by problems with the LIMS or the LIMS/patient administration system (PAS) interface in five cases and two of these cases were new IT systems that did not perform as expected – one where the analyser did not transmit results to the LIMS and another where the LIMS did not transmit results to a general practice (GP) surgery.

There were discrepancies between the PAS and LIMS resulting in blood delays in four cases and one case where the wrong pack of a 2-pack apheresis platelet donation had been recorded as issued so the remaining pack could not be issued either.

**Case 11a.12: Electronic prescribing does not include blood components and this causes confusion (Case 11a.2 above)**

*Prophylactic fresh frozen plasma (FFP) was not given to a patient undergoing a difficult endoscopic retrograde cholangiopancreatography (ERPC) procedure for obstructive jaundice and this was thought to have contributed to the peri-procedural bleeding. One cause of this omission was the fact that fluids and drugs were prescribed electronically but blood components were not so the prescription was overlooked and the component, thawed for use by the laboratory, was not transfused.*

The remaining five cases were mainly errors due to specific requirement flags being absent, inaccessible or incorrect.



### Learning point

- New ways of working may improve patient safety but if incorrectly implemented they may pose a risk. Electronic prescribing of blood is increasingly being used where ordercomms and an electronic patient record are in place. This is an area where shared experience between organisations could be beneficial and perhaps encourage implementation of blood prescribing in line with other drugs and fluids

### Commentary

It is disappointing that 7 years after the National Patient Safety Agency notice about provision of blood components in an emergency (NPSA 2010) patients continue to be put at risk because the MHP are not working well, most often due to failures in communication or misunderstandings. Delays may be exacerbated by short-staffing as demonstrated in some of these cases, and this should be discussed with managers. Emergency protocols should be practised to ensure they function as intended. At least three instances are noted where porters were not appropriately available after MHP activation, and in another the clinical staff did not appreciate the need to inform the laboratory.



### Learning point

Every hospital should clarify the delivery times for emergency O D-negative, group-specific or crossmatched units as shown in the example at Appendix 11.1

### References

NPSA: Rapid Response Report NPSA/2010/017 **The transfusion of blood and blood components in an emergency.** <http://www.nrls.npsa.nhs.uk/alerts/?entryid45=83659> [accessed 17 March 2017]

NPSA: Rapid Response Report NPSA/2010/017 **The transfusion of blood and blood components in an emergency. October 2010, Supporting information.** <http://www.nrls.npsa.nhs.uk/EasySiteWeb/getresource.axd?AssetID=83689&> [accessed 17 March 2017]



Appendix 11.1: Example of a transfusion aide memoire (Manchester Royal Infirmary)

**Life threatening haemorrhage**

**Urgent Red Cells (for acute but not life threatening haemorrhage)**

Group specific uncrossmatched red cells will be available 30 mins following receipt of sample in the lab fully crossmatched blood will be available in 60 mins\*

It is safer to wait for fully crossmatched blood if time allows

\*if antibodies are present, turnaround time will be determined on a case by case basis

**Urgent Platelets for urgent management of thrombocytopenia**

A small stock of platelets is kept in the lab for life threatening emergencies telephone the transfusion laboratory

If further platelets need to be ordered:  
Blue light delivery time: 1 hour  
Standard delivery time: 2 hours

**Urgent Prothrombin Complex Concentrate (PCC) (for reversal of warfarin)**

**ED patients:**  
Quick reference guide can be found on Staffnet Departments > Blood Transfusion > Policies or follow the Critical Clinical Links (Staffnet front page) and click Clinical Emergency Information

**Do not delay in administering this product**  
In patients with life threatening bleeding or head injury or who require emergency surgery, PCC should be administered before INR results are available

**Supply of PCC in the ED Blood Fridge**  
Please inform transfusion laboratory if PCC has been used so that stock can be replenished

**Follow the Massive Haemorrhage Pathway (See Blood Transfusion pages on Staffnet)**

Dial xxxx

State 'massive haemorrhage adult / child & location'  
Request emergency response porter to attend clinical area (if a sample needs to be collected) or go to lab (if no sample and blood already available in lab for collection)  
Stay on line and you will be put through to transfusion lab  
State emergency blood requirements and patient's details and the weight if a child

**Wards:**

Please contact haematology registrar for advice on indication and dosing

**Do not delay in administering this product**  
In some patients that are bleeding, PCC is required before INR results are available

**Quick reference guide can be found on Staffnet Departments > Blood Transfusion > Policies**  
Order PCC from lab via CWS and telephone call to the transfusion laboratory

Complete the request form and Fax the form to the lab on xxxxx

**Group specific uncrossmatched blood**

will be available 30 mins after sample arrives in lab

**Massive haemorrhage pack 1**

Comprises:  
4 units red cells  
4 units FFP  
(Platelets are not included in MHP1 unless requested)

If you need blood immediately, send a member of the team to collect emergency Group O Negative blood from the nearest blood fridge

**Emergency O Negative locations:**

Adult Emergency Department  
1<sup>st</sup> Floor theatres  
Central Delivery Unit – Adult and Neonates  
Paediatric Theatre  
Paediatric Emergency Department

**Emergency Transfusion**

**Urgent Platelets for urgent management of thrombocytopenia**

**Procedure for emergency blood collection:**

Massive Haemorrhage: ring xxxx and you will be allocated an emergency response porter


**Urgent blood collection:** This may be when the massive haemorrhage pathway is not necessary but clinically you cannot delay in sending for blood/blood components/products via the routine collection route. You must confirm the location of the components and can then phone the portering team directly on xxxxx

**Transfusion laboratory ext xxxx**

**'Out of hours' bleep xxx**

**Massive haemorrhage activation: xxxx**

**Urgent blood collection: xxxx**



# 11b Avoidable Transfusions n=114 (n=116 in 2015)

## Definition:

Where the intended transfusion is carried out, the blood/blood component is suitable for transfusion and compatible with the patient, but where the decision leading to the transfusion is flawed. This includes transfusions based on poor knowledge, communication failures, incorrect decisions or poor prescribing.

## Key SHOT messages

- Transfusion can usually be avoided in iron, B12 and folate deficiency. Oral iron for iron deficiency is usual, however, where this cannot be tolerated, single dose intravenous (IV) iron is safe and very effective, and is now a recommended treatment for iron deficiency (Auerbach and Deloughery 2016) particularly before surgery (NICE 2015). Anaphylaxis may occur but is uncommon with currently available preparations. Adrenaline should be available where IV iron is used (McCulley et al. 2016). B12 and folate deficiency should be treated with the missing vitamin
- It is important to ask patients about their beliefs (religion) to avoid transfusion of blood components to those to whom they are not acceptable, particularly Jehovah Witnesses
- Group O D-negative red cells are not safe for everybody particularly patients with irregular antibodies. They will always be incompatible for patients with anti-c. If the emergency is so great that there should be no delay, the consultant in charge of the patient should make the decision. The patient should not die from exsanguination. See SHOT Bite 8 available on the SHOT website (<https://www.shotuk.org/wp-content/uploads/SHOT-Bites-No8-Massive-Haemorrhage-Delays-1.pdf>). If the antibody screen subsequently shows that incompatible red cells have been transfused, discuss with a haematologist whether to give IV methylprednisolone 1g and/or intravenous immunoglobulin (IVIg) cover. In addition, follow up and observe for haemolysis including deterioration in renal function and further alloimmunisation
- Unexpected thrombocytopenia should always prompt film examination and review of previous results. Biomedical scientists should not release results which they know or suspect to be inaccurate. Clinical staff should make a diagnosis before transfusing platelets as there may be specific contraindications

## Overview

There were 11 deaths in this group only one of which was possibly related to the transfusion. No instances of major morbidity were recorded although there was one case of transfusion-associated circulatory overload which is reported in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO).

The age range was from one day to 94 years.

This section includes avoidable use of emergency O D-negative blood where group-specific or crossmatched blood was readily available for the patient. Three cases are reported in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO).

Jehovah Witness 5  
 Haematinics 8  
 Avoidable O neg 18  
 Other 86

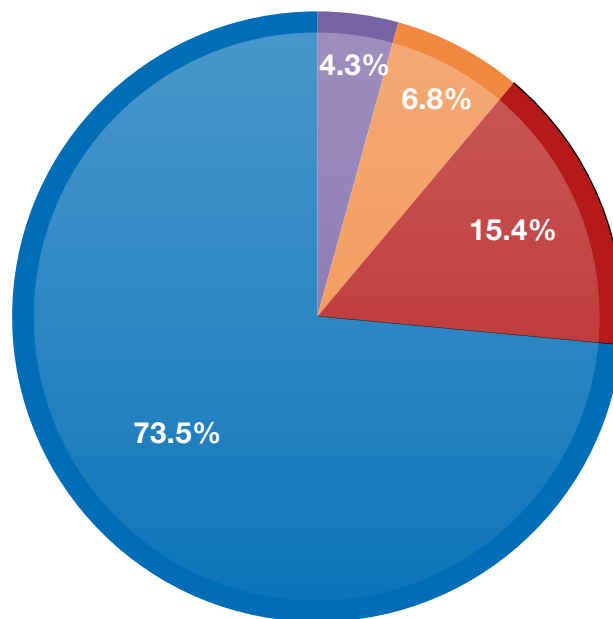


Figure 11b.1: Reasons for avoidable transfusions n=117 (3 cases added from TACO\*)

\*Additions from TACO: megaloblastic anaemia n=1; inappropriate FFP for anticoagulant reversal n=2

## Deaths n=1

### Case 11b.1: Unnecessary use of two units where one would do, associated with cardiac decompensation

A 94-year-old lady attended the ED unable to manage at home and with malnutrition. Her Hb was 76g/L and she had a low potassium. She had no symptoms or signs of anaemia or bleeding. The ED junior doctor wrote a care plan to transfuse two units, correct potassium and transfer to the elderly care unit off site. The patient weighed 50kg. The transfusion plan was not reassessed at the treating unit. Following transfusion the Hb was 160g/L. More than 24 hours post transfusion the patient developed fast atrial fibrillation (AF), cardiac failure and subsequently died. The transfusion was considered possibly contributory but there were other medical factors.

The reporter considered that one unit at a time with a check Hb would have been appropriate given her age, weight and additional risk factors. Poor communication between the two locations was identified as a factor. Although medical and nursing staff at the community hospital receive annual blood transfusion training from the transfusion practitioner, it was noted before this incident that there was generally poor attendance by doctors, which had been notified to the matron.

### Case 11b.2: An avoidable transfusion (where specific requirements were not met) to a transplant patient who then needed repeat stem cell harvests

An 11-year-old girl with a recurrent malignant tumour was scheduled for autologous haemopoietic stem cell transplant (HSCT). She was admitted on a Sunday evening and an irradiated unit of red cells ordered for the next day. A different BMS issued two units of non-irradiated red cells electronically (despite the need for irradiation noted in three places on the request). These were transfused with a two-person check at the bedside in relation to two stem cell collections on the Monday and Tuesday. When it was noted that these were non-irradiated cells, the stem cell harvests had to be wasted and the child underwent repeat harvesting six weeks later following further stimulation with granulocyte-colony stimulating factor.

Another instance was reported under specific requirements not met (SRNM). A 4-year-old child with neuroblastoma received non-irradiated platelets three days prior to stem cell harvest. At the time of autologous harvest the specialist nurse noted that red cells provided to prime the machine were not irradiated. These units were returned to the hospital transfusion laboratory (near miss) and irradiated red cell units issued. It was then discovered that non-irradiated platelets had been transfused three days previously.

### Red cell transfusion to Jehovah Witness patients n=5

These were emergency (1) or urgent (4) transfusions to older patients (62, 72, 83, 90 and 94 years of age) who were not always able to understand (language or clinical state) or give consent. In some cases the information was available in the case notes but not seen by the staff or prescriber in an urgent situation. One patient had been in hospital for 3 months; another was transferred from a care home where the information about his religion was available. Another report commented that staff find it intrusive to ask patients about their religion and that this box on the admissions form is frequently not completed. An audit noted that religion had been recorded as 'unknown' in 31% of admissions and that this is a 'routine violation'.



#### Learning point

- Clerical staff need to understand the importance of recording a patient's religion and realise how this may affect their management

### Transfusion of patients with haematinic deficiency n=8

There were 2 cases with megaloblastic anaemia and 6 with iron deficiency. One of these was a postnatal woman with Hb 78g/L not tolerating oral iron and the transfusion was prescribed by the general practitioner in the community. There is evidence that IV iron is more effective than oral iron for treatment of fatigue after postpartum haemorrhage (Holm et al. 2017).

#### Case 11b.3: Inappropriate treatment of megaloblastic anaemia

*A haematology registrar authorised transfusion of four units to a 51-year-old woman with megaloblastic anaemia due to lack of knowledge. Her Hb was 42g/L and she was generally unwell with development of sepsis.*

This case demonstrates a surprising lack of knowledge. Patients with megaloblastic anaemia are best treated with haematinics to which they respond rapidly. Transfusion is rarely required and should be limited <http://www.transfusinguidelines.org.uk/transfusion-handbook/8-effective-transfusion-in-medical-patients/8-1-haematinic-deficiencies>. Excessive transfusion puts the patient at unnecessary risk; patients with B12 deficiency have increased mortality from pulmonary oedema compared with those with iron deficiency (Lawson et al. 1972). Cardiac muscle is also B12-deficient. Another patient with megaloblastic anaemia who was transfused developed TACO and is discussed (and counted) in Chapter 18b, Transfusion-Associated Circulatory Overload (TACO).



#### Learning point

- In a normal setting haematinics, in particular oral iron for iron deficiency, can be effective. However, where this cannot be tolerated, single dose intravenous (IV) iron is safe and very effective, and is now a recommended treatment for iron deficiency (Auerbach and Deloughery 2016) particularly before surgery (NICE 2015). Anaphylaxis may occur but is uncommon with currently available preparations. Because of this risk, adrenaline should be available where IV iron is used (McCulley et al. 2016). B12 and folate deficiency should be treated with the missing vitamin



## Avoidable use of emergency O D-negative units n=18

Sixteen of these were either emergency (n=13) or urgent (n=3) transfusions. The priority was not known for two cases. The majority were in theatre (n=7), the ED (n=4) and wards (n=4) with two in intensive care units and one in a neonatal unit, Case 11b.5 below.

The reasons for these transfusions were:

- Delayed provision of correct components due to earlier errors n=5
- O D-negative units used when crossmatched (n=6) or type-specific (n=2) units were available n=8
- Other n=5

### Case 11b.4: Obstetric patient with anti-Jk<sup>a</sup> transfused emergency O D-negative unit that might have been incompatible

*A woman presented with an antepartum haemorrhage and required urgent caesarean section. The transfusion laboratory was advised that red cells would be required. The first blood sample was haemolysed, and the second sample received 30 minutes later had an incorrect date of birth. The woman had a known anti-Jk<sup>a</sup> so theatre staff were advised that the emergency O D-negative units may not be compatible. Due to misunderstanding of the consultant haematologist's advice one unit of emergency O D-negative red cells was used one hour after the initial telephone call. Crossmatched blood was available within 30 minutes of this. Fortunately, as 76% of Caucasian donors are Jk(a+), retrospective matching of this unit confirmed it was compatible. Three units of red cells were transfused in total.*

When a patient with known antibodies requires emergency transfusion this should, if possible, be authorised by a consultant haematologist. It may be possible to rapidly select a compatible unit from the transfusion laboratory as several additional antigen specificities are noted on the labels (depending on the antibody). In this instance there was miscommunication between the consultant haematologist and the anaesthetist as to whether this blood was to be given and whether it was needed in an emergency. The consultant haematologist had advised that the blood could only be used in an emergency but this had been misinterpreted as him giving the go ahead to transfuse the unit.

This case is a reminder that group O D-negative red cells are not safe for everybody particularly patients with irregular antibodies. They will always be incompatible for patients with anti-c and laboratory staff can provide a more suitable unit very quickly. If the emergency is so great that there should be no delay, the consultant in charge of the patient should make the decision. The patient should not die from exsanguination. This is discussed in SHOT Bite 8 available on the SHOT website (<https://www.shotuk.org/wp-content/uploads/SHOT-Bites-No8-Massive-Haemorrhage-Delays-1.pdf>).

### Case 11b.5: An infant with haemolytic disease of the fetus and newborn (HDFN) due to anti-c was transfused with emergency O D-negative red cells

*A pregnant woman presented at 39 weeks because of reduced fetal movements. She was sent home, but was found to have new anti-c. She was readmitted and underwent emergency section later that evening. The baby was unwell, Hb 65g/L and was transfused with emergency O D-negative blood. The maternity staff had not handed over to neonatal unit staff that the mother had anti-c. The baby then received exchange transfusion with appropriate red cells.*

#### Learning point

- Group O D-negative red cells are not safe for everybody. They may or may not be compatible with other irregular antibodies and are not compatible with anti-c which is a risk in pregnancy and may result in haemolytic disease of the fetus and newborn (HDFN)

Generally (where there are no known irregular antibodies), use of emergency O D-negative units has a low risk of adverse outcomes and transfusion should not be delayed in an emergency. If the antibody screen subsequently shows that incompatible red cells have been transfused, discuss with a haematologist whether to give IV methylprednisolone 1g and/or IVIg cover. In addition, follow up and observe for haemolysis including deterioration in renal function and further alloimmunisation.



### **Case 11b.6: Avoidable transfusion of O D-negative units to a pregnant patient with sickle cell disease due to misunderstanding**

*A pregnant woman known to have sickle cell disease with a low Hb (69g/L) (normal for her) was taken to theatre. She was not actively bleeding. The doctor wanted two units of O D-negative blood for the patient and did not want to wait for crossmatched units. The first unit was started but was stopped by a haematology registrar after approximately 20mL had been transfused. She did not need transfusion at all.*

The use of O D-negative rather than an appropriately selected phenotyped unit could have resulted in alloantibody formation. The patient did not require any blood following the surgery.

### **Avoidable transfusion of platelets n=23**

The reasons included inaccurate results: 14/23 had wrong full blood count (FBC) results; 7/14 had platelet clumping on the film which had not been detected prior to release of the FBC result; in one case a flag on the LIMS was ignored. Four other samples were clotted, one transfusion was based on the result from another patient and reasons were not given in two. Clinical indications for at least six of these transfusions were not justified and were against platelet transfusion guidelines.



#### **Learning point**

- Unexpected thrombocytopenia should always prompt film examination and review of previous results. Biomedical scientists should not release results which they know or suspect to be inaccurate. Clinical staff should make a diagnosis before transfusing platelets; there are three conditions where platelet transfusions should not be given (immune thrombocytopenia, heparin-induced thrombocytopenia and thrombotic thrombocytopenic purpura)

### **Miscellaneous n=3**

Three patients received inappropriate transfusions due to failure of patient identification, being identified only by their bed number.

#### **Case 11b.7: Avoidable transfusion where patient identified by bed number**

*A 60-year-old man received red cells as a result of a prescription based on a FBC result from another patient. The patient's bed number was used to communicate which patient needed a transfusion. However, the patients' beds had changed. An incorrect patient was crossmatched and prescribed two units of blood. This patient was then given one unit of red cells, but when the error was recognised no further blood was given.*

### **Near miss avoidable cases n=4**

There were 4 near miss cases related to avoidable transfusions. These included 2 requests based on erroneous results, 1 FBC wrong blood in tube (WBIT), and 1 where the transfusion was not prescribed.

### **Information technology (IT)-related avoidable transfusion cases n=6**

#### **Transfused on the wrong result n=6**

IT systems or equipment failure contributed to the following unnecessary transfusions.

In three patients the platelets were low due to clumping or clotting but these spuriously low results, which should not have been transmitted to the ward results enquiry system, resulted in patients being given unnecessary platelet transfusions. On another occasion a short neonatal coagulation sample gave an incorrect fibrinogen result and cryoprecipitate was given unnecessarily. Another patient was transfused based on a wrong Hb following an autologous stem cell harvest where the timing of the sample was not clear.

## Commentary

It is surprising that patients with megaloblastic anaemia were transfused as this carries a particular risk of TACO due to cardiac dysfunction. Low platelet counts should always be investigated, initially by examination of a film to confirm that this result is not due to clumping. It is important to make a diagnosis of thrombocytopenia as there are conditions where platelet transfusion is inappropriate (e.g. immune thrombocytopenia) or contraindicated (thrombotic thrombocytopenia purpura and heparin-induced thrombocytopenia).

Group O D-negative red cells are not safe for everybody, particularly those with anti-c and other irregular antibodies. The transfusion laboratory may be able to immediately issue more appropriate units where the antibody is known.

# 11C Under or Overtransfusion n=21

Eleven of these were children under the age of 16 years (6 less than a year of age), 9/11 were transfused excessive amounts of red cells or platelets (based on a wrong weight or wrong calculations) and two received less than planned (a one-unit exchange transfusion where only one suitable donation was available, and one error in the calculation for the infusion pump).

Ten adults received inappropriate amounts: 5/10 received inadequate amounts of FFP. Another was given excessive cryoprecipitate because a consultant haematologist (locum) did not accept advice that the current packs of cryoprecipitate are pools from 5 donations and prescribed 10 bags (equivalent to 50 single donor units).

Four adult patients received excessive transfusion of red cells. One of these was an elderly patient with a haematological condition who was transfused regularly over several months without checking Hb measurements and who developed iron overload.

## Near miss incorrect volume cases n=3

There were 3 near miss cases related to incorrect volumes. These included 2 where the incorrect volume was requested, and 1 case where an incorrect dose was prescribed. All 3 patients were babies under 6 months old, that could have been overtransfused.

## Information technology (IT)-related undertransfusion cases n=1

### Case 11c.1: Undertransfusion because blood label specification was incorrect

*A neonatal exchange transfusion was required because of maternal red cell antibodies causing haemolytic disease of the fetus and newborn (HDFN). The volume required to undertake the exchange was calculated by the clinical area and this amount was ordered from the transfusion laboratory. Unfortunately, when the unit was re-processed by the Blood Service to provide the correct specification for the procedure, the initial volume was printed on the label, not the new (lower) volume with the result that the neonate received an exchange transfusion with insufficient blood.*

# Incidents Related to Prothrombin Complex Concentrates (PCC) n=10

# 11d

Ten cases related to PCC alone. A further 2 cases also involved delays of other blood components and have been counted in the numbers in the section on delays, however, all 12 cases are described in this section.

## Key SHOT messages

- Delay in administration of prothrombin complex concentrate (PCC) for bleeding, particularly intracranial haemorrhage, puts patients at risk
- PCC is a blood product which should be carefully prescribed to ensure that the treatment is appropriate and traceable
- Junior medical staff should be trained in the indications for and use of PCC

Twelve cases were reported, 6 with delayed administration, 3 avoidable infusions, 2 that were given to the wrong patients, and one with misunderstanding (Case 11d.5 below). In two instances PCC was used because vitamin K was not available. Two cases had delayed administration due to inadequate supplies in the hospital. Several of the reported cases demonstrate delay in prescription, confusion about where to prescribe, delay in release from the laboratory with consequent excessive interval between decision and treatment in vulnerable elderly patients (8/12 aged >70 years) on warfarin in emergency settings. PCC should be administered immediately (NICE 2015) and certainly within an hour of the decision being made, particularly in cases of intracranial haemorrhage (ICH) or major bleeding. A research study from Germany (19 centres) noted reduced rates of haematoma enlargement in ICH (853 cases analysed) where the INR was reduced to <1.3 within 4 hours of admission (Kuramatsu et al. 2015). A simplified dosing algorithm was associated with more rapid international normalised ratio (INR) reversal in a small series using a fixed low dose of 25IU/kg (Appleby et al. 2017).

Many patients who need anticoagulation are now being treated with direct oral anticoagulants (DOAC). While there is some evidence that PCC may be of benefit in a bleeding emergency (Makris et al. 2013; Makris 2014; Keeling et al. 2016), specific antidotes are becoming available. In particular idarucizumab is a specific reversal agent for dabigatran (Glund et al. 2015; Pollack et al. 2015). This is licensed and should be available in any hospital likely to treat such emergencies. Reversal agents for the anti-Xa inhibitors (such as rivaroxaban) have been developed and are expected to be licensed soon (Connolly et al. 2016a; Connolly et al. 2016b).

### Case 11d.1: Delay in administration of PCC to a patient with ICH (1)

*A 77-year-old man on warfarin had ICH confirmed on a computerised tomography (CT) performed at 20:26. PCC was requested at 22:15 but not issued until 23:06; collected by the ward at 23:50 and given at 00:05, a delay of about 3.5 hours. The INR was repeated at 01:00 and recorded as 1.4. The laboratory standard operating procedure (SOP) has been revised.*

### Case 11d.2: Delay in administration of PCC to a patient with ICH (2)

*An elderly man on warfarin suffered a fall resulting in an ICH (INR 2.8). He was prescribed 3000IU of PCC but only 1000IU was given initially. Further stock was obtained from another hospital and given 4.5 hours later. He recovered and survived. The PCC stock had not been re-ordered when getting low. As a result of this incident the base stock level was increased and an increased number of staff were authorised to reorder it.*

### Case 11d.3: Communication issues cause delay in release of PCC

*A patient was in theatre for a heart transplant. The consultant anaesthetist requested PCC for emergency reversal of warfarin. The BMS on duty asked that this be authorised by the haematology registrar. This registrar cover is provided by another organisation, which often results in delays in communication. The request for PCC was appropriate, and according to the laboratory SOP, authorisation by a haematology doctor was not required. Thus the PCC should have been issued in a matter of minutes, but as a result of delays trying to make contact with the haematology team the issue was delayed by 30 minutes. The BMS on duty was relatively new to the department, having previously worked in an organisation which required authorisation of PCC by the haematology team.*

The turnaround time for patients undergoing transplantation (being informed, admitted and proceeding to surgery) is very short so that there was unlikely to be time to plan warfarin reversal in advance.

### Case 11d.4: Administration of PCC to the wrong patient

*A request form for PCC was completed for the wrong patient. The product was issued by the laboratory for the patient on the request form but was given to a different patient (who was the intended recipient) by the anaesthetist despite all paperwork and labels having details for the patient on the request form.*

### Case 11d.5: Misunderstanding of the indications for and use of PCC

*A 66-year-old lady was readmitted via the ED 7 days after total abdominal hysterectomy and salpingo-oophorectomy for malignancy. She had developed postoperative pulmonary embolism and was on warfarin for this. PCC 2750IU was given prior to theatre (for a second look) to reverse the warfarin which was stopped. Postoperatively she was treated with low molecular weight heparin. The following day a junior doctor requested further PCC and was informed by laboratory staff that the patient had had a dose the day before to reverse the warfarin. The doctor stated he had discussed it with the haematologist who agreed. A dose of 3000IU PCC was collected but 5 days later was found in the patient's drawer. The transfusion practitioner discussed the incident with the consultant haematologist who stated he was not informed of the full facts.*

This alerted ward and department managers to ensure that their staff are up to date with transfusion training including giving information as handouts about PCC. Blood transfusion is now on the reporting organisation's training matrix and is updated monthly with reports sent to managers and clinical leads.

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# Reflections on Blood Component Wastage in the Emergency Department in the UK

*Author: Rangaswamy Mothukuri*

Blood component transfusion is a very important part of resuscitation of critically unwell patients. The indications for blood transfusion range from major trauma needing a massive transfusion, upper gastrointestinal (GI) bleeding, lower GI bleeding, haemoptysis, obstetric emergencies, catastrophic bleeding from tonsillectomy etc.

One of the key areas in hospitals requiring blood components on a regular basis is the emergency department (ED). Many factors lead to blood components wastage for example unnecessary transfusion, incorrect indications, blood not being returned to the refrigerator within thirty minutes. The Annual SHOT Report for 2015 (Bolton-Maggs et al. 2016) included 3288 reports of adverse events relating to transfusion of which 77.7% had errors as an underlying cause. The complicating factor in the ED is the fact that on many occasions, there is either very little history of what is going on and/or minimal warning of the patient arriving to the ED. In these situations, whenever blood is requested urgently or as part of the major haemorrhage protocol (MHP), on most occasions, the blood is used appropriately but given the complexity of the situation and resuscitation of critically unwell patients, sometimes blood gets wasted. This adds not only to the financial burden to the healthcare but also raises an ethical issue about the wastage of blood which is generously and willingly donated by people. 'Blood cannot be made, it has to be donated' (from a talk by Alister Jones 2014).

Over the years there has been a significant improvement in the practice of blood component usage in hospitals mainly due to teaching and training of healthcare professionals highlighting the importance of the blood component wastage. Other changes include the introduction of MHP in many hospitals. Despite those measures, it is well-known that there is still a significant amount of blood component wastage. It is acceptable that some blood component wastage will occur for unavoidable reasons, for example if the patient dies before components are administered. However, there is room to improve avoidable wastage. NHS Blood and Transplant (NHSBT) provide wastage target levels to help hospitals measure their performance. This is measured as 'wastage as a percentage of issues' (WAPI) and is set for red cells at <2.3% and platelets at <3.8%. According to Blood Stocks Management Scheme (BSMS) data, over a 2-year period almost 10,000 units were taken to clinical areas but not used and then wasted (BSMS 2014). The most common reason for red cell wastage in the clinical area was given as 'out of temperature control outside of the laboratory.' For platelets the reasons were components 'ordered (medically or surgically) but not used.' Further avoidable wastage occurred for laboratory reasons.

A retrospective case note review of patients requiring blood component usage in one ED prior to 2007 (Kelly et al. 2013) demonstrated that out of the total number of blood components requested, only 66.4% were transfused, 24% were recycled, 8.7% were discarded and 0.9% were unaccounted for. Following the study, various improvement measures were introduced including staff education, use of online e-learning modules, having a dedicated ED transfusion consultant and an ED transfusion link nurse together with availability of an ED resuscitation refrigerator. Their practice was reviewed again in 2011 and they demonstrated a significant reduction in the ordering of blood components by 64% and a 96% reduction in the unaccounted units.

Another group conducted a retrospective case note review of blood component usage and wastage over a 12-month period in their ED in 2007 (Beckwith et al. 2010). They showed that out of all the blood components ordered only 39.5% were used, 47.8% were recycled, 3.2% wasted and 9.5% were unaccounted for.



A review of literature identified various studies looking at blood component wastage in hospitals but very few specifically focussing on the ED. There have been significant improvements in dealing with blood wastage but reviewing current transfusion practices and blood component usage and wastage in various ED in UK will give a better and wider picture of the scale of the problem. Various suggestions for improvement of practices to avoid wastage already exist and could be better applied if we can demonstrate the seriousness of the situation.

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# 12 Near Miss Reporting (NM) n=1283

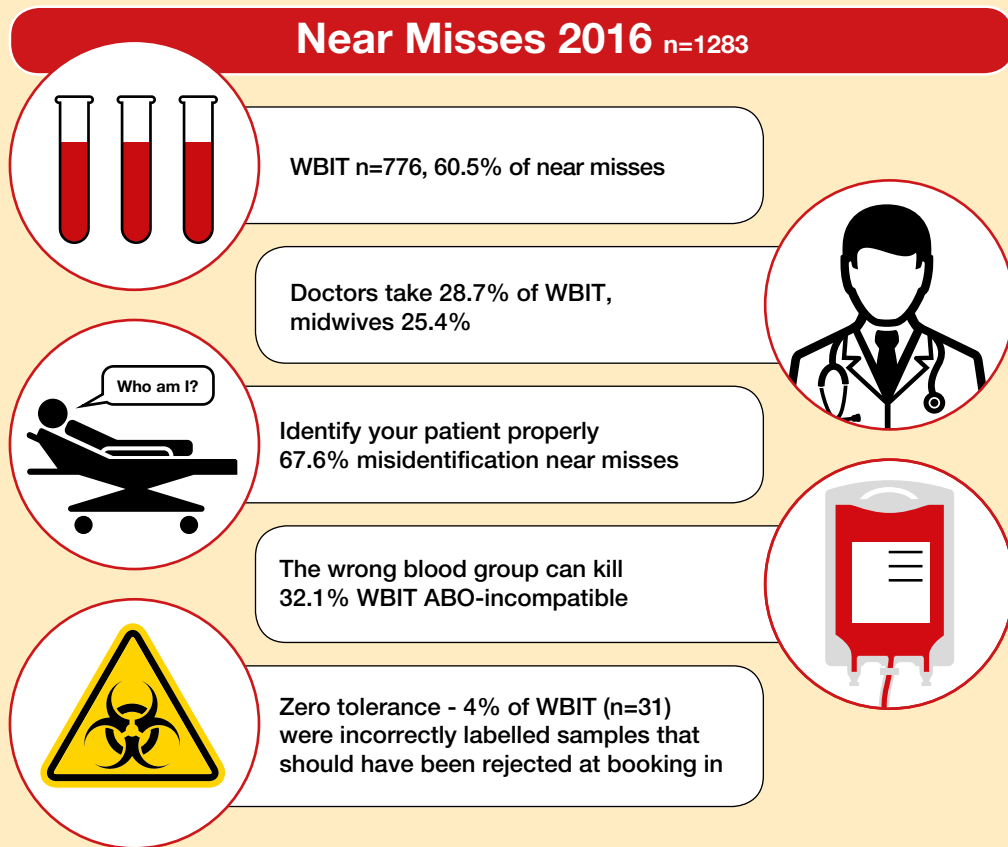
Authors: Alison Watt and Katy Cowan

## Definition:

A 'near miss' event refers to any error which if undetected, could result in the determination of a wrong blood group or transfusion of an incorrect component, but was recognised before the transfusion took place.

The number of reports of near misses continues to increase, n=1283 from n=1243 in 2015. It is important to learn from near miss cases and SHOT strongly encourages reporting of these incidents.

## Key SHOT messages



WBIT=wrong blood in tube

Figure 12.1:  
Near miss key  
messages

## Discussion of near miss errors in other categories

Full discussion of these cases can be found in each relevant chapter. Table 12.1 details the subcategorisation of near miss events according to SHOT definitions.

Category of outcome had the near miss incident not been detected		Discussed in chapter	Number of cases	%
Incorrect blood component transfused (IBCT)	Wrong component transfused (WCT)	Chapter 10	881	68.7
	Specific requirements not met (SRNM)	Chapter 10	121	9.4
Handling and storage errors (HSE)		Chapter 9	124	9.7
Right blood right patient (RBRP)		Chapter 8	121	9.4
Adverse events related to anti-D immunoglobulin (Anti-D Ig)		Chapter 14	29	2.3
Avoidable, delayed or undertransfusion (ADU)		Chapter 11	7	0.5
<b>Total</b>			<b>1283</b>	<b>100</b>

**Table 12.1:**  
Possible outcomes from near miss incidents if not detected

## Near miss wrong blood in tube samples (WBIT), caution with testing rejected samples

The largest number of near misses in a single category continues to be WBIT incidents 776/1283 (60.5%).

Some reporters are submitting cases where they have detected a WBIT when there is evidence that the sample should have been rejected at the booking-in stage, 31/776 (4.0%) of all WBIT. These incidents have been accepted as SHOT-reportable, because the laboratory staff have tested and confirmed the sample as WBIT, not simply a labelling error, but this practice of testing inadequately or poorly labelled samples should be discouraged. Zero tolerance (i.e. some error in the labelling) requires that such samples should be rejected immediately at booking-in. Laboratory staff would need to be very careful if testing a sample that should have been rejected, because of the risk of those tests becoming accidentally validated and used inappropriately as historical results for the wrong patient.

### Learning point

- Full implementation of zero tolerance requires that all incorrectly or incompletely labelled samples should be discarded without testing and this applies to all pathology samples, not only those in transfusion



## ABO incompatibility prevented by detection of near miss incidents n=264

Near miss incidents could have resulted in ABO-incompatible red cell transfusions. In a total of 881 near miss potential incorrect blood component transfused (IBCT) cases, 264/881 (30.0%) would have resulted in an ABO-incompatible transfusion. The highest risk error is one that results in group A red cells being given to a group O recipient, because anti-A titres tend to be higher than anti-B titres and the anti-A titre tends to be higher in group O subjects than group B (Klein and Anstee 2014). Half the ABO-incompatible near misses could have resulted in group A red cells being given to a group O patient (130/264, 49.2%). This is discussed in more detail in Chapter 3, Headline Data: Deaths, Major Morbidity and ABO-Incompatible Transfusions.

The majority of potential ABO-incompatible transfusions result from WBIT samples, 249/264 (94.3%). The 249 ABO-incompatible WBIT out of a total of 776 WBIT, means 32.1% of all WBIT incidents could have resulted in an ABO-incompatible transfusion. All but 4 of the total 264 ABO-incompatible near misses resulted from clinical errors.

Table 12.2:  
Cause of potential  
ABO-incompatible  
transfusions n=264

Cause of potential ABO-incompatible transfusions	Number of cases	%	
WBIT	249	94.3	Clinical error n=260
Component collection/administration error	9	3.4	
Sample error	2	0.8	
Wrong group component selected	2	0.8	Laboratory error n=4
Grouping/testing error	2	0.8	
<b>Total</b>	<b>264</b>	<b>100</b>	

The seriousness of the error is not determined by the patient outcome. A nurse was convicted of manslaughter in December 2016 after transfusing an ABO-incompatible red cell unit to a patient (TheLawpages.com, 2017). Any of the 264 near miss cases that were potential ABO-incompatible transfusions could have resulted in the same outcomes. Although criminal charges are seldom warranted, this case showed that such a result is possible. According to the concept of 'Just Culture' (Dekker 2012) staff members should not be punished unless there has been wilful violation or gross negligence. Full investigation of all contributory factors in each incident may be more beneficial than placing blame on individuals. Further information can be found in Chapter 6, Human Factors in SHOT Error Incidents where there is additional discussion of whether it is appropriate in some cases to score 10 for individual error and nothing for other contributory human factors such as environment, organisation or high level government factors (Case 6.1).

In 2016 SHOT included a question in the near miss reporting questionnaire to assess whether the introduction of a group-check policy as recommended in the British Society for Haematology (BSH) guidelines for pre-transfusion compatibility (BSH Milkins et al. 2013) is helping to detect WBIT. In 529/776 (68.2%) WBIT reports the hospital laboratory had a group-check policy in place, but 213/776 (27.4%) indicated there was no policy in place and 34/776 (4.4%) did not answer the question.

#### Case 12.1: Group-check policy detects original sample was of transfused blood, not patient's

*The first sample from an emergency department (ED) patient grouped as O D-negative and the second sample 30 minutes later showed mixed field O D-positive. The patient had been brought in by air ambulance and was given two units of O D-negative emergency blood in transit. Unfortunately there was no pre-transfusion sample taken by the helicopter emergency medical service (HEMS) staff. Subsequent samples taken in the intensive therapy unit (ITU) grouped as O D-positive (mixed field). The most probable cause of the discrepant blood group is that most of the original sample consisted of the emergency O D-negative unit that was being transfused instead of an uncontaminated sample of patient blood.*



#### Learning point

- It is important to obtain a pre-transfusion sample before giving an emergency blood transfusion, but if this is not possible, and a sample is obtained during the transfusion, it should be taken distant from the transfusion site and the laboratory should be informed

#### Value of historical samples

SHOT data from WBIT reports in 2016 show that 49/776 (6.3%) WBIT were historical samples. Although many of these historically incorrect samples were taken in the same patient episode or close to the repeat sample that demonstrated the error, the dates of historical WBIT errors were recorded as far back as 1995. Local group-check policies should consider the criteria for a valid historical record in that institution. An addendum to the BSH guidelines (BSH addendum 2015) for pre-transfusion compatibility procedures in blood transfusion laboratories includes a set of scenarios of possible combinations of historical and current samples that can be used to inform local policy in hospital transfusion departments and reference laboratories.

### Quality management systems

Quality management systems (QMS) and checking procedures can detect errors and prevent incorrect transfusions, but not all near miss incidents can be detected by the QMS. There was good fortune in the accidental detection of 291/1283 (22.7%) of near miss cases and 612/1283 (47.7%) were found as a result of testing anomalies, where detection is only possible if current results differ from a historical sample.

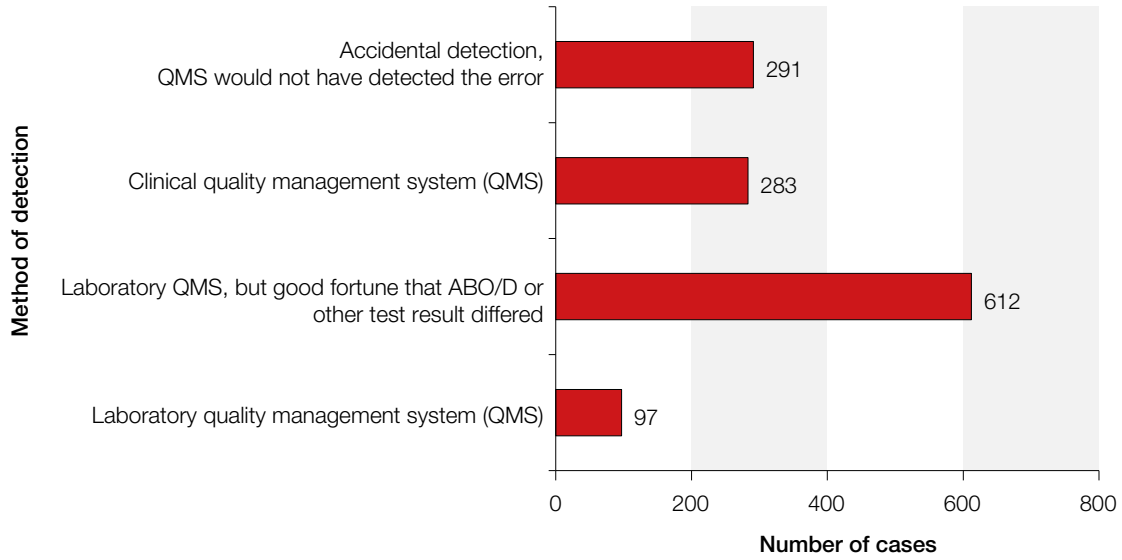


Figure 12.2: Near miss incidents – how are they detected?

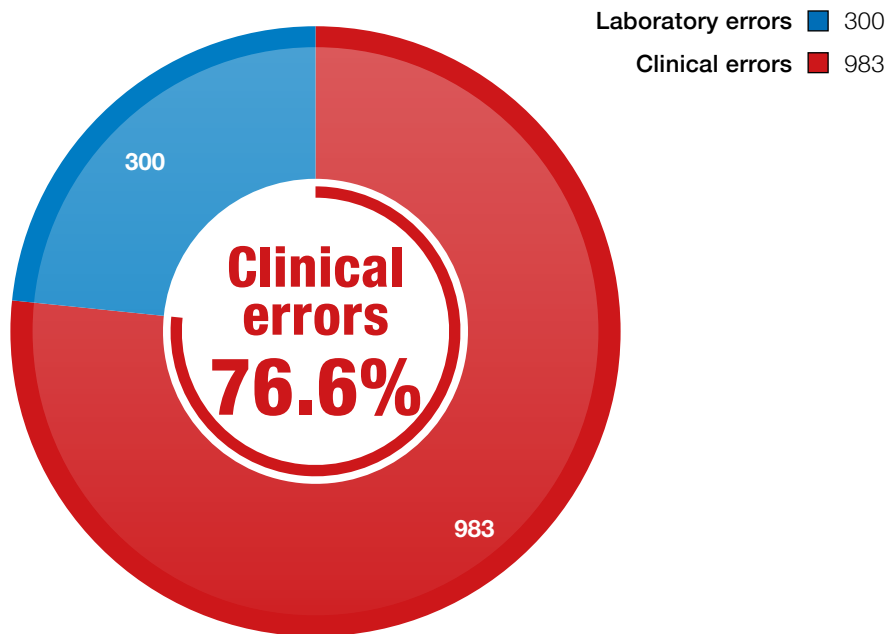
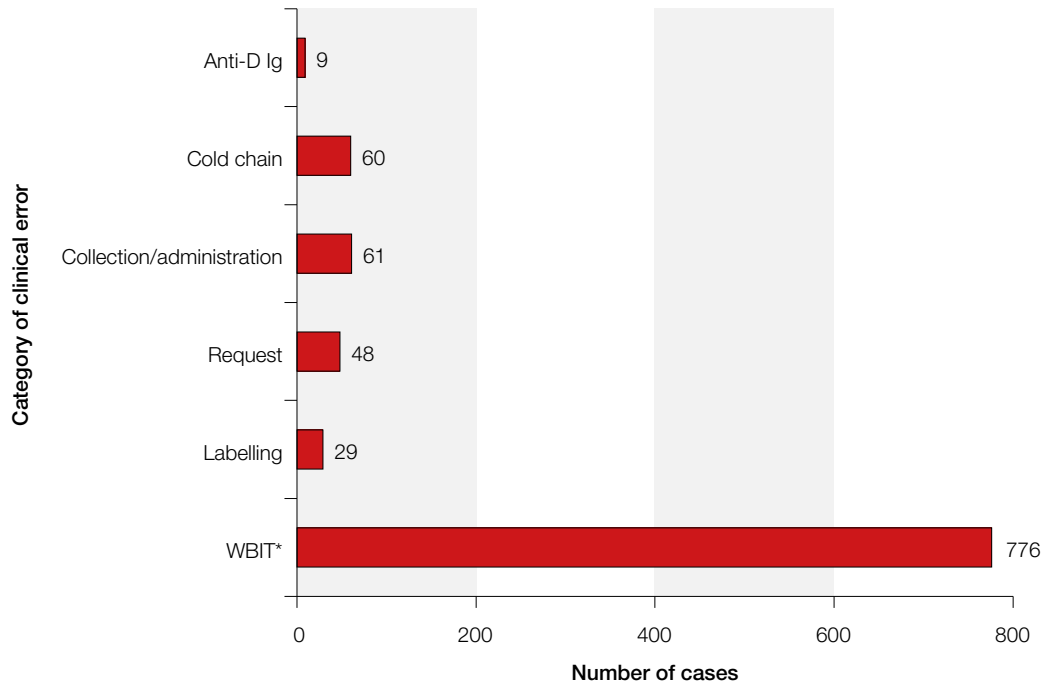


Figure 12.3: Number of near misses originating in clinical or laboratory area (total n=1283)

## Near miss clinical errors n=983

Figure 12.4:  
Near miss clinical  
errors according to  
category



\*Includes 1 full blood count (FBC) WBIT error where transfusion could have taken place based on an incorrect result

### Case 12.2: WBIT error for full blood count (FBC) sample fortunately results in no harm

A transfusion sample was labelled with the correct patient details and handwritten at the bedside, but the haematology and biochemistry samples were mislabelled with details from another baby who had the same surname and date of birth, but a different hospital number. The haematology and biochemistry sample labels were printed away from the patient using an electronic system and the doctor used the patient name rather than hospital number to search for details on the electronic system. The incorrectly labelled sample for FBC was found to have a haemoglobin (Hb) of 54g/L. Fortunately the correct baby was transfused.

### Wrong blood in tube (WBIT) n=776

#### Definition of wrong blood in tube incidents:

- Blood is taken from the wrong patient and is labelled with the intended patient's details
- Blood is taken from the intended patient, but labelled with another patient's details

#### Staff responsible for wrong blood in tube incidents

Denominator data have been supplied by the Oxford University Hospitals NHS Foundation Trust. Total Oxford samples n=14,678, in a 3-month period December 2016 to February 2017, population 670,000 in 2015. Doctors remain the staff group most likely to be responsible for wrong blood in tube errors, accounting for 28.7% (223/776) but this has fallen from 35.0% (273/780) in 2015. Midwives and doctors are over-represented when compared against the percentage of samples taken by those staff groups in the Oxford region.

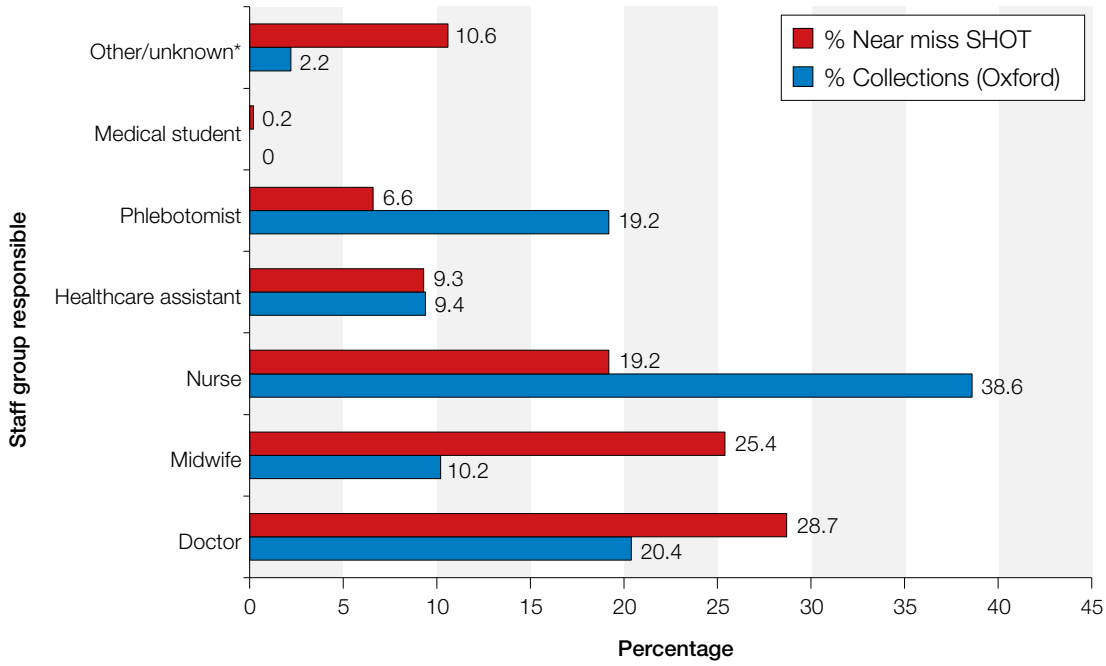


Figure 12.5: Staff responsible for taking the near miss WBIT sample

\*Includes historical WBIT incidents reported to SHOT where details are unknown  
 With thanks to Professor Mike Murphy and colleagues for supplying the Oxford data

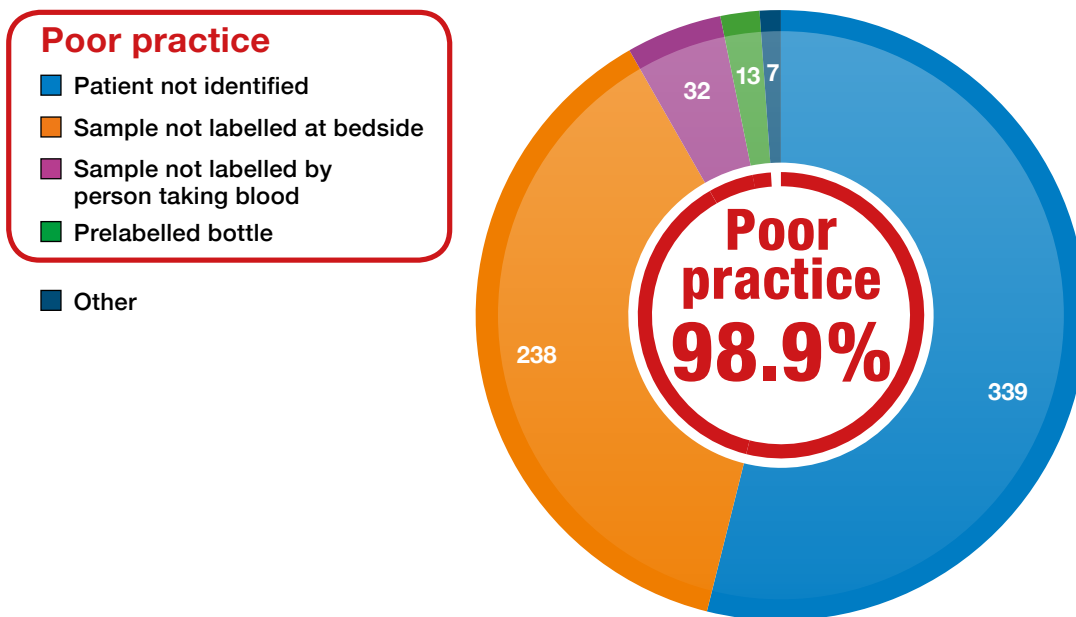


Figure 12.6: Practices leading to near miss WBIT n=629

The majority of WBIT samples result from failure to identify the patient correctly and labelling the sample away from the bedside, together 577/629, 91.7% (in 147 the procedures were not stated; these are not included in Figure 12.6). One way of reminding staff to complete the process correctly is the use of posters on the wards with the ‘sample circle’ promoted by Joy Murphy, a transfusion nurse practitioner, noting that unlabelled samples must not leave the sample circle.

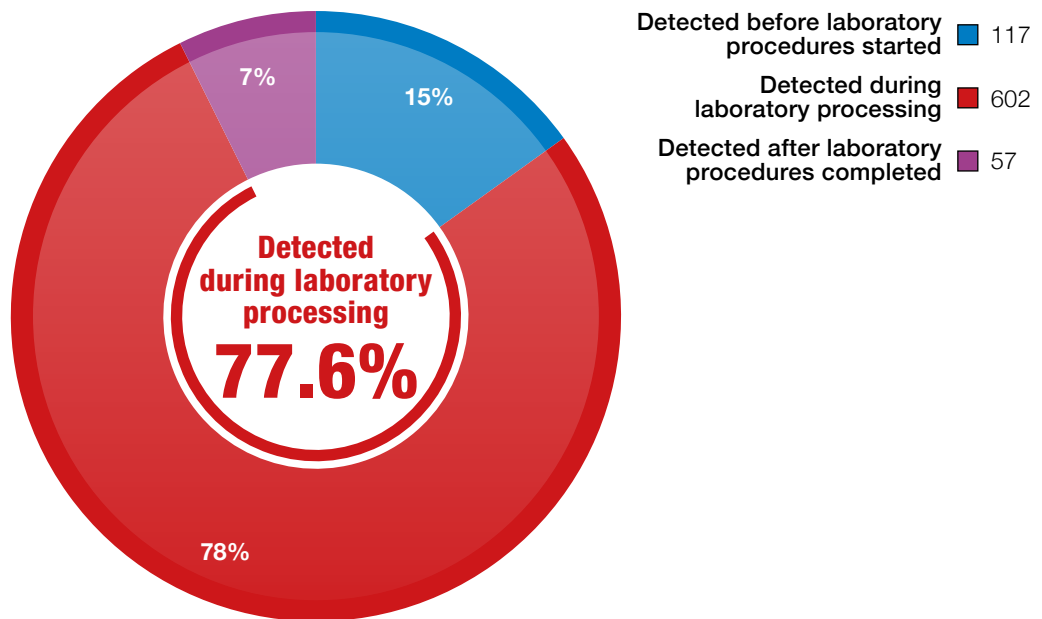
Figure 12.7:  
The sample circle



**All samples must be labelled at the bedside from the wristband details.  
Unlabelled blood samples **MUST NOT** leave the **SAMPLE CIRCLE**.  
Unlabelled blood samples outside the circle should be disposed of.**

The majority of WBIT are detected during laboratory testing, Figure 12.8.

Figure 12.8:  
Detection of near miss WBIT





## Near miss laboratory errors n=300

Please see Chapter 7, Laboratory Errors for further information on category of error.

### Near miss information technology (IT) errors

Case 12.3 was initially reported and included in the numbers for the 2015 Annual SHOT Report. The case is reported in full here as there are important learning points which have emerged after detailed analysis. This is a reminder that IT systems are not always as safe as users might expect, and that there may be a time delay in implementing the correction which was made in early 2017.

#### Case 12.3: Auto-validation by laboratory information management system (LIMS) assigns incorrect ABO group to the patient record

*A blood sample on a patient previously unknown to the transfusion laboratory was tested on the Galileo Echo analyser and, having required no manual editing, the test result was suitable for auto-validation so was exported to the CliniSys WinPath v5 LIMS. The result assigned to the patient record was B D-positive but the result produced and interpreted by the analyser was O D-positive. No blood transfusion was required so the patient came to no harm. This was extensively investigated by the LIMS provider and a notification issued to all users of the same software highlighting the potential, albeit very unlikely, whereby a patient's blood group could be transposed with the results of another patient, under a very specific set of circumstances and that there will shortly be a point upgrade to the software to resolve the issue and mitigate the risk.*

CliniSys state that 'The approved methodology to auto-validate a batch of blood group results from BT Analyser is to click the auto-validate button and wait until the queue is fully processed and the checking has completed'. They have discovered that 'should a user scroll down the queue, minimise the screen, or cause the validate grid to refresh in any way while the auto-validate process is still running, a patient's blood group *may* be written against the wrong patient record.' However they also noted 'that this has *only* been seen and recreated when a degradation in network connectivity and/or performance is experienced, hence the rarity of the occurrence'.

Due to the action taken by CliniSys, all transfusion laboratories using a specific version of their software have now been informed to take appropriate action to prevent any patient harm. However there are some learning points for all transfusion laboratories and the SHOT recommendation for software providers to work together with transfusion professionals to learn from errors and provide fit for purpose software is relevant to this case.

#### Learning points

- Implementation of the group check provides additional safety to prevent issue of wrong blood. The principle of the group check is to ensure correct patient identification but group check also detects discrepancy if the wrong sample is tested and, in this situation, the allocation of the wrong result to the patient record
- Previous blood grouping errors have been reported where the interface between the analyser and the LIMS transmits the wrong result and validation protocols can be used to test the integrity of interfaces. It is important to note this error is not due to the interface but due to interrupting an auto-validation programme which is much more difficult to validate unless there is an inbuilt check to read and compare the group with a historical group already assigned to that patient. The software upgrade provided in response to this error will include such a check but is not going to be effective in first-time patients

#### Case 12.4: Analyser error that could not be detected by quality management system

*A crossmatch was processed on the analyser, which gave the result as negative, i.e. compatible. Another biomedical scientist (BMS) put the same sample on the analyser a couple of hours later not realising the crossmatch had already been performed. The re-run of the crossmatch gave results as*



*positive i.e. incompatible. On review of both crossmatch results it was noted that on both occasions the unit was incompatible with the patient's plasma, but the analyser had incorrectly called the initial crossmatch compatible. This anomaly has been investigated further by the analyser manufacturer. They identified that the picture from the rear of the cassette gave a query (?) result, but the picture from the front had a value below the level to trigger a ? result. As a front-and-back average feature is used, and this average was below the threshold, the result was given as negative. A correction should follow in one of the next software versions and in the meantime results are being reviewed by a BMS prior to transmission from the analyser to the LIMS.*

## Further analysis of total near miss errors n=1283

Tables showing the subcategorisation of near miss errors consistent with those in previous Annual SHOT Reports (2010-2015) can be found in the supplementary information on the SHOT website [www.shotuk.org](http://www.shotuk.org).

## Commentary

The key messages are the same as previous years, with failure of correct patient identification as a common root cause of near miss cases 867/1283 (67.6%). WBIT incidents remain the most commonly reported near miss error and accounted for 776/1283 (60.5%) of all near misses in 2016. Many near miss incidents, particularly WBIT, are potential ABO-incompatible transfusions. In 2016 264/881 near miss IBCT could have been ABO incompatible (30.0%).

The practice of testing poorly labelled samples to confirm if they are WBIT is questionable and SHOT has previously recommended full zero tolerance for all pathology samples. There is a risk that test results on unacceptably labelled samples could be accidentally validated and used inappropriately as a historical result when the sample was from the wrong patient.

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 [Accessed 08 March 2017]

# Information Technology (IT) Incidents

# 13

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## Definition:

This chapter covers transfusion adverse events that relate to laboratory information management systems (LIMS) as well as other IT systems and related equipment used in the delivery of hospital transfusion services.

Cases selected include events where IT systems may have caused or contributed to the errors reported, where IT systems have been used incorrectly and also includes cases where IT systems could have prevented errors but were not used. Where the corrective and preventive action suggested by hospitals in response to errors included IT solutions, these have been included.

## Key SHOT messages

- **Knowledge and training** – IT systems can make transfusion safer by supporting and controlling clinical and laboratory tasks but they do not replace knowledge about the supported task and are only safe if timely and accurate training to undertake the role is provided. You can not rely on IT to replace knowledge – you need both
- **Leadership, supervision and personal responsibility** – Although procurement and implementation of new IT systems, or system upgrades, require the leadership of subject matter experts (SME) it should be the responsibility of managers and supervisory staff to ensure appropriate role-based training and for individuals to ensure that they are trained and confident in their use of systems, including a clear understanding of the limitations of these systems
- **IT, electronic systems and equipment ‘fit for purpose’** – The design and configuration of IT, and other electronic systems, has to meet current requirements and be flexible enough to take account of developments in blood safety and changes in practice, whether they be anticipated or unexpected. Analysis of SHOT errors has shown weaknesses in some systems and this information should be taken into account for the benefit of all when upgrading existing or developing new systems. There is a challenge for software and equipment providers to listen to and work with the UK transfusion community so that together we can maximize the promise of IT and electronic systems for patient benefit. Using alerts, warnings and flags as an example – we need to learn from what works well, share good practice and standardise
- **Sharing information** – Communication is critical to good care in transfusion practice but lack of connectivity and interoperability between IT systems repeatedly fails to enhance the potential benefits of secure electronic transfer of information. Any manual steps required to transfer or transcribe information introduce a source of error and potential delay. There could be, and should be, IT solutions to make test results and other information available between hospitals, between hospital and reference laboratories and also across country boundaries. This would improve the care of complex and shared care patients, and also improve the experience of patients who have repeated samples because their care is delivered in more than one healthcare setting



In 2016 there were 297 reported incidents of errors related to IT systems. The cases included are drawn from the other chapters of this report as shown in Table 13.1 and these are categorised in Table 13.2 according to the errors and the reason for the error based on the reporter's classification and the author's interpretation of the report. The commentary relating to these cases is included in the relevant chapters.

**Table 13.1:**  
Source of cases  
containing  
errors related  
to information  
technology

Error	2016
Incorrect blood component transfused (IBCT-WCT)	29
Specific requirements not met (SRNM)	161
Right blood right patient (RBRP)	57
Avoidable, delayed and undertransfusion (ADU)	26
Handling and storage errors (HSE)	3
<b>Total</b>	<b>276</b>
Anti-D immunoglobulin (Ig) errors (Anti-D Ig)	21
<b>Total including anti-D</b>	<b>297</b>

In 2016, 57.9% (172/297) of the IT incidents originated in the transfusion laboratory and 42.1% (125/297) originated in the clinical area.

Excluding the anti-D Ig cases and where the relevant information was provided by the reporter, the majority of incidents related to transfusion in adults (230/262 87.8%) with 20 cases in children under 18 years and 12 cases in neonates or infants. The incident involved red cells in 210/273, 76.9%, platelets in 25/273, 9.2%, FFP/cryoprecipitate in 23/273, 8.4% and multiple components in 15/273, 5.5% of cases where the component was stated. Most incidents were said to take place in normal working hours 138/178, 77.5%, but there were many cases where a specific time was not recorded. Where the urgency of the transfusion was stated 149/257, 58.0%, were classified 'routine', 80/257, 31.1% 'urgent' and 28/257, 10.9% 'emergency' cases.

## Deaths n=0

There were no transfusion-related deaths where IT systems contributed.

## Major morbidity n=3

There were two cases with major morbidity due to alloimmunisation in women of childbearing potential. These both developed anti-K as a result of transfusion of K-positive red cells. A third case suffered serious haemolysis due to anti-S where IT systems contributed.

## Minor or moderate morbidity n=6

There was an additional case of significant haemolysis in a solid organ transplant patient where IT systems contributed to moderate morbidity.

There were two cases classified as minor morbidity who were alloimmunised (anti-e and anti-c) but with no haemolytic transfusion reaction where incorrect use of IT systems contributed.

There were two delays where surgery was cancelled because blood components were not available (minor morbidity) and following another blood delay the patient died due to underlying injuries, not blood delay.

All the other cases did not result in any harm to the recipient of the components transfused.

## IT flags, alerts and warnings

Once again nearly half of the errors (48.2%, 133/276) related to IT systems can be attributed to the failure in some way of laboratory information management systems (LIMS) and electronic blood management systems (EBMS) to prevent wrong blood and missed specific requirements including 'right blood, right patient errors' where there was a discrepancy in one of the core patient identifiers but blood was still issued, collected, checked at the bedside and administered.

Whilst robust clinical systems for identifying patients and communicating their age- gender- or disease-specific requirements to the transfusion laboratory cannot be replaced with IT systems, it is disappointing that the functionality of these systems has not been standardised so that clinical and laboratory users can have the confidence that ABO-incompatible red cell transfusion will be prevented and that complex and vulnerable patients can receive blood components of the exact specification they require.

An example in 2016 was the introduction of hepatitis E virus (HEV)-screened components for allogeneic haemopoietic stem cell transplant (HSCT) and solid organ transplant (SOT) patients. This was widely discussed and debated before implementation and yet, at the point of implementation, not all LIMS systems were able to provide this new alert with the result that there were 23 cases where failure to use the LIMS correctly to flag these patients was the predominant cause of failure to provide HEV-screened components (21/23).

In previous SHOT reports, and at the SHOT symposia, we have been encouraged to learn as much from **what goes right** as well as learning from the relatively small numbers of human and system failures reported to SHOT. In this spirit we should critically review the methods for existing flags, alerts and warnings used by the software in clinical and laboratory use in the UK and decide what works best in different situations. It should no longer be acceptable to tolerate workarounds and patches that can solve one problem only to create another unanticipated effect.

## Recommendation

- Clinicians, laboratory scientists, information technology (IT) professionals and IT providers should work together to develop an industry standard for flags, alerts and warnings that prevent harm from wrong blood but still ensure timely and accurate availability of blood components for clinical use

**Action: IT/software providers with UK Transfusion Laboratory Collaborative**

## IT vulnerability: Serious Trust/Health Board-wide IT incidents

In 2016 two large Trusts in England had serious problems with their IT systems.

### Failure of the pathology IT system

At the first site the laboratory information system failed. This was supporting three different hospitals. The root cause of this was progressive failure of 3 hard drives where hardware warnings had not been acted on. The back-up processes had also not been robust leading to difficulty in restoration. The LIMS was not available for blood transfusion for a total of 8 days and in the interim arrangements were made with other hospital laboratories to perform the analyses and return the results. Elective surgery was cancelled. This downtime resulted in 27 SHOT-reportable incidents (25 SRNM, 1 HSE and 1 RBRP).

The second site identified an issue with malevolent intrusion which threatened all of the IT support.

### Incident affecting two linked Trusts/Health Boards (T/HB-1 and T/HB-2)

T/HB-1 was subject to a type of malware attack known as 'ransomware'. Manual systems were quickly put in place in order to continue some services. T/HB-1 is part of a networked organisation and is linked to a second Trust/Health Board (T/HB-2).

Throughout the incident the pathology laboratory information management system (LIMS) was not affected or switched off, because it uses a different IT language and was not considered at risk. Therefore, LIMS access for T/HB-1 was maintained throughout the incident, but staff at T/HB-2 took the decision to sever the IT links with T/HB-1 until they could be assured there was no risk to their systems from the ransomware.

As T/HB-1 pathology was fully functional, non-urgent work from T/HB-2 sites was transferred to T/HB-1 sites. For any transfusion work that could not be transferred, T/HB-1 staff were able to provide patient history to staff on T/HB-2 sites, because the LIMS had shared patient records across all sites.

The incident review demonstrated that not all sites had the required paper copies of documents critical to service provision in the event of IT failure. No site was without access to key information or documents during the incident, because these were available on other sites and shared either by fax or email.

No SHOT or MHRA-reportable incidents occurred during this IT downtime.



### Learning points

- Trusts/Health Boards should evaluate what documentation might be required in the event of IT failure and ensure paper master copies are available wherever needed
- Trusts/Health Boards should test cyber security regularly, including network threat monitoring and have a cyber incident response contract in place for expert advice during an incident

**Table 13.2:**  
Summary of errors related to information technology

Error	Reports	Right BC	Wrong BC	Unit transfused when specific requirements not met						Wrong group HSCT/SOT	HSE	ADU
				Not irradiated	Not CMV	Not VIP	Not phenotyped	Not HLA-matched	Not HEV-			
Failure to consult or identify historical record	36	-	3	11	5	-	13	-	2	1	-	1
Failure to link, merge or reconcile computer records	13	6	-	1	-	-	4	-	-	-	-	2
Wrong record selected on LIMS or PAS	9	6	-	1	-	-	-	-	-	-	-	2
Warning flag in place but not heeded	22	-	5	5	-	1	3	-	2	4	-	2
Warning flag not updated or removed in error	20	-	1	11	-	-	4	-	4	-	-	-
Failure to use flags and/or logic rules	91	-	1	45	-	7	11	3	15	6	1	2
Computer or other IT systems failure	7	1	2	-	-	-	-	-	-	-	-	4
Errors related to computer system	5	-	-	-	-	-	-	-	-	-	-	5
Errors related to electronic blood management system	8	1	2	-	-	-	-	-	-	-	1	4
Other equipment failure	7	2	-	-	-	-	1	-	-	-	2	2
Incorrect result or data entered or accessed manually	23	18	2	-	-	-	2	-	-	-	-	1
Discrepancy between LIMS and PAS	13	12	-	-	-	-	-	-	-	-	-	1
Blood issued against wrong patient ID (sample or request form)	11	10	1	-	-	-	-	-	-	-	-	-
Electronic blood ordering/OBOS	7	-	1	-	-	5	-	1	-	-	-	-
Crossmatched blood labelled as uncrossmatched	1	1	-	-	-	-	-	-	-	-	-	-
Inappropriate EI (+17 counted in another category)	3	-	(1)	-	-	-	3 (13)	(1)	-	(1)	-	(1)
<b>Totals</b>	<b>276</b>	<b>57</b>	<b>18</b>	<b>74</b>	<b>5</b>	<b>13</b>	<b>41</b>	<b>4</b>	<b>23</b>	<b>11</b>	<b>4</b>	<b>26</b>

BC=blood component; CMV=cytomegalovirus; VIP=virally inactivated plasma; HLA=human leucocyte antigen; PAS=patient administration system; EI=electronic issue



# Adverse Events Related to Anti-D Immunoglobulin (Ig): Prescription, Administration and Sensitisation

## n=409

# 14

Authors: Lilian Parry and Clare Denison

### Definition:

**An adverse event related to anti-D immunoglobulin (Ig) is defined as related to the prescription, requesting, administration or omission of anti-D Ig which has the potential to cause harm to the mother or fetus immediately or in the future.**

### Key SHOT messages

- A total of 409 reports related to errors involving anti-D Ig were reviewed by SHOT in 2016, of which 81.4% related to the omission or late administration of anti-D Ig. This is a continuing and worrying trend that is resulting in a large number of women being put at risk of sensitisation to the D antigen
- There continues to be a lack of knowledge by both clinical and laboratory staff regarding the theory underpinning the clinical need for both routine antenatal anti-D Ig prophylaxis (RAADP) and also anti-D Ig prophylaxis in response to a potentially sensitising event (PSE), including labour. This has again resulted in both inappropriate administration of anti-D Ig and incorrect, most importantly insufficient doses of anti-D Ig being administered
- While 75.8% of the errors reported this year occurred in the hospital environment, there are numerous examples of errors that have occurred as a result of poor communication between hospital and community teams
- The term 'early pregnancy' is defined by The National Institute for Health and Care Excellence (NICE) as up to 13 completed weeks of pregnancy (NICE 2012), whereas the British Society for Haematology (BSH) guideline defines this as up to 12 weeks (BSH Qureshi et al. 2014). It is therefore important, as previously recommended by SHOT in 2014, that there is consistency of practice within hospitals, regardless of which professional guideline may influence the detail of local policy

### Recommendations

- Hospital Transfusion Committees should ensure regular and active participation from obstetric and midwifery teams including those based both within the hospital and the community, in order to develop and oversee local policies for the requesting, issue and administration of anti-D Ig and the investigation of adverse incidents associated with anti-D Ig

#### **Action: Hospital Transfusion Committees, Obstetric Departments, Midwifery Teams**

- All staff involved in the requesting, issuing or administration of anti-D Ig should have appropriate training and education in relation to anti-D, such as completion of the anti-D module within the Learn Blood Transfusion (LBT) e-learning package ([www.learnbloodtransfusion.org.uk](http://www.learnbloodtransfusion.org.uk))

#### **Action: Hospital Transfusion Laboratories, Hospital Transfusion Committees, Trust/Health Board Chief Executive Officers (CEO), Obstetric Departments, Community Midwifery Teams**

- All clinical facilities, both NHS and private clinics, that provide care to women and are involved in the administration of anti-D Ig should report errors associated with anti-D Ig to SHOT

#### **Action: Trust/Health Board/Private clinic Chief Executives**

**Good practice points:**

- Hospitals should consider implementing, via a Blood Service reference laboratory, high throughput non-invasive prenatal testing for fetal D genotype, as recommended by NICE (NICE 2016). The testing will identify D-negative women carrying a D-positive fetus with the aim being to streamline the RAADP programme and prevent the administration of an unnecessary medicinal blood product when the fetus is D-negative and is therefore not at risk of haemolytic disease of the fetus and newborn (HDFN)

There should also be a robust system for making sure that fetal blood group results are acted upon appropriately and an awareness that fetal blood group results may be different in subsequent pregnancies so that any results linked to a maternal record should be accurately recorded and indexed to a specific pregnancy

- Hospitals should have a team consisting of consultant obstetricians, hospital and community-based midwives and laboratory staff to help develop a clear policy regarding the use of anti-D Ig. The introduction of midwifery champions as a point of reference in hospital and community teams will ensure education is continuous and lead to a better understanding of the policy. A named contact(s) in the laboratory should be available to ask for advice in understanding Blood Service reference laboratory reports, including antibody levels and additional sampling requirements
- Hospital blood transfusion laboratories should have systems in place to identify any anti-D Ig that has been issued for a woman but not collected from the laboratory. The system should include a mechanism to escalate the urgency of the anti-D Ig administration to ensure that it is administered before the 72-hour time limit has elapsed
- Hospitals should have clear pathways of communication between the hospital and community teams. Regular meetings between the teams to discuss communication failures are essential in improving the service for the users

**i****Learning points**

- Hospitals should ensure a robust system is in place for the regular education of emergency department (ED) staff and midwives regarding the clinical indications for anti-D Ig. Rapid early pregnancy pathways should be available for the administration of anti-D Ig following a potential sensitising event in D-negative women
- Hospitals should develop clear processes for checking historical blood group records prior to the requesting of anti-D Ig by clinical staff or issue of anti-D Ig by laboratory staff in order to prevent inappropriate requests and administration
- Where mother and cord samples are received in the laboratory, a system should be in place to ensure that the results of the cord sample are linked to the maternal record. This will guarantee that any required postnatal anti-D Ig is appropriate (i.e. infant blood group has been confirmed as D-positive) and that the correct dose has been issued (i.e. based on the fetomaternal haemorrhage (FMH) testing result). There must be a robust system in place for entering results into the laboratory information management system (LIMS), including any received from the Blood Service reference laboratory. This will ensure that all information, including the infant blood group, is easily retrievable in the event of a query from clinical staff
- Positive patient identification means asking a woman 'What is your name?' not asking 'Is this your name?'

**Commentary**

This year's report again highlights recurring key issues in the provision of anti-D Ig. These include poor knowledge and understanding by both clinical and laboratory staff about appropriate use of anti-D Ig, failure to follow standard operating procedures and failure to refer to the blood grouping results of both women and infants before both requesting and issuing anti-D Ig.



These errors all emphasise the need for clear and unambiguous local protocols in both the clinical area, most importantly in clinical areas outside the maternity departments e.g. the ED and in the blood transfusion laboratory.

These protocols should be complemented by robust training programmes for clinical and laboratory staff that ensure all staff are able to correctly request and issue anti-D Ig for a woman that may present with a need for anti-D Ig regardless of the department she presents in.

The use of a checklist in the laboratory in order to escalate the requirement for anti-D Ig issued but not collected should ensure that it is administered before the 72-hour deadline. A key contact (champion) in the clinical area should be identified to act on these cases.

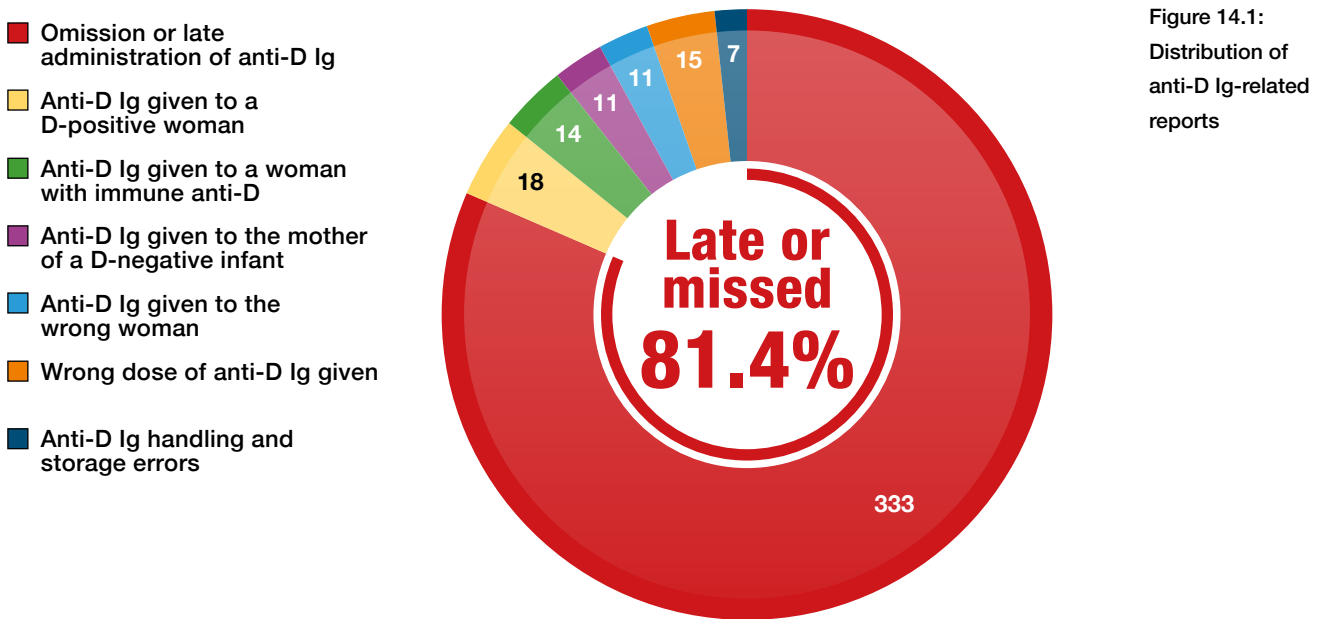


Figure 14.1: Distribution of anti-D Ig-related reports

Most errors occurred in hospital, 310, 75.8%, and 99, 24.2% in the community.

**Deaths n=0**

There were no deaths reported related to errors associated with anti-D Ig in 2016.

**Major morbidity n=2**

Two women developed immune anti-D following errors in clinical management. One was failure to administer anti-D Ig following a PSE, and the other was failure to administer anti-D Ig appropriately during a first pregnancy in 2012 which resulted in sensitisation and detection of immune anti-D in a subsequent pregnancy in 2015.

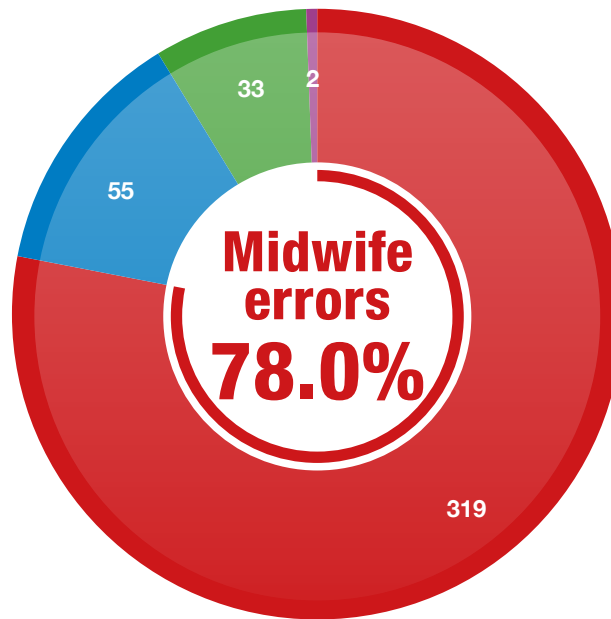
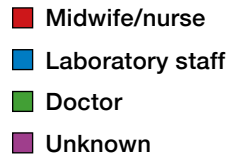
**Potential for major morbidity n=331**

In addition to the 2 sensitisations above, 331/409 (80.9%) case reports related to the omission or late administration of anti-D Ig. This is a worrying situation, putting many women at risk of potential sensitisation to the D antigen.

**Overview of cases**

Most errors (377/409, 92.2%) occurred during normal working hours.

**Figure 14.2:**  
Staff group  
responsible for  
primary error  
associated with  
anti-D Ig



Clinical staff were responsible for 352/409, 86.1%, of the errors reported with 33/409, 8.1%, involving doctors, including consultant obstetricians.

The majority of errors by laboratory staff were made by biomedical scientists (BMS); however there were also errors involving unregistered staff e.g. associate practitioners (AP), including errors in the selection and issue of anti-D Ig from the blood transfusion laboratory.

### **Omission or late administration of anti-D Ig n=333 (81.4%)**

A total of 333/409 (81.4%) case reports related to the omission or late administration of anti-D Ig. The majority, 305/333 (91.6%) were caused by clinical staff, and 28/333 (8.4%) by laboratory staff. Most errors occurred in hospital (244/333, 73.3%) and 89 (26.7%) in the community.

Common themes identified in this category include:

- Failure to administer anti-D Ig within 72 hours when a woman attended the ED for a PSE
- General lack of understanding of national guidance on administration of anti-D Ig following a PSE
- Failure of timely collection of anti-D Ig from the laboratory
- Late administration of postnatal anti-D Ig following early discharge of the woman from hospital
- Communication failures when women have shared care between hospital and community midwifery teams

### **Case 14.1: Failure to administer postnatal anti-D Ig results in the formation of immune anti-D**

*A D-negative woman developed an immune anti-D in her second pregnancy. It is possible she did not receive all appropriate anti-D Ig during her first pregnancy. The woman was informed that her first baby was D-negative and anti-D Ig was not required. As no cord blood sample was ever received for this pregnancy, it is unclear where this information came from. It does appear as if the woman had been sensitised to the D antigen prior to her second pregnancy. It has been highlighted that the same woman probably did not receive the postnatal standard dose of anti-D Ig at the time of her first pregnancy, as clinicians believed it was only given if the Kleihauer test indicated so.*

### **Case 14.2: Lack of knowledge by clinical staff in the ED about the need for administration of anti-D Ig for a PSE resulting in sensitisation to the D antigen**

*At approximately 18 weeks gestation a D-negative woman attended the ED following a road traffic accident (RTA). No anti-D Ig was administered, as a result it appears that this woman has been sensitised to the D antigen. The routine 28-week blood sample showed the presence of low level immune anti-D. The woman previously had a negative antibody screen at booking.*

### **Handling and storage errors related to anti-D Ig n=7 (1.7%)**

These 7 incidents originated in the clinical area in 6 and one in the laboratory; 4 incidents occurred in the community and 3 in hospital.

### **Case 14.3: Failure to return product ordered in error to the laboratory**

*RAADP was requested for a woman by a community midwife. This was not administered on the date originally required because the midwife who had completed the request form wrote an incorrect date. The anti-D Ig that was issued was not returned to the laboratory and was kept in a drawer in the community midwives' office. The woman was given the anti-D Ig 3 weeks later but required a further dose of RAADP as the one given may not have been sufficient to protect her against D-sensitisation. This is because it is unclear if the product would still remain effective as the storage conditions specified by the manufacturer were not followed. The product manufacturer states that it is stable at 4-8°C but can be kept at room temperature for a maximum of 4 days.*

### **Case 14.4: RAADP issued during previous pregnancy administered after expiry**

*1500IU anti-D Ig was administered to a woman for whom it had been prescribed and issued during her previous pregnancy 15 months earlier. The dose had expired.*

### **Anti-D Ig given to D-positive women n=18 (4.4%)**

Staff groups and locations involved: 9 clinical staff and 9 laboratory staff errors; 17 in hospital and 1 in the community.

Four errors that occurred in the laboratory related to women typed as 'weak D-positive' and therefore should be regarded as D-positive. Two occurred as a result of failure to investigate equivocal D-typing results.

These errors also highlighted a lack of knowledge by laboratory staff regarding the classification of women typed as 'weak-D' as D-positive who therefore do not require anti-D Ig prophylaxis at any stage of pregnancy or at delivery (BSH Qureshi et al. 2016).

It is important to note however that where clear cut results cannot be obtained in D-typing, women should be classified as D-negative until the D status is confirmed and anti-D Ig prophylaxis administered accordingly. This is particularly important in cases where samples are referred to a Blood Service reference laboratory for confirmation of D-typing where the result is not available within 72 hours of a PSE.

The main theme identified in this category was failure to check the woman's blood group on historical records prior to ordering/issuing anti-D Ig.

### **Case 14.5: Historical blood group record not checked prior to issuing anti-D Ig**

*Cord and maternal blood samples were received in the laboratory for a postnatal woman despite her being grouped as D-positive. The cord sample was typed unnecessarily and anti-D Ig issued inappropriately by a BMS before checking the maternal blood group.*

### **Anti-D Ig given to women with known immune anti-D n=14 (3.4%)**

Staff group and locations involved: 7 clinical staff, 3 laboratory staff and 4 involved both groups; 13 were in hospital and 1 in the community.

The themes identified within this category include:

- Failure to check historical records
- Laboratory staff ignoring flags on the LIMS
- Lack of understanding by clinical, particularly midwifery staff, and also a consultant obstetrician

#### **Case 14.6: Lack of knowledge by clinical staff about immune anti-D**

*It was standard practice for midwives to administer anti-D Ig to all women that deliver a D-positive baby. A postnatal dose of anti-D Ig was issued and administered to a D-negative woman who was under a fetal medicine unit for the management of HDFN due to high levels of immune anti-D. She had undergone previous intrauterine transfusions (IUT) (described in Case 10.1).*

#### **Case 14.7: Lack of knowledge by consultant obstetrician**

*Postnatal anti-D Ig was requested for a woman known to have immune anti-D (>15IU/mL), but although the BMS informed the consultant who made the request that anti-D Ig was not indicated, the consultant insisted that it was administered regardless.*

### **Anti-D Ig given to the mother of a D-negative infant n=11 (2.7%)**

The staff involved in the primary error associated with the administration of anti-D Ig to the mother of a D-negative infant were laboratory staff in 8/11 cases (often where postnatal anti-D Ig was issued before the infant blood group had been confirmed as D-positive), and clinical staff in 1/11. In one it was unclear and in the other case, both were implicated. All errors reported in this category occurred in hospital.

### **Anti-D Ig given to the wrong woman n=11 (2.7%)**

Nine errors were made by a midwife or nurse, 2 by doctors. Nine occurred in hospital and 2 in the community.

The themes identified in this category of reports were:

- Insufficient identification checks of the woman prior to administration of anti-D Ig
- Anti-D Ig administered was labelled with details of a different woman

#### **Case 14.8: Patient misidentification followed by a deliberate deviation**

*Both Woman A and Woman B attended the antenatal clinic for administration of RAADP. The midwife called out the name of Woman B but Woman A followed her into the clinic room. The midwife mentioned the name of Woman B again and Woman A acknowledged this was her name. RAADP was administered, but then following discussion Woman A stated that this was not her name. When questioned Woman A thought that it was her name being called. Woman B was then called into a separate clinic room and administered a dose of RAADP despite it being labelled for Woman A.*

### **Wrong dose of anti-D Ig given n=15 (3.7%)**

Eight were caused by clinical staff, 6 by laboratory staff and 1 was unclear.

In 12/15 cases in this category the dose of anti-D Ig administered exceeded the recommended minimum dose. This was either in breach of local policy or occurred as a result of a clinical or laboratory error that resulted in the incorrect dose being administered, for example the patient was dosed twice, or where the local policy was to give 500IU but 1500IU was given, or the dose was based on an erroneous Kleihauer result. In 3/15 cases insufficient anti-D Ig was administered.

The theme identified in this category was errors in selection of the appropriate dose required for a PSE, particularly when women had repeated bleeding during pregnancy.

**Case 14.9: Insufficient postnatal anti-D Ig administered following confirmation of a large fetomaternal haemorrhage**

A Kleihauer test confirmed a fetomaternal bleed following delivery which would require additional anti-D Ig prophylaxis. The sample was sent to the reference laboratory who confirmed a bleed of 21mL. The BMS in the laboratory miscalculated the dose of anti-D Ig required and only issued 2000IU. This was administered. Laboratory checks identified that 3000IU anti-D Ig was required and a further 1500IU anti-D Ig was issued and administered however this was administered more than 72 hours following delivery.

**Near miss anti-D Ig cases n=29**

Point in the process	Type of error made	Number of cases	%
Request	Requested for a D-positive woman	2	13.8
	Requested for a woman with immune anti-D	1	
	Requested for the incorrect patient	1	
Sample receipt	Entered into the incorrect record	1	3.5
Testing	Incomplete testing prior to issue	4	24.1
	Transcription error	2	
	Misinterpretation	1	
Component selection	Issued to a woman with immune anti-D	5	17.2
Component labelling	Anti-D Ig mislabelled	5	17.2
Collection	Collection of incorrect anti-D Ig	1	3.5
Administration	Anti-D Ig not given in timely manner	4	20.7
	Attempted administration to the wrong patient	1	
	Inappropriate storage in the clinical area	1	
<b>Total</b>		<b>29</b>	<b>100</b>

Table 14.1: Near misses that could have led to errors related to anti-D Ig n=29

Midwives are one of the largest staff groups who make sampling errors leading to wrong blood in tube (WBIT) incidents, 197/776 (25.4%) (Figure 12.5). This appears to be an over-representation when compared to data supplied by the Oxford University Hospitals NHS Foundation Trust, which indicates midwives take 10.2% of all samples.

**Information technology (IT)-related anti-D Ig cases n=21**

Error	Reports	Unnecessary anti-D Ig administered	Failure to administer anti-D Ig or excessive delay	Wrong dose anti-D Ig
Error when manually transcribing data	2	1	1	
LIMS not updated with reference laboratory result	3	2	1	
Failure to consult historical record	5	3	1	1
Failure to use flags, logic rules	6	4		2
Electronic device not working	1			1
Computer downtime	4		4	
<b>Total</b>	<b>21</b>	<b>10</b>	<b>7</b>	<b>4</b>

Table 14.2: IT-related anti-D Ig cases n=21

In Table 14.2 above and cases below there are a number of examples where the use of IT systems flags, logic rules or algorithms would have prevented women getting anti-D Ig unnecessarily (10 cases), ensured that the correct dose of anti-D Ig was given (4 cases) and perhaps prevented omissions or delays in anti-D Ig prophylaxis (7 cases).

**Case 14.10: LIMS can prompt correct anti-D Ig administration, but only if you put the right information in**

*A woman with a D-negative baby was given postnatal anti-D Ig unnecessarily. The LIMS was configured to guide whether anti-D Ig was needed postnatally if the cord blood group was recorded against the maternal FMH test request. On this occasion a locum BMS recorded the cord blood group somewhere else on the LIMS so it did not prevent issue of anti-D Ig.*

**Case 14.11: Highlighting changes in advice on electronic records**

*A woman was typed as O D-positive at booking and did not receive any RAADP or postnatal anti-D Ig. However, repeat samples requested to investigate a D-grouping anomaly and sent to a reference laboratory for testing, showed a D variant that does require anti-D Ig. However despite this report being uploaded onto the LIMS and a paper copy sent to the maternity unit the clinical team continued to act on the original (incorrect) result.*

**Case 14.12: RAADP worklist failed after computer downtime**

*After a laboratory computer failure was fixed the RAADP list was printed but four patients were missed and did not get timely RAADP although all had appropriate postnatal anti-D Ig prophylaxis.*

**Case 14.13: Manual transcription of the wrong result onto maternity records**

*A D-negative woman had a D-positive baby and was given anti-D Ig. Unfortunately the RAADP had been missed because the wrong blood group had been transcribed onto the maternity system manually.*

## Commentary

It is possible to use the LIMS or other IT systems to support anti-D Ig prophylaxis to make the process more robust and to ensure the right women receive anti-D Ig.

Ideally the LIMS is used to record and then use the **results of testing** to support laboratory and clinical policies for **anti-D Ig prophylaxis**. This includes:

### During pregnancy

- The maternal blood group and the outcome of any anomalous D-typing investigations
- The maternal antibody screen and results of any associated reference tests used to distinguish passive from immune anti-D

### At delivery

- The fetal blood group
- The maternal Kleihauer test and results of any additional confirmatory FMH tests

Flags or logic rules can be used to guide when anti-D Ig prophylaxis is needed and when contraindicated based on these testing results. For example to identify:

- D-negative women with no immune anti-D who need RAADP
- D-positive women or D-negative women with immune anti-D who do not need RAADP

The risk for error is greater when manual transcription is required. Entering the results of reference tests into the LIMS, along with the interpretation and associated clinical advice has resulted in errors in anti-D Ig administration. Similarly, mistakes can occur when copying the blood grouping results into the maternity record. Electronic transmission of data is preferred because it reduces the risk of transcription error and provides the ability to see real-time and updated results which supports effective decision-making and correct anti-D Ig prophylaxis.

Finally the benefits of having anti-D Ig assigned to a named patient in the LIMS enables audit of the completeness of the process. Another development is that some electronic blood management systems are now able to control the issue of anti-D Ig as well as other blood components and this is a useful and positive step.

## Learning points

In the future high-throughput non-invasive prenatal testing (NIPT) using cell-free-fetal deoxyribonucleic acid (DNA) will be available for D-typing the fetuses of D-negative women to see if anti-D Ig prophylaxis is required in pregnancy (NICE 2016). It is of some concern that similar patterns of errors could arise as have been seen in this anti-D Ig prophylaxis pathway already. For example, care should be taken to avoid:

- Transcription errors when putting paper-based reference laboratory results into the LIMS
  - Think! Right patient – Right result – Right pregnancy
- Transcribing both the correct fetal genotyping result and the correct maternal D-typing result into the maternity record

There have been no errors reported to SHOT that fall into this category but laboratories and antenatal clinics should be vigilant to prevent such errors when implementing this new technology



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# 15

## Immune Anti-D in Pregnancy: Cases reported up to the end of 2016: More questions than answers so far

Author: Jane Keidan

### Questions arising from the data:

- Do twin pregnancies pose a higher risk of alloimmunisation during pregnancy as well as the already recognised risk of increased fetomaternal haemorrhage at delivery?
- Should laboratories proactively chase up cases where anti-D immunoglobulin (Ig) prophylaxis has been issued but confirmation of administration is not received?
- Why does apparently 'ideal' care result in immunisation in some cases? Data from National Health Service Blood and Transplant (NHSBT) Alloimmune Resource (AIR) study (looking for genetic influences that predispose women to developing red cell alloantibodies during pregnancy) may be informative to identify women at higher risk of immunisation
- Should obese women receive modified routine antenatal anti-D Ig prophylaxis (RAADP) - higher or more frequent dosing, or intravenous administration?
- Should extra doses of RAADP be given to women whose pregnancy extends beyond 40 weeks?
- Is anti-D Ig prophylaxis indicated for medical termination with no instrumentation?
- How do we encourage reporters to send in fully completed datasets?

### Key SHOT messages

- The terms 'standard dose' and 'higher dose' of anti-D Ig should be avoided in any guidance issued, and the minimum recommended dose for each clearly specified clinical scenario should be given in international units (IU)
- All healthcare professionals, including laboratory staff, are responsible for ensuring that women who become immunised to the D antigen in pregnancy are reported to SHOT with an accurate and complete dataset

### Recommendation

- United Kingdom (UK) guidance for use of anti-D Ig prophylaxis from both National Institute for Health and Care Excellence (NICE 2008 and 2012) and British Society for Haematology (BSH 2014) should be reviewed to avoid conflicting and thus confusing advice, especially in early pregnancy

**Action: BSH Guidelines Transfusion Task Force**

### Introduction

To improve understanding of the causes of continuing anti-D immunisations, SHOT is conducting a prospective study of women who have produced alloimmune anti-D detected for the first time in the current (index) pregnancy.

## Results

In 2016 a total of 40 cases were reported, although some datasets were incomplete (only 14 (35.0%) datasets were satisfactorily completed at initial submission, in the other cases SHOT staff had to contact the reporter for more details or clarifications). There were 9 cases in women with no previous pregnancies (NPP) and 31 in women with previous pregnancies (PP), 28 of which resulted in live birth. Cumulatively SHOT now has data on 42 women with no previous pregnancy (NPP) and 115 women with previous pregnancies (PP).

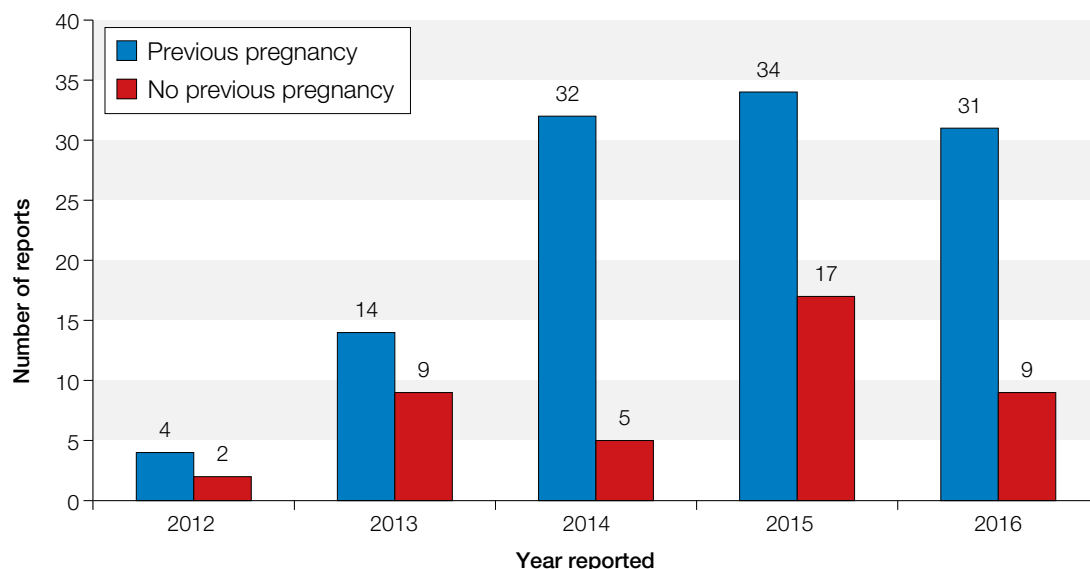


Figure 15.1: Number of reports of anti-D immunisation in pregnancy by year, 2012-2016

### No previous pregnancy (NPP) n=9 in 2016, cumulative n=42

#### When was the anti-D detected?

	Number of new cases 2016	Number of cases cumulative total
Before 28 weeks	0	4
At or after 28 weeks, before delivery	4	11
At delivery	4	25
Other	1*	1
No information	0	1
<b>Total</b>	<b>9</b>	<b>42</b>

\*Alloimmune anti-D was detected 6 months postpartum after large fetomaternal haemorrhage (FMH) of 12.7mL at delivery managed correctly

Table 15.1: When immune anti-D was detected NPP

#### What was the booking weight?

Weight at booking in kg	Number of new cases 2016	Number of cases cumulative total
<68	5	21
68-80	0	4
>80 (obese)	3	7
No information	1	10
<b>Total</b>	<b>9</b>	<b>42</b>

Table 15.2: Booking weight NPP

## Did the women receive appropriate RAADP?

Table 15.3:  
Details of RAADP  
for eligible NPP  
cases n=9 (2016)  
n=39 (cumulative)

RAADP regimen	Number of new cases 2016	Number of cases cumulative total
Single dose 1500IU at 28 weeks	7	33
Single dose 1500IU at 30 weeks	2	
Two-dose regimen 500IU	0	1
Not given	0	5
<b>Total</b>	<b>9</b>	<b>39</b>

The route was specified in 6 cases from 2016 as intramuscular into deltoid, one case into gluteal region and the rest were not specified.

## Details of potentially sensitising events (PSE)

Table 15.4a:  
Details of PSE  
NPP n=9

Number of cases	PSE	Management
7	None	
1	Twin pregnancy	
1	Large FMH at delivery	Appropriate anti-D Ig dose and follow up. Immune anti-D detected at 6-month follow up

Table 15.4b:  
Details for all  
PSE NPP cases  
reported since 2012

PSE	Number of cases
None	30
7 antepartum haemorrhage (APH) 2 interventions (chorionic villus sample, amniocentesis) 1 fall 1 large FMH at delivery 1 twin pregnancy	Some women had more than one PSE

## Pregnancy outcomes

In 2016 all 9 pregnancies resulted in 10 live births (one twin pregnancy) of which 2 babies were D-negative, 7 had no complications, and 1 case required exchange transfusion.

Cumulatively, all 42 pregnancies resulted in 43 live births, of which 27 had no complications, 11 babies required phototherapy and 4 cases required exchange transfusion. No details were given in one case.

## Summary of 2016 NPP data

The majority of women (8/9) were found to be immunised during the third trimester or at delivery, and all received apparently 'ideal' care, with timely RAADP and no identifiable sensitising episodes. In 3 cases the women were obese, and one pregnancy delivered beyond term at 41 weeks. There was one twin pregnancy, one where RAADP administration was incompletely documented but otherwise received 'ideal' care and one where information on booking weight was missing. One further case had alloimmune anti-D detected 6 months postpartum after a large FMH at delivery which was apparently managed correctly with increased dose of postpartum anti-D Ig and appropriate follow up.

## Case studies:

### Case 15.1: Twin pregnancy

*Primipara aged 26 years. Booking weight 66kg (body mass index (BMI) 22.8). Received RAADP (single dose of 1500IU anti-D Ig at 28 weeks by intramuscular injection into deltoid region). Alloimmune anti-D was detected (15.4IU/mL) at 36 weeks when she delivered twins. Twin one (D-positive) required exchange transfusion, twin two was D-negative.*

**Question:** Do twin pregnancies pose a higher risk of alloimmunisation during pregnancy as well as the already recognised risk of increased fetomaternal haemorrhage at delivery?

**Case 15.2: Incomplete documentation of RAADP administration**

*Primipara aged 20 years. Booking weight 57.7kg (BMI 24). Antenatal notes document that she received RAADP (1500IU anti-D Ig at 31 weeks) but the batch number and confirmation of transfusion form was not logged and the form was not returned to the transfusion laboratory. Alloimmune anti-D was detected (13.9IU/mL) at delivery at 38 weeks. The baby required no interventions for haemolytic disease of the fetus and newborn (HDFN).*

**Question:** Should laboratories proactively chase up cases where anti-D Ig has been issued but confirmation of administration is not received?

**Case 15.3: Apparently ‘ideal’ care but obese**

*Primipara aged 25 years. Booking weight 107kg (BMI 36.95). Received RAADP (single dose of 1500IU anti-D Ig at 28 weeks by intramuscular injection into deltoid region). Alloimmune anti-D was detected (3.8IU/mL) at delivery at 40 weeks. The baby required no interventions for HDFN.*

**Question:** Should obese women receive modified RAADP-higher or more frequent dosing, intravenous administration?

**Case 15.4: Apparently ‘ideal’ care**

*Primipara aged 26 years. Booking weight 59.4kg (BMI 24). Received RAADP (single dose of 1500IU anti-D Ig at 28 weeks). Alloimmune anti-D was detected (1.9IU/mL) at 29 weeks, peaking to a level of 4.8IU/l at 36 weeks gestation. There were no PSE. The baby was delivered at 37 weeks and required no interventions for HDFN.*

**Question:** Why does apparently ‘ideal’ care result in immunisation in some cases? Data from the NHSBT AIR study (looking for genetic influences that predispose women to developing red cell alloantibodies during pregnancy) may be informative to identify women at higher risk of immunisation.

**Previous pregnancies (PP) n=31 in 2016, cumulative n=115 cases**

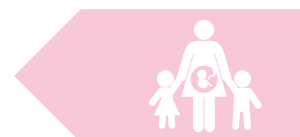
**When was the anti-D detected in index pregnancy?**

Time of anti-D detection	Number of new cases 2016	Number of cases cumulative total
At booking (if first trimester)	9	50 (43.5%)
After booking to 28 weeks (includes late booking)	2	4
At or after 28 weeks	10	39 (33.9%)
At delivery	9	16 (13.9%)
Other	1*	6**
<b>Total</b>	<b>31</b>	<b>115</b>

\*One at preoperative assessment 15 months after pregnancy

\*\*Two at preoperative assessment following pregnancy, two at planned follow up of large FMH at delivery where correct dose of anti-D Ig had been given, two unknown

Where alloimmune anti-D was detected at booking in the index pregnancy, only the events in the preceding pregnancy are relevant to the sensitisation (assuming no other exposure to the D antigen occurred e.g. transfusion, an unlikely event in healthy fertile women). Where anti-D is detected later in the index pregnancy, the relative contribution of events in the previous and index pregnancy is less certain.



**Table 15.5:**  
When immune anti-D was detected PP

### Information about the pregnancy immediately preceding index pregnancy

In 2016 one woman underwent medical termination of her third pregnancy at 9 weeks and received 250IU anti-D Ig, another case underwent a termination (TOP) but no further details were available, one woman sustained fetal loss at 8 weeks gestation with no surgical intervention, leaving 28 cases that proceeded to live birth.

### Did the women receive appropriate anti-D Ig prophylaxis for pregnancy loss?

One woman received an appropriate dose (250IU) of anti-D Ig after medical termination at 9 weeks, one required no anti-D Ig after early (8 week) spontaneous fetal loss and no information was available in the other woman who underwent a termination.

### What was the booking weight in the preceding pregnancy?

Table 15.6:  
Booking weight for  
PP cases

Weight at booking in kg	Number of new cases 2016	Number of cases cumulative total
<68	8	36
68-80	2	11
>80 (obese)	5	14
No information	13	41
<b>Total</b>	<b>28</b>	<b>102*</b>

\*13 cases did not go to term

### Did the women who carried to term receive RAADP in the preceding pregnancy?

Table 15.7:  
Details of RAADP

RAADP	Number of new cases 2016	Number of cases cumulative total
PP Single dose	17	60
Two doses	0	7
Not given	1*	16**
No information	10	19
<b>Total</b>	<b>28</b>	<b>102</b>

\*Before practice adopted

\*\*Learning difficulties, concealed pregnancy, needle phobic, prior to RAADP introduction (3), delivered abroad (3), no reason given (5), declined (2)

In 8 cases the route was specified as deltoid, in the other cases it was not known.

### Details of potentially sensitising events in the preceding pregnancy

Table 15.8:  
Details of potentially sensitising events  
PP

Number of PSE	Details
8 PSE reported	<ul style="list-style-type: none"> <li>2 APH (33 weeks and 30 weeks) both managed correctly with Kleihauer test and correct timely dose of anti-D Ig</li> <li>1 spontaneous miscarriage at 8 weeks, no anti-D Ig indicated</li> <li>2 TOP: 1 no information, 1 managed correctly with 250IU anti-D Ig</li> <li>3 falls/abdominal trauma (19, 34 and 37 weeks) managed correctly with Kleihauer test and correct timely dose of anti-D Ig</li> </ul>
12 cases had no PSE reported	
10 cases had no information on PSE	

Since reporting began in 2013, a total of 28 PSE have been reported in the preceding pregnancies of which 19 (67.9%) were correctly managed.

### Method of delivery of preceding pregnancy

Type	Number of new cases 2016	Number of cases cumulative total
No information	12	40
Vaginal	9	37
Instrumental	2	6
Elective caesarean section (CS)	3	8
Emergency CS	2	11
<b>Total</b>	<b>28</b>	<b>102</b>

Table 15.9:  
Mode of delivery  
for PP cases

### Gestation more than 40 weeks at delivery of preceding pregnancy

Gestation at delivery (weeks)	Number of new cases 2016
40 weeks or less	12
More than 40 weeks	1 case 40 <sup>+3</sup> 2 cases 40 <sup>+5</sup> 2 cases 40 <sup>+7</sup> 1 case 41
No information	10
<b>Total</b>	<b>28</b>

Table 15.10:  
Gestation at  
delivery PP

Cumulatively (data collected from 2015 onwards), 9/58 pregnancies (15.5%) in PP women who became immunised lasted more than 40 weeks. NHS maternity statistics 2014-2015 indicate 17.5% pregnancies extended beyond 40 weeks (NHS Digital 2015).

### Postpartum prophylaxis (PPP) in preceding pregnancy

What happened?	Number of new cases 2016	Number of cases cumulative total
Kleihauer test and appropriate dose of anti-D Ig	12	62*
No prophylaxis	1	6**
Incorrect dose of anti-D Ig	0	2***
No information	12	27
D-negative baby	3	5
<b>Total</b>	<b>28</b>	<b>102</b>

Table 15.11:  
Details of  
postpartum anti-D  
Ig prophylaxis PP

\*Includes 4 cases requiring higher doses as a result of Kleihauer test

\*\*2 from overseas, 1 with learning difficulties, 1 needle-phobic, 1 declined

\*\*\*1 dose 250IU, 1 dose given late

### Anti-D detected at first trimester booking of index pregnancy n=9

The details of the preceding pregnancy may provide information on the cause of immunisation in these cases.

**Table 15.12:**  
Details of  
management in  
previous pregnancy  
n=9

Details	Details of preceding pregnancy
Case 002*	Not obese, correct RAADP, no PSE, delivery route not specified, correct PPP
Case 004	Delivered by caesarean section, no other information provided
Case 005*	Medical termination of pregnancy at 9 weeks, 250IU anti-D Ig given
Case 011*	Not obese, correct RAADP, no PSE, delivered by caesarean section at 36 weeks gestation, correct PPP
Case 014	TOP, no other details known
Case 018	No further information available
Case 021	Booking weight not known, RAADP not given as before policy introduced, APH correctly managed, vaginal delivery, no information on PPP
Case 024*	Booking weight not reported, correct RAADP, no PSE. Weak anti-D detected at term and confirmed at 3 months which was at booking for next pregnancy
Case 026*	Not obese, correct RAADP, fall at 34 weeks correctly managed, vaginal delivery but no PPP as baby D-negative, alloimmune anti-D detected at booking of index pregnancy at very low level, D-negative baby

\*Cases with apparently 'ideal' management with no risk factors

Missing data for these cases make analysis difficult, but as in NPP reports there are cases where apparently 'ideal' management with no risk factors still resulted in immunisation.

### Anti-D detected after first trimester in index pregnancy n=21

Further information is requested about the index pregnancy when alloimmune anti-D is detected after the booking (first trimester) sample, as it may be that the sensitisation occurred in the index pregnancy rather than in the preceding pregnancy.

### What was the booking weight in the index pregnancy?

**Table 15.13:**  
Booking weight in  
index pregnancy  
PP

Weight at booking in kg	Number of new cases 2016	Number of cases cumulative total
<68	9	27
68-80	2	10
>80	5	7
No information	5	15
<b>Total</b>	<b>21</b>	<b>59</b>

### RAADP in index pregnancy

**Table 15.14:**  
Details of RAADP  
in index pregnancy  
PP

RAADP given or not	Number
Single dose 1500IU	11
RAADP given but no details	3
Not given:	
Late booker: alloimmune anti-D present at 28 week visit	6
No clinic appointment made	1
<b>Total</b>	<b>21</b>



### Details of potentially sensitising events in index pregnancy

Number of women	Details
8 cases where PSE reported	<ul style="list-style-type: none"> <li>• Fall at 33 weeks, no Kleihauer test performed, no anti-D Ig given</li> <li>• APH at 15 weeks, 500IU anti-D Ig given</li> <li>• External cephalic version (? gestation), Kleihauer test negative, 1500IU anti-D Ig given</li> <li>• APH at 18 weeks, 250IU anti-D Ig given</li> <li>• Abdominal trauma at 16 weeks, 250IU anti-D Ig given; fall at 32 weeks, no Kleihauer test performed and no anti-D Ig given</li> <li>• APH at 30 weeks, Kleihauer test negative, 1500IU anti-D Ig given</li> <li>• Abdominal trauma (road traffic accident) at 18 weeks, no anti-D Ig given</li> <li>• APH at 23 weeks, Kleihauer test negative 500IU anti-D Ig given</li> </ul>
8 cases no PSE reported	
5 cases no information on PSE	

Table 15.15: Details of potentially sensitising events in index pregnancy PP

### Outcomes of pregnancies reported in 2016

Outcome	Number of cases
Live births	28
<i>No treatment (5 D-negative babies)</i>	15
<i>Required phototherapy</i>	11
<i>Required phototherapy and intravenous immunoglobulin</i>	1
<i>Required phototherapy and exchange transfusion</i>	1
No information	2
Not pregnant: anti-D detected at follow up of previous pregnancy	1

Table 15.16: Outcome of pregnancies reported in 2016 PP

### Summary of 2016 PP data

In 9 cases women were found to be immunised at the first trimester booking indicating that sensitisation had probably occurred in the preceding pregnancy. Although the data are incomplete, we continue to see cases where despite apparently ‘ideal care’ in the preceding pregnancy, sensitisation to the D antigen occurs and alloimmune anti-D develops in the subsequent pregnancy. Cumulatively since data collection began in 2012, 18/50 PP cases (36.0%) found to be immunised at booking received apparently ‘ideal care’ in the preceding pregnancy.

In 6/28 of the previous pregnancies to term (21.4%) lasted longer than 40 weeks and cumulatively, since 2015, 9/58 pregnancies (15.5%) in PP women who became immunised lasted longer than 40 weeks. **Should extra doses of RAADP be given to women whose pregnancy extends beyond 40 weeks?**

NHS maternity statistics 2014-2015 show 17.5% pregnancies extended beyond 40 weeks (NHS Digital 2015).

In 21 cases alloimmune anti-D was detected later in the index pregnancy so that the relative contribution of previous pregnancies is less clear.

### Case studies

#### Case 15.5: Medical termination of early pregnancy with apparent failure of prophylaxis

*A woman had two previous live births with no alloimmune anti-D detected at the second delivery. She then had a medical termination of pregnancy (MTO) at 9 weeks gestation. A sample for group and antibody screen could not be obtained. Anti-D Ig (250IU) was given following the MTO. At booking for her next pregnancy alloimmune anti-D (29IU/mL) was detected. The baby was D-negative.*

### Case 15.6: Obesity

*Preceding pregnancy booking weight 149kg (BMI 50.4). RAADP administered at 28 weeks gestation (1500IU intramuscularly into deltoid area). Antepartum haemorrhage occurred at 30 weeks with negative Kleihauer, 1500IU anti-D Ig given intramuscularly into deltoid area within 24 hours of event. D-positive baby delivered by caesarean section at 37 weeks gestation. Postpartum prophylactic anti-D Ig (500IU) was given. Anti-D was detected 15 months later when the woman attended the emergency department with abdominal pain.*

3/9 NPP women were obese (booking weight >80kg), as were 5/28 PP women in their preceding pregnancy and 5/21 PP women in their current pregnancy. None received prophylactic anti-D Ig intravenously.

**Question:** Should obese women receive modified RAADP: higher or more frequent dosing, intravenous administration?

### Case 15.7: Early fetal loss

*The preceding pregnancy ended in early fetal loss at 7-8 weeks gestation. This was treated medically with no surgical intervention. In the index pregnancy, no alloimmune anti-D was detected at booking at 10 weeks. Alloimmune anti-D was detected at 28 weeks (12.4IU/mL). The baby was delivered at 36 weeks gestation and required phototherapy and exchange transfusion.*

**Question:** Is anti-D Ig prophylaxis indicated for early medical termination with no instrumentation?

## Conclusion

The SHOT anti-D immunisation dataset continues to expand as more cases are reported each year. In some, an obvious error is identified and indeed, in Chapter 14, Adverse Events Related to Anti-D Immunoglobulin (Ig) of this year's report, 409 reports related to errors involving anti-D Ig are reviewed, of which 81.4% relate to the omission or late administration of anti-D Ig, putting these women at risk of sensitisation.

There is guidance on the use of anti-D Ig prophylaxis from the National Institute for Health and Care Excellence (NICE 2008 and 2012) and the British Society for Haematology (BSH Qureshi et al. 2014). However, despite the use of prophylactic anti-D Ig (both RAADP and post sensitising events) being founded on sound research and approved by BSH and NICE, a number of questions remain and are highlighted by the immunisation data reported here, including whether obesity, gestation beyond term and twin pregnancies require additional doses of anti-D Ig. While the Royal College of Obstetricians and Gynaecologists green top guidance has been archived in favour the BSH guideline, we are concerned that the guidance from BSH and NICE related to events in early pregnancy is not identical, with BSH recommending prophylaxis for ectopic pregnancies whereas NICE does not recommend anti-D Ig prophylaxis where the ectopic pregnancy is medically managed. Similarly, BSH advises anti-D Ig in some cases of threatened miscarriage where NICE guidance does not.

SHOT experts are also aware some centres have developed 'bespoke' guidance containing terms such as 'standard dose' and 'higher dose' anti-D Ig. Such terms should be avoided in any guidance issued, and the minimum recommended dose for each clearly specified clinical scenario should be given in international units (IU) to avoid confusion.

The SHOT data suggest that even where 'ideal' care in terms of anti-D Ig prophylaxis has been given during the previous or index pregnancy, women can become sensitised/immunised. Data from the NHSBT AIR' study (looking for genetic influences that predispose women to developing red cell alloantibodies during pregnancy) may be informative to identify women at higher risk of immunisation.

The responsibility for ensuring women receive appropriate, timely and adequate anti-D Ig prophylaxis (both RAADP and following PSE) must be shared between the woman herself, midwifery and obstetric services, other departments the pregnant woman may be in contact with, including general practice and emergency care, and transfusion laboratories who issue anti-D Ig. One question arising from this year's data is whether transfusion laboratories should proactively chase up cases where antenatal anti-D Ig

prophylaxis has been issued but confirmation of administration is not received. Appendices 15.1 and 15.2 show examples of such good practice.

All healthcare professionals, including laboratory staff, involved in the care of pregnant women must be encouraged to send in fully completed datasets on newly identified cases of anti-D immunisation in pregnancy, as the SHOT anti-D immunisation data may be the only way the important questions posed at the beginning of this chapter will be answered, particularly why women with apparently ideally managed pregnancies are still becoming immunised.

#### \*The AIR study for pregnant women with red cell antibodies

The AIR study is a research project funded by NHSBT and aims to collect 2000 deoxyribonucleic acid (DNA) samples from alloimmunised women for a genome wide screening study to identify genes that may enhance the likelihood of antibody production.

## References

BSH Qureshi H, Massey E et al. (2014) **Guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn.** *Transfus Med* 24(1), 8-20

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## Appendices

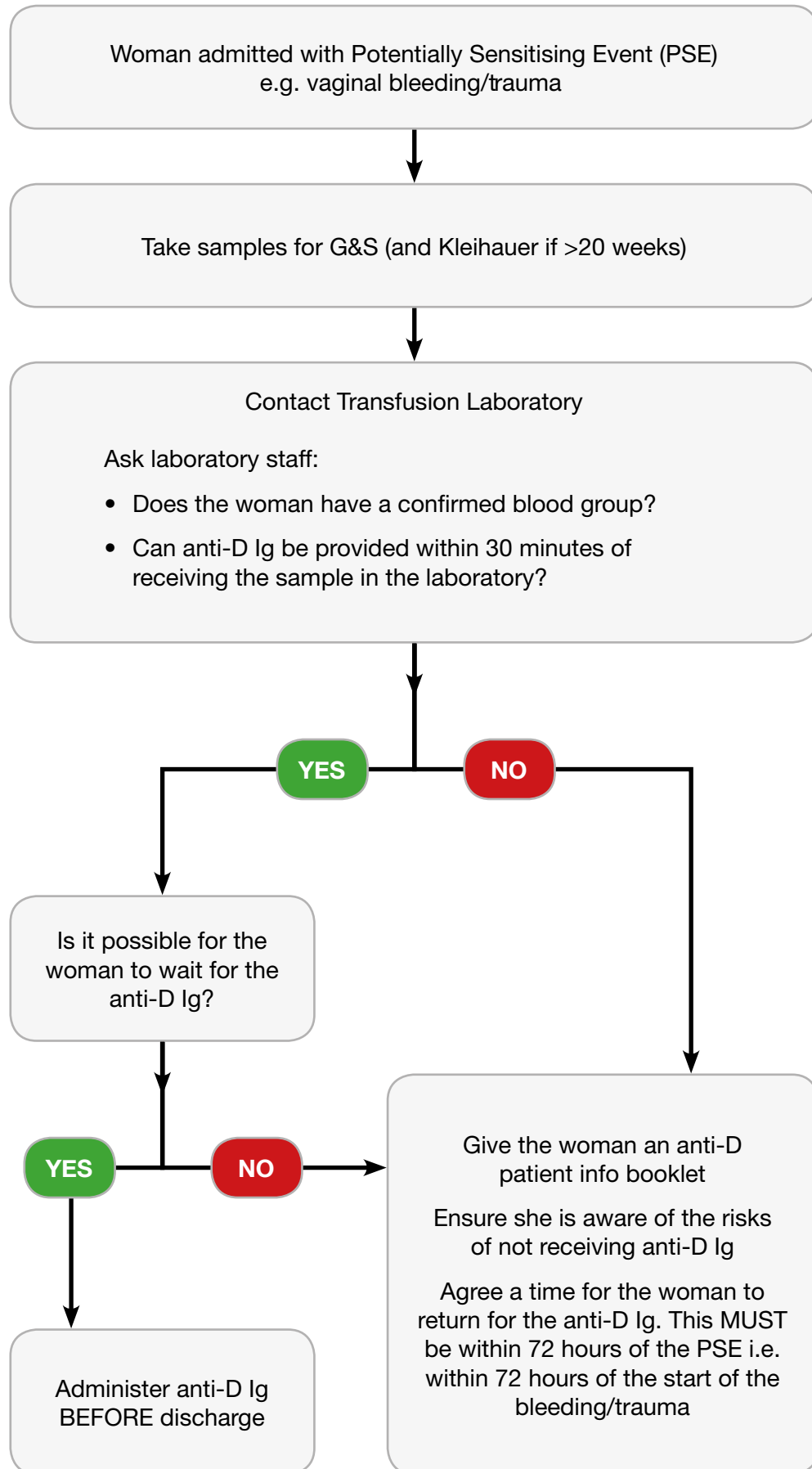
### Description of Test

Take action **BEFORE 72 hours** has passed from a potentially sensitising event

1. Contact the ward responsible for the patient, if unable to identify the ward responsible for the patient go to step 2
2. Ask a senior member of staff to locate patient using LE 2.2, if unable to identify the ward responsible for the patient go to step 3
3. Contact the Gynaecology Registrar & inform a senior member of transfusion staff. (There is an agreement in place with the Obstetric Department to escalate to the gynaecology registrar if a woman cannot be located and is at risk of breaching the 72 hour deadline)

Appendix 15.1:  
Example of the escalation process for transfusion laboratory staff if a patient cannot be located and is at risk of breaching the 72-hour deadline for the administration of anti-D Ig

Appendix 15.2:  
Example of the  
procedure for  
requesting anti-D  
immunoglobulin  
from the  
transfusion  
laboratory



# REACTIONS IN PATIENTS

## Definition: Serious adverse reactions (SAR) are defined for EU reporting as follows:

An unintended response in a donor or in a patient that is associated with the collection, or transfusion of blood or blood components that is fatal, life-threatening, disabling or incapacitating, or which results in or prolongs hospitalisation or morbidity. Blood Establishments and the person responsible for the management of a hospital blood bank shall notify the Secretary of State (Competent Authority) of any serious adverse reactions observed during or after transfusion which may be attributable to the quality or safety of blood or blood components:

- (i) Collected, tested, processed, stored or distributed by the blood establishment, or
- (ii) Issued for transfusion by the hospital blood bank

**These must be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) (a legal requirement).**

These reactions are described under the following headings:

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# 16

## Acute Transfusion Reactions (Allergic, Hypotensive and Severe Febrile) (ATR) n=253

Authors: Janet Birchall and Fiona Regan

### Definition:

**Acute transfusion reactions are defined in this report as allergic, hypotensive and severe febrile reactions, occurring up to 24 hours following a transfusion of blood or components, for which no other obvious cause is evident.**

### Introduction

These reactions are classified according to the International Haemovigilance Network/International Society for Blood Transfusion (IHN/ISBT) definitions which are summarised in Table 16.2, available on-line (ISBT/IHN 2011) and have been adopted by the British Society for Haematology (BSH) (BSH Tinegate et al. 2012).

Cases of acute reaction due to incorrect component transfused, haemolytic reaction, transfusion-related acute lung injury (TRALI), transfusion-associated circulatory overload (TACO), transfusion-associated dyspnoea (TAD) or those due to bacterial contamination of the component are excluded.

### Key SHOT message

- A reduction in the number of ATR reported corresponds with the decrease in blood components issued. This relationship is most evident for commonly-used components such as red cells and platelets and provides support for the message that only patients likely to benefit should receive blood

### Recommendation

- Platelets suspended in platelet additive solution (PAS) are associated with a reduction in allergic response (BSH Estcourt et al. 2017). Hospitals should consider preferential use of readily available pooled platelets suspended in PAS in patients with a history of allergic reactions. This should include paediatric patients where apheresis platelets are usually the platelet component of choice. If reactions continue, despite antihistamine cover, then platelets resuspended in 100% PAS can be supplied

#### Action: Hospital Transfusion Teams (HTT)

- Give appropriate targeted treatment and if needed, preventive cover for future transfusion (BSH Tinegate et al. 2012), as indicated below:

#### Action: HTT

Table 16.1:  
Targeted  
treatment for  
future transfusion  
reactions

Reaction	Treatment	Prevention of recurrent reactions
Febrile	Paracetamol	Paracetamol 60 minutes before anticipated time of reaction
Allergic	Antihistamine (steroid should not be used routinely)	If previous reaction with apheresis platelets try pooled platelets in PAS If recurrent, give antihistamine before transfusion
	If anaphylaxis, adrenaline is essential	If recurrent, consider washed platelets/red cells; for fresh frozen plasma (FFP) try a pooled component e.g. solvent-detergent treated plasma

Key recommendations from previous years can be found in the supplementary information on the SHOT website [www.shotuk.org](http://www.shotuk.org).

	1 = Mild	2 = Moderate	3 = Severe
<b>Febrile type reaction</b>	A temperature $\geq 38^{\circ}\text{C}$ and a rise between 1 and $2^{\circ}\text{C}$ from pretransfusion values, but no other symptoms/signs	A rise in temperature of $2^{\circ}\text{C}$ or more, or fever $39^{\circ}\text{C}$ or over and/or rigors, chills, other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion	A rise in temperature of $2^{\circ}\text{C}$ or more, and/or rigors, chills, or fever $39^{\circ}\text{C}$ or over, or other inflammatory symptoms/signs such as myalgia or nausea which precipitate stopping the transfusion, prompt medical review AND/OR directly results in, or prolongs hospital stay.
<b>Allergic type reaction</b>	Transient flushing, urticaria or rash	Wheeze or angioedema with or without flushing/urticaria/rash but without respiratory compromise or hypotension	Bronchospasm, stridor, angioedema or circulatory problems which require urgent medical intervention AND/OR, directly result in or prolong hospital stay, or Anaphylaxis (severe, life-threatening, generalised or systemic hypersensitivity reaction with rapidly developing airway and/or breathing and/or circulation problems, usually associated with skin and mucosal changes
<b>Reaction with both allergic and febrile features</b>	Features of mild febrile and mild allergic reactions	Features of both allergic and febrile reactions, at least one of which is in the moderate category.	Features of both allergic and febrile reactions, at least one of which is in the severe category.
<b>Hypotensive reaction</b>		Isolated fall in systolic blood pressure of 30 mm or more occurring during or within one hour of completing transfusion and a systolic blood pressure 80 mm. or less in the absence of allergic or anaphylactic symptoms. No/minor intervention required.	Hypotension, as previously defined, leading to shock (e.g. acidaemia, impairment of vital organ function) without allergic or inflammatory symptoms. Urgent medical intervention required.

**Table 16.2:**  
Classification of reactions

## Number of reactions and reaction rates n=253

### Deaths n=0

There were no deaths related to the transfusion reaction.

### Major morbidity n=76

Severe reactions, as classified above, are used to define major morbidity reactions.

Reactions have been classified as follows:

	Moderate	Severe	Total
Febrile	98	26	124
Allergic	61	46	107
Mixed allergic/febrile	14	4	18
Hypotensive	4	0	4
<b>Total</b>	<b>177</b>	<b>76</b>	<b>253</b>

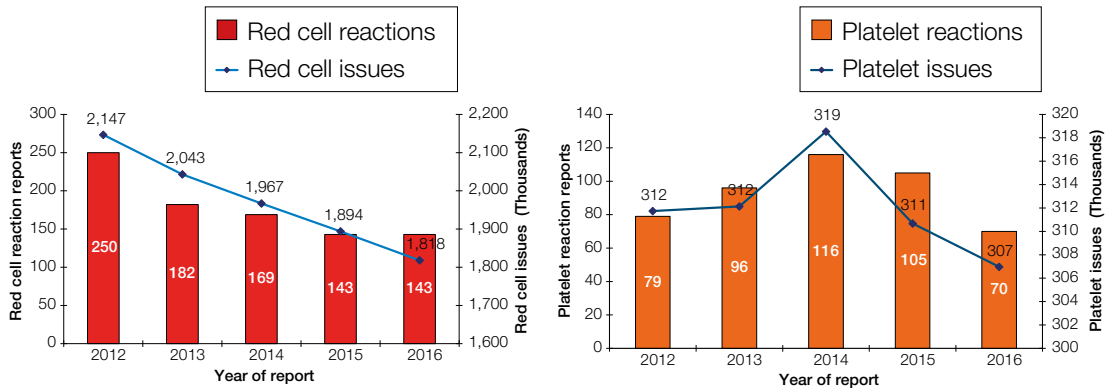
**Table 16.3:**  
Classification of ATR in 2016

*N.B. in 40 of the 76 reactions classified as severe this was primarily because the patient was admitted*



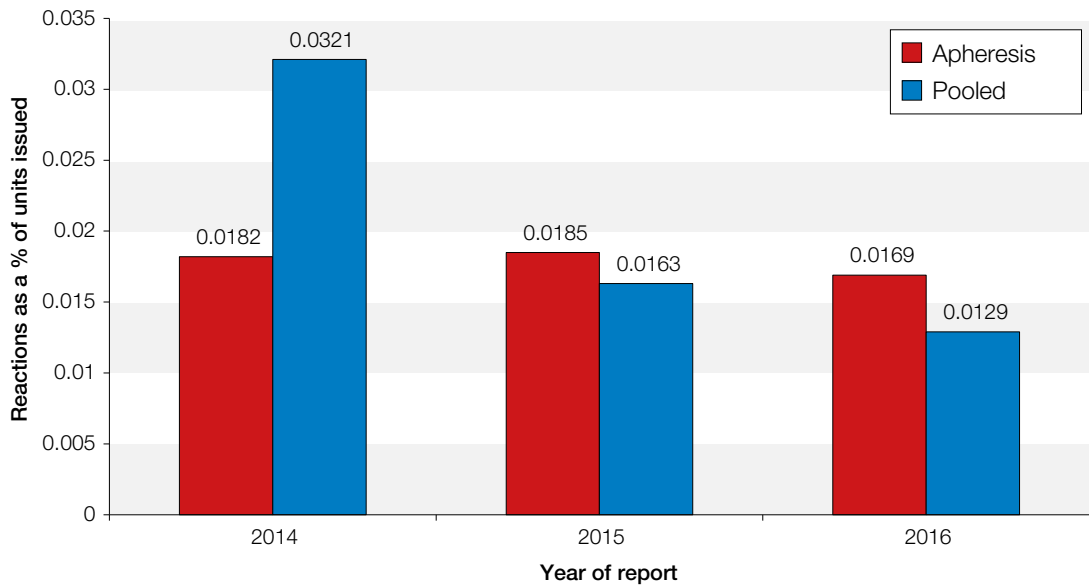
The total number of reactions reported over the last few years has reduced in keeping with the fall in total blood component demand. For the two most commonly used blood components, red cells and platelets, the relationship between units issued and reactions reported is striking; Figure 16.1. There is less correlation with other blood components likely because of the smaller number of reactions reported.

**Figure 16.1:**  
Reactions related to the number of issues from UK Blood Services



In addition to the reduction in platelet demand, suspension of pooled platelets in PAS, which is now universal in England and Wales, is also likely to have contributed to the reduction in reactions. This year, in these countries, in keeping with 2015 data, allergic reactions associated with pooled platelets are fewer than with apheresis platelets. This is in contrast to reaction rates in 2014 when both components were suspended in plasma; Figure 16.2.

**Figure 16.2:**  
Percentage of allergic reactions 2014 to 2016



### Type of reactions by component

This remains similar to previous reports; Figure 16.3. Red cells are usually associated with febrile-type reactions (~75%) whereas plasma and platelets more commonly cause allergic reactions (~80% and ~60% respectively). Only one reaction associated with methylene blue treatment was reported. The percentage of severe reactions remains similar to 2014 and 2015 at 30.0% (76/253). As in previous years, many reactions were difficult to classify as a result of insufficient information, the IHN/ISBT grade of reaction not being used and because of the difficulty distinguishing true transfusion reactions from symptoms and signs associated with the patient's underlying condition.

Analysis of reactions remains comparable in the following parameters:

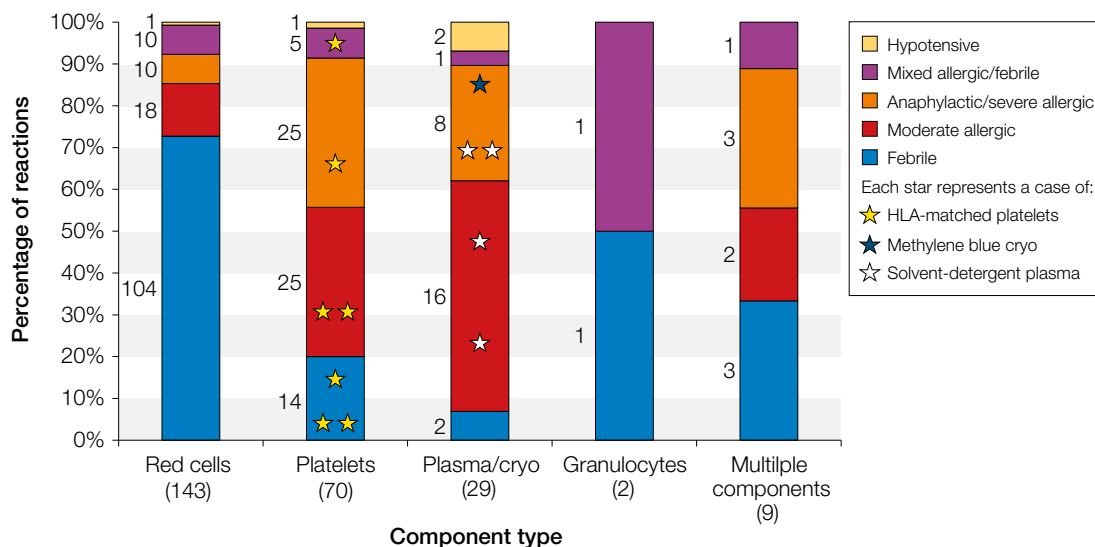


Figure 16.3: Reaction by component type

Characteristic	Occurrence
Age distribution	About 90% of patients were aged 18 years or over
Gender	Similar numbers of male and female cases
Urgency of transfusion	70% were given routinely
Timing of transfusion	About 60% occurred within standard hours
Location	About 50% were on wards and 20% in outpatient/day case units

Table 16.4: Characteristics of ATR

### Treatment of reactions

Similar to previous years an antihistamine with or without steroid continues to be a common treatment of reactions with only febrile/inflammatory type symptoms and/or signs; Table 16.5. In addition to no evidence of benefit, the use of steroids may immunosuppress some already immunocompromised patients and increase the risk of side effects such as infection and other adverse events (Waljee et al. 2017).

Following a pure febrile reaction, in cases where details of subsequent management were provided, 42.9% planned use of an antihistamine with or without steroids; Table 16.6.

Given the evidence for reduced allergic reactions to pooled platelets suspended in PAS compared to apheresis platelets, analysis of future management following allergic reactions to apheresis platelets was identified. Thirty-one allergic reactions to apheresis platelets occurred and future management was stated in 18/31. In 10/18 premedication was advised, in 4/18 washed platelets were advised, in 1/18 human leucocyte antigen (HLA)/human platelet antigen (HPA) testing was advised and in only 3/18 were pooled platelet components recommended.

**Table 16.5:**  
Treatment of  
reported reaction

	Number	Medication stated	Antihistamine +/- steroid
<b>Febrile</b>			
2016	124	102/124 (82.3%)	51/102 (50.0%)
2015	142	101/142 (71.1%)	57/101 (56.4%)
2014	144	97/144 (67.4%)	42/97 (43.3%)
	Number	Medication stated	Paracetamol
<b>Allergic</b>			
2016	107	101/107 (94.4%)	11/101 (10.9%)
2015	122	106/122 (86.9%)	10/106 (9.4%)
2014	139	112/139 (80.6%)	14/112 (12.5%)

**Table 16.6:**  
Planned treatment  
for subsequent  
febrile reactions

	Number where treatment stated	Antihistamine +/- steroid
2016	21	9/21 (42.9%)
2015	9	7/9 (77.8%)
2014	24	9/24 (37.5%)

### Illustrative cases

#### Case 16.1: A febrile reaction treated with hydrocortisone and chlorphenamine

*An adult male with sickle cell disease attended an outpatient department to receive an exchange blood transfusion. After the first unit of red cells he developed rigors. Observations revealed a temperature of 38.6°C and a rise of 2°C. His blood pressure was also increased compared to pre-transfusion observations but there were no respiratory signs or symptoms. The transfusion was discontinued and he was given hydrocortisone and chlorphenamine. He recovered in less than one hour and was subsequently admitted to the ward for antibiotics to treat a possible chest infection. Repeat serology and blood culture of the patient and implicated unit were negative.*

Although admission may have been required to manage a possible underlying infection it is difficult to understand why hydrocortisone and chlorphenamine were considered to be appropriate.

#### Case 16.2: A moderate febrile reaction resulting in transfer of the patient from a community hospital to a larger hospital with an emergency department

*An elderly male with myelodysplastic syndrome (MDS) received two units of red cells in a community hospital. He was known to have anti-C, anti-Kp<sup>a</sup> and a non-specific autoantibody. Following transfusion of his second unit routine observations identified a temperature rise from 36.9°C prior to transfusion to 38.7°C. An ambulance was called and the patient transferred to the emergency department at a larger hospital. On arrival he was given paracetamol, his temperature settled and he was discharged home. Repeat serology, and culture of the patient and implicated unit revealed nil significant.*

Febrile-type reactions, although not serious, can alarm clinical staff and result in significant time and resource to investigate and manage.

#### Case 16.3: An allergic reaction to apheresis platelets

*An elderly male with MDS and possible sepsis but no bleeding received a unit of apheresis platelets. Ten minutes after starting the transfusion he developed a swollen tongue and was unable to talk. His observations were stable, the transfusion was discontinued and he was given intravenous hydrocortisone. The reaction resolved and a decision made that further platelet transfusion should routinely be covered with both hydrocortisone and chlorphenamine.*

A patient with MDS at an increased risk of infection may have benefitted more from prudent use of platelet transfusion and pooled platelets suspended in platelet additive solution as an alternative to premedication for apheresis platelets, if required.

**Case 16.4: A severe reaction in a patient with IgA deficiency**

*An adult female received transfusion of red cells to treat a postpartum bleed on the delivery ward. Within 15 minutes of the start of the transfusion she developed a fever, chest tightness and throat swelling associated with a temperature rise of more than 2°C to 39.7°C, dyspnoea and visible angioedema. She received paracetamol, an antihistamine, hydrocortisone and intravenous adrenaline. After 4 hours her observations settled. Subsequent investigation identified that she was IgA deficient with IgA antibodies and IgA deficient or washed red cells were recommended for any future transfusion.*

Reactions associated with IgA deficiency are rare despite a prevalence of IgA deficiency of around 1 in 200. In this case symptoms of allergy were present, which are considered standard, but in addition a fever occurred more typical of a febrile type reaction. A similar reaction was reported last year and included in the illustrative cases.

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# 17 Transfusion-Transmitted Infections (TTI) n=1

Authors: Rachael Morrison and Su Brailsford

## Definition of a TTI:

A report was classified as a transfusion-transmitted infection if, following investigation:

- The recipient had evidence of infection following transfusion with blood components, and there was no evidence of infection prior to transfusion, and no evidence of an alternative source of infection

and either:

- At least one component received by the infected recipient was donated by a donor who had evidence of the same transmissible infection

or:

- At least one component received by the infected recipient was shown to contain the agent of infection

Note that for the purposes of the European Union (EU) legislation, serious adverse reactions (SAR) are defined as any reactions in patients that are 'life-threatening, disabling or incapacitating, or which result in or prolong hospitalisation or morbidity.'

These must be reported to the Medicines and Healthcare Products Regulatory Agency (MHRA) (a legal requirement). This includes all confirmed transfusion-transmitted infections.

## Key SHOT messages

- Bacterial screening of platelets has been shown to be useful in reducing the risk of contaminated platelets entering the blood supply, however, there is still a small residual risk that bacteria may not be detected
- The risk of transfusion-transmitted hepatitis B virus (HBV), hepatitis C virus (HCV) or human immunodeficiency virus (HIV) is very low in the UK
- Clinicians investigating suspected viral TTI should explore all possible risk exposures in parallel with the Blood Service investigations, in order to determine the patient's most likely source of infection. For example, hepatitis E virus (HEV) is commonly transmitted by food. Investigation includes checking records and if available, testing samples, including non-transfusion samples, taken prior to the implicated transfusion(s) to check that the recipient did not already have infection

## Introduction

This chapter describes the possible transfusion-transmitted infection incidents investigated by the United Kingdom (UK) Blood Services and reported to the National Health Service Blood and Transplant (NHSBT)/Public Health England (PHE) Epidemiology Unit in 2016.

## Summary of reports made to the NHSBT/PHE Epidemiology Unit in 2016

During 2016, UK Blood Services investigated 108 suspected bacterial cases and 18 suspected viral incidents (Figure 17.1). From these suspected cases, there have been:

- One transfusion-transmitted HEV incident, following multiple transfusions between October 2015 and January 2016
- Three bacterial near miss incidents from Northern Ireland
- One bacterial near miss incident in England

Further information about how and what to report can be found in 'SHOT Bites no. 7 Transfusion-transmitted infections' at <https://www.shotuk.org/wp-content/uploads/SHOT-Bites-No7-TTI.pdf>

### Major morbidity n=1

A patient with a confirmed case of transfusion-transmitted HEV suffered a serious reaction (Case 17.5).

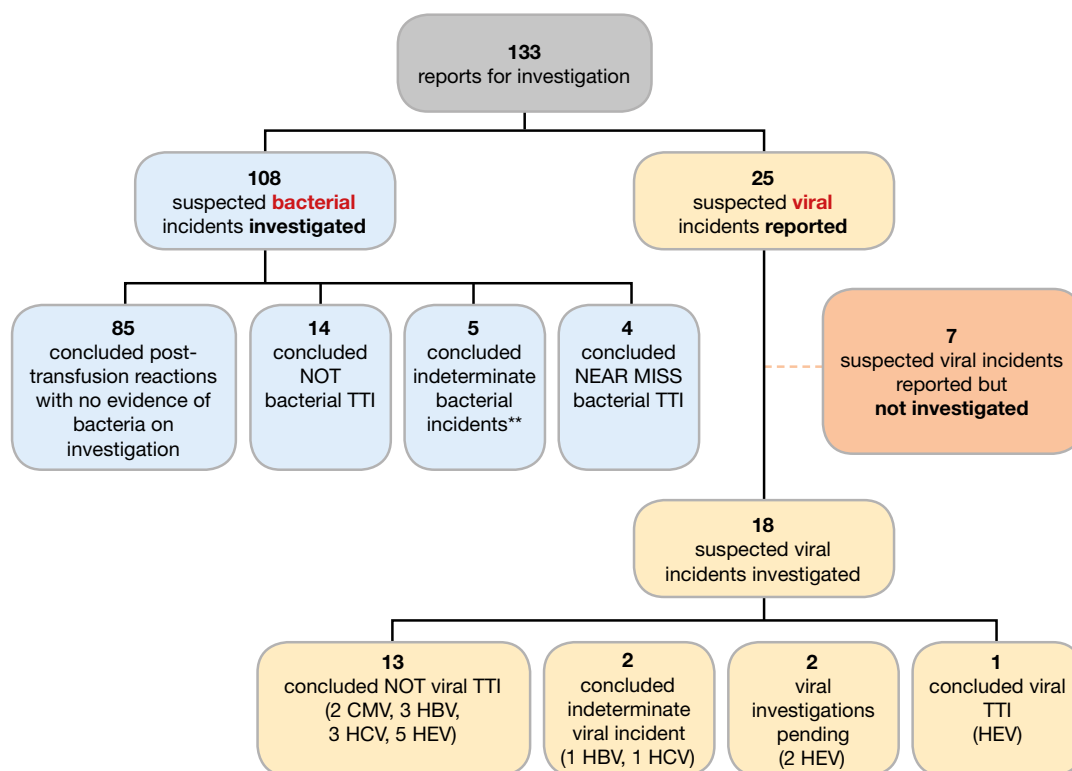


Figure 17.1: Outcome of reports of suspected TTI made to the NHSBT/PHE Epidemiology Unit in 2016\*

\*HCV investigations where the transfusion was prior to screening are not included in the above Figure (2 HCV incidents in 2016)

\*\*No packs to test but investigation based on information received indicates unlikely to reflect a TTI

CMV=cytomegalovirus

### Bacterial TTI reports 2016

In 2016, there were no reported and confirmed bacterial transfusion-transmitted infections, however there were three near miss incidents reported by the Northern Ireland Blood Transfusion Service (NIBTS) of which two occurred in 2016 and one in 2014, and one near miss event in 2016 reported by NHSBT. The four UK Blood Services all use the BacT/ALERT system for bacterial screening but each country uses different methods for sampling platelet packs as shown in Table 17.1. For example NHSBT is the only Blood Service that samples each split apheresis pack; the Welsh Blood Service resamples platelets at day 4 to prolong the shelf life and NIBTS do not sample the packs until 48 hours have passed since donation.

**Case 17.1: Near miss 1**

*One unit of apheresis platelets was issued and transfused as a 3-day-old pack without event. Pack 2 of the same donation was requested for the same patient, however, on inspection prior to transfusion, staff noted a clump of material in the 5-day-old pack and returned the pack to NIBTS for investigation. Staphylococcus aureus was isolated from pack 2, bacterial screening results for both packs were negative at day 7. The donor was a regular donor who had given over 100 platelet donations. The donor was recalled and permission given for samples to be taken including peripheral blood cultures and swabs from the antecubital fossa (venepuncture site, pre and post cleansing) nasal and oral cavities; axilla; and inguinal areas. Staphylococcus aureus was only cultured from the left nostril. Molecular typing gave indistinguishable results for the isolates from both the pack and the donor and as such represent a single strain. The donor was permanently withdrawn.*

**Case 17.2: Near miss 2**

*Packs 1, 2 and 3 of an apheresis platelet donation were issued on day 3 to a local hospital. Pack 3 was transfused without any symptoms or signs of a transfusion reaction. Pack 2 was requested for another patient, however, clumps of white material were noted in the platelet pack by one of the nursing team prior to transfusion. Platelet packs 1 and 2 were returned to NIBTS. The donor was a regular donor with no obvious ill health. All three packs were negative on bacterial screening at day 7. Pack 1 was retested and was negative. Pack 2 was re-sampled and cultured and Staphylococcus aureus confirmed. The donor was recalled for samples and peripheral blood cultures and swabs were taken from the antecubital fossa (venepuncture site – pre and post cleansing) nasal and oral cavities; axilla; and inguinal areas. Staphylococcus aureus was not isolated from the blood cultures or skin swabs of the donor. The donor has been temporarily deferred until the investigation concludes.*

**Case 17.3: Near miss 3**

*Two packs of apheresis platelets from one donation were received at one of the NHSBT stock-holding sites. One of the platelet packs looked abnormal and was described as looking like 'scrambled egg in orange juice'. Pack 2 appeared normal on visual inspection. Both units were returned for bacteriological investigation. Small Gram-negative rods were seen on Gram stain from the index, visually abnormal pack, and the organism was subsequently identified as Serratia marcescens. All processes were reviewed and no errors observed. The donor was a regular donor who was well at the time of donation. The most likely source of contamination was thought to be environmental whereas a subclinical infection in the donor was less likely. The implicated platelet pack was sent for pressure testing to exclude this as a source of the contamination, there was no evidence of any leaks. Environmental monitoring records of both the donor centre and manufacturing site were checked and found to be as expected. Despite extensive investigations no obvious source of the contamination was found.*

**Case 17.4: Near miss case from 2014**

*Transfusion laboratory staff noted obvious visible clumping in a day 6 apheresis platelet pack (pack 1). Cultures of both aerobic and anaerobic BacT/ALERT samples were negative at 12 days. The pack was resampled and Staphylococcus aureus was confirmed on resampling from pack 1 only. Pack 2 was negative on resampling. The donor was recalled and a number of skin abrasions were noted, the donor had recently played rugby. Swabs and peripheral blood cultures were taken from the donor and Staphylococcus aureus was isolated from the left nasal cavity. Molecular typing showed the pack and donor isolated were indistinguishable. The donor was permanently removed from active panel.*

**Bacterial TTI 1996 – 2016**

Screening of platelet components cannot guarantee freedom from bacterial contamination. Packs are released for issue as 'negative-to-date' which may be before bacteria have multiplied sufficiently to trigger an initial screening reaction. On the other hand, an initial screen reactive result may be a false positive result, or related to bacteria which are of low pathogenicity and unlikely to cause any noticeable reaction in the recipient. The last confirmed bacterial TTI was in 2015. Prior to 2015, the previous



documented confirmed bacterial TTI was in 2009, predating universal bacterial screening of platelets throughout the UK Blood Services (2011). There have been 8 near misses (7 in platelets) reported to the unit between 2011 and 2016. Overall, a total of 37/44 bacterial transfusion-transmissions to individual recipients (34 incidents) have been caused by the transfusion of platelets, and 7/44 by red cells (Table 17.3) since reporting began.

Haemovigilance systems for bacterial TTI are passive and as such rely on clinical colleagues to report suspected TTI. Following the introduction of bacterial screening of platelets, colleagues were reminded that there was still the possibility of TTI occurring from both platelet and red cell transfusion and the numbers of reported suspected TTI have remained almost constant. Current British Society for Haematology (BSH) guidance recommends that patients are advised to report any symptoms that occur within 24 hours of transfusion (BSH Tinegate et al. 2012) although our experience suggests that patients with confirmed TTI become unwell very rapidly. Within NHSBT, post-dated platelets are randomly sampled for the presence of bacteria, and to date, there is no evidence that bacterial screening is routinely failing to detect potentially pathogenic bacteria.

	Time of sampling (hour)	Volume sampled (mL)	Apheresis sample	Time at release (hour)	Length of screening
NHSBT	36	2 x 8	Post-split	6	Day 7
NIBTS	48	2 x 8	Pre-split	6	Day 9
SNBTS	18	2 x 7	Pre-split	6	Day 7
WBS	16	2 x 10	Pre-split	From start of screening	Day 7*

\*Additional 10mL sample taken at day 4 to extend shelf-life from 5 to 7 days

**Table 17.1:**  
Bacterial screening methods used by the UK Blood Services

## Viral TTI reports 2016

In 2016, there was one confirmed transfusion-transmitted HEV incident.

### Case 17.5: Confirmed viral HEV TTI case (major morbidity)

*A male patient in his 70's with a diagnosis of aplastic anaemia was receiving regular blood transfusions with two units of red cells every month. In February 2016 the patient was found to have abnormal liver function tests (LFT). A blood sample was reported in March 2016 as anti-HEV IgM and IgG positive and ribonucleic acid (RNA) positive with a viral load of 410,000IU/mL. Records of all donors of the implicated packs were examined and archive samples of the donations transfused between December 2015 and January 2016 were retrieved and tested (6 donors); all tested HEV RNA negative. Earlier transfusions given between October to November 2015 were then investigated (4 donors); one of the samples from a donor who donated in October 2015 was confirmed to be HEV RNA positive with a viral load of 3574 IU/mL. The donor cleared the infection and remains on the donor panel.*

### Update on viral TTI reports from 2015

There were two pending HCV and one HEV case in 2015, all of which were found to be NOT a viral TTI.

### Viral TTI 1996 to 2016

The year of transfusion may be many years prior to the year in which the case is investigated and reported to SHOT because of the chronic nature, and therefore late recognition, of some viral infections. Since 1996, 30 confirmed incidents of transfusion-transmitted viral infections have been documented, involving a total of 37 recipients. HBV is the most commonly reported proven viral TTI in the UK. This is partly because the 'window period' where an infectious donation from a recently infected donor cannot be detected by the screening tests is longer than for HCV or HIV, despite nucleic acid testing (NAT).

## Risks of HBV, HCV or HIV being transmitted by transfusion

The risks of a potentially infectious HBV, HCV or HIV window period donation not being detected on testing in the UK are very low (Table 17.2) (PHE 2016).

**Table 17.2:**  
The estimated risk of a potentially infectious HBV, HCV or HIV window period\* donation entering the UK blood supply: 2013-2015

	HBV	HCV	HIV
Number per million donations	0.79	0.025	0.18
95% confidence interval	0.22-1.30	0.01-0.04	0.12-0.27
At 2.3 million donations per year testing will miss a potentially infectious window period donation every:	0.6 years	19-20 years	2-3 years

\*The window period is the time at the start of an infection before the tests can detect it

Far fewer TTI are observed in practice than estimated in Table 17.2, partly because the estimates have wide uncertainty and the model is based on the risk in all donations tested. The model does not incorporate pack non-use, recipient susceptibility to infection, or under ascertainment/under reporting, for example due to recipients dying from an underlying medical condition before a chronic asymptomatic viral condition is identified, or, in the case of HBV, an asymptomatic acute infection.

## HEV testing 2017

Following a review by the Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO 2016) in October 2016, UK Blood Services have implemented 100% HEV-screening. 100% HEV-screened red cells were available in England from 1<sup>st</sup> May, from 3<sup>rd</sup> April in Wales, and in Scotland from 5<sup>th</sup> April 2017. Replacement of frozen components followed as stocks were used up.

## Parasitic TTI

There were no reported parasitic infections for investigation in 2016. There have been two proven malaria TTI reported to SHOT, the last in 2003 (Table 17.3). Malaria antibody testing was not applicable at the time according to information supplied at donation, and the donor selection guidelines were updated after these incidents to minimise the risk of further malaria TTI (Kitchen et al. 2005). The current selection guidelines on deferral and additional testing for malaria can be accessed at the UK transfusion guidelines web pages at <http://www.transfusinguidelines.org.uk/red-book>.

## Variant Creutzfeldt-Jakob Disease (vCJD) 2016

There were no vCJD investigations in 2016.

## vCJD 1996-2016

Three vCJD incidents (Table 17.3) took place prior to the introduction of leucodepletion and other measures taken by the UK Blood Services to reduce the risk of vCJD transmission by blood, plasma and tissue products. All these measures have been reviewed and endorsed by SaBTO (SABTOa 2013). Risk assessment and research into vCJD continues however currently there is no suitable blood test available for screening blood donations for vCJD.

More information can be found here [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/407681/measures-vcjd.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/407681/measures-vcjd.pdf).

Year of transfusion**	Number of incidents (recipients) by infection											Implicated component				
	Bacteria	HAV	HBV	HCV	HEV	HIV	HTLV I	Parvovirus (B19)	Malaria	vCJD/prion	Total	RBC	Pooled platelet	Apheresis platelet	FFP	Cryo
Pre 1996	-	-	1 (1)	-	-	-	2 (2)	-	-	-	3 (3)	3	-	-	-	-
1996	-	1 (1)	1 (1)	1 (1)	-	1 (3)	-	-	-	1 (1)	5 (7)	5	1	-	1	-
1997	3 (3)	-	1 (1)	1 (1)	-	-	-	-	1 (1)	2 (2)	8 (8)	6	1	1	-	-
1998	4 (4)	-	1 (1)	-	-	-	-	-	-	-	5 (5)	2	1	2	-	-
1999	4 (4)	-	2 (3)	-	-	-	-	-	-	‡ (1)	6 (8)	5	3	-	-	-
2000	7 (7)	1 (1)	1 (1)	-	-	-	-	-	-	-	9 (9)	1	5	3	-	-
2001	5 (5)	-	-	-	-	-	-	-	-	-	5 (5)	-	4	1	-	-
2002	1 (1)	-	1 (1)	-	-	1 (1)†	-	-	-	-	3 (3)	2	1	-	-	-
2003	3 (3)	-	1 (1)	-	-	-	-	-	1 (1)	-	5 (5)	1	1	3	-	-
2004	††	-	-	-	1 (1)	-	-	-	-	-	1 (1)	1	-	-	-	-
2005	2 (2)	1 (1)	1 (1)	-	-	-	-	-	-	-	4 (4)	1	3	-	-	-
2006	2 (2)	-	-	-	-	-	-	-	-	-	2 (2)	-	1	1	-	-
2007	3 (3)	-	-	-	-	-	-	-	-	-	3 (3)	2	1	-	-	-
2008	4 (6)	-	-	-	-	-	-	-	-	-	4 (6)	-	2	4	-	-
2009	2 (3)	-	-	-	-	-	-	-	-	-	2 (3)	1	-	2	-	-
2010	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2011	-	-	1 (2)	-	1 (2)	-	-	-	-	-	2 (4)	2	-	-	2	-
2012	-	-	1 (1)	-	1 (1)	-	-	1 (1)	-	-	3 (3)	2	-	-	1	-
2013	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2014	-	-	-	-	2 (3)	-	-	-	-	-	2 (3)	1	-	-	2	-
2015	1 (1)	-	-	-	2 (3)	-	-	-	-	-	3 (4)	-	2	1	-	1
2016	-	-	-	-	1 (1)	-	-	-	-	-	1 (1)	1	-	-	-	-
<b>Number of incidents</b>	<b>41</b>	<b>3</b>	<b>12</b>	<b>2</b>	<b>8</b>	<b>2</b>	<b>2</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>76</b>					
Number of infected recipients	44	3	14	2	11	4	2	1	2	4	87	36	26	18	6	1
Death due to, or contributed to, by TTI	11	-	-	-	1	-	-	-	1	3	16					
Major morbidity	29	2	14	2	6	4	2	1	1	1§	62					
Minor morbidity	4	1	-	-	4	-	-	-	-	-	9					
<b>Implicated component</b>																
RBC	7	1	11	2	4	2	2	1	2	4	36					
Pooled platelet	21	2	1	-	1	1	-	-	-	-	26					
Apheresis platelet	16	-	1	-	1	-	-	-	-	-	18					
FFP	-	-	1	-	4	1	-	-	-	-	6					
Cryoprecipitate	-	-	-	-	1	-	-	-	-	-	1					

Numbers in brackets refer to recipients

\*No screening was in place for vCJD, human T cell lymphotropic virus (HTLV), hepatitis A virus (HAV), HEV or parvovirus B19 at the time of the documented transmissions. In both malaria transmissions, malaria antibody testing was not applicable at the time according to information supplied at donation

\*\*Year of transfusion may be prior to year of report to SHOT due to delay in recognition of chronic infection

\*\*\*HCV investigations where the transfusion was prior to screening are not included in the above Figure

†The two HIV incidents were associated with window period donations (anti-HIV negative/HIV RNA positive) before HIV NAT screening was in place. A third window period donation in 2002 was transfused to an elderly patient, who died soon after surgery. The recipient's HIV status was therefore not determined and not included

††In 2004 there was an incident involving contamination of a pooled platelet pack with Staphylococcus epidermidis, which did not meet the TTI definition because transmission to the recipient was not confirmed, but it would seem likely. This case was classified as 'not transfusion-transmitted'

‡Same blood donor as one of the 1997 transmissions so counted as the same incident; note: counted as two separate incidents in previous reports

§A further prion case died but transfusion was not implicated as the cause of death. The outcome was assigned to major morbidity instead because although there was post-mortem evidence of abnormal prion proteins in the spleen the patient had died of a condition unrelated to vCJD and had shown no symptoms of vCJD prior to death

Table 17.3: Number of confirmed TTI incidents\*, by year of transfusion\*\* with total infected recipients and outcomes (death, major morbidity, minor morbidity) in the UK between October 1996 and December 2016 (Scotland included from October 1998)

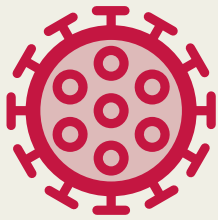


## Safe supplies: A picture for policy

Joint working of NHS Blood and Transplant and Public Health England

# Blood donations UK, 2015

**The risk that testing would NOT detect a HBV, HCV or HIV infection is less than one in a million**



	Estimated that testing would NOT detect an infection every:	Last proven transfusion-transmitted infections in the UK
Hepatitis B	8 months	2012
Hepatitis C	19 years	1999
HIV	2-3 years	2002

**42 million**



Age 17-66 years in the UK

**2.1 million**

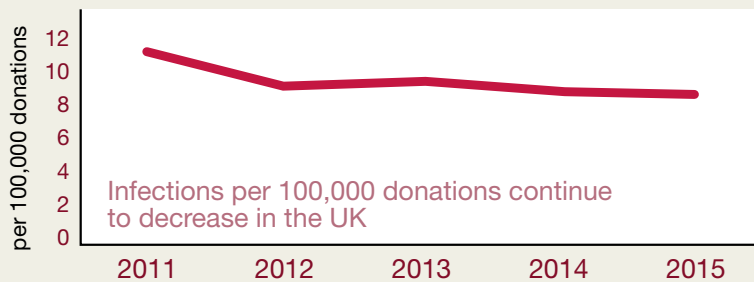


Blood and platelet donations

**199 infections detected**



Mostly chronic hepatitis B and syphilis

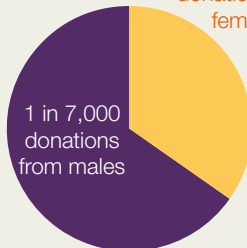


- 64** Hepatitis B
- 64** Syphilis
- 49** Hepatitis C
- 13** HIV
- 9** HTLV

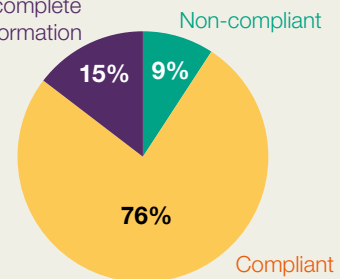
1 in 55,000 donations from repeat donors



1 in 17,000 donations from females



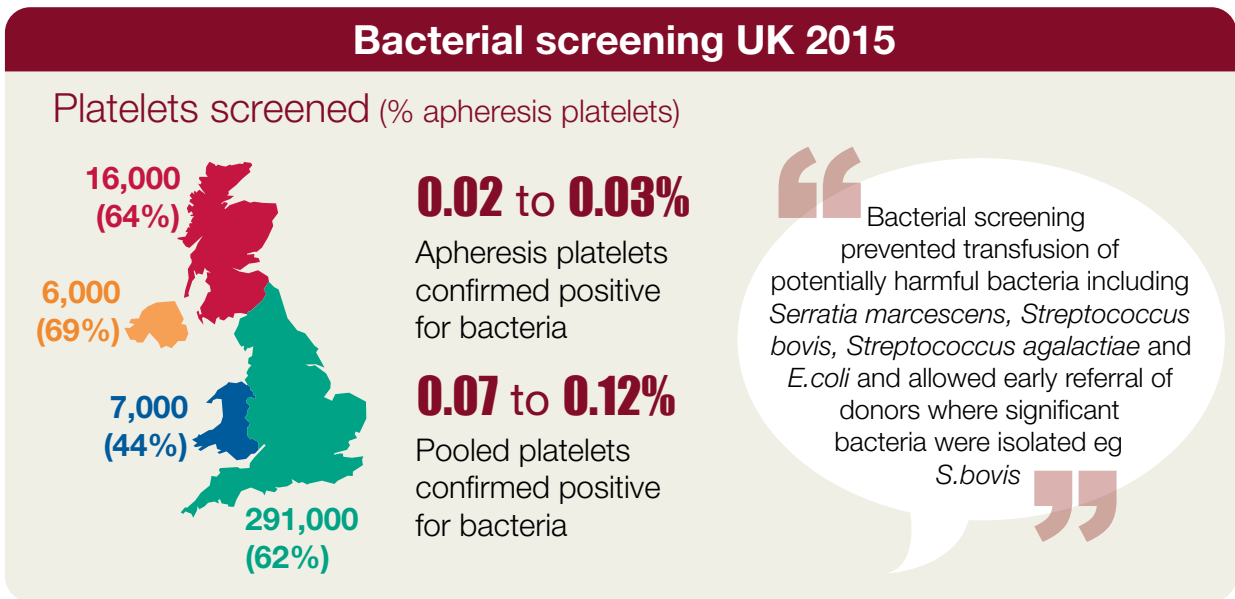
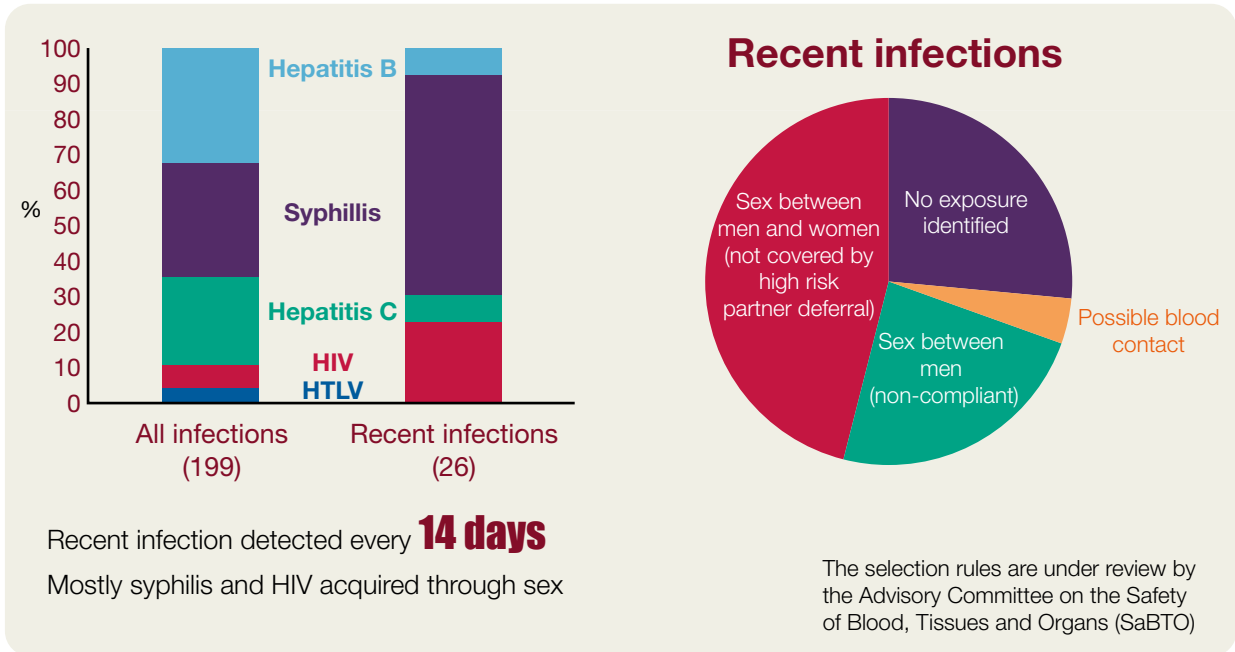
Not known, incomplete information



**Infections more common in new donors and male donors**

Most positive donors had complied with the donor selection rules

PHE publications gateway number: 2016xxx



### Additional testing NHSBT

	Instead of travel deferrals		
	<b>Tested 67,000</b>	<b>POSITIVE</b>	
		0/1460 Chagas disease	490/27,090 Malaria
	<b>4%</b>	Donations gained through additional testing	

Data source: Data supplied to the NHSBT/PHE Epidemiology Unit by NHSBT, WBS, NIBTS & SNBTS.

PHE publications gateway number: 2016453 © Crown copyright

For further information or alternative breakdown of data please contact the National Coordinator for Transfusion-Transmitted Infections via the NHSBT/PHE Epidemiology Unit at [epidemiology@nhsbt.nhs.uk](mailto:epidemiology@nhsbt.nhs.uk).

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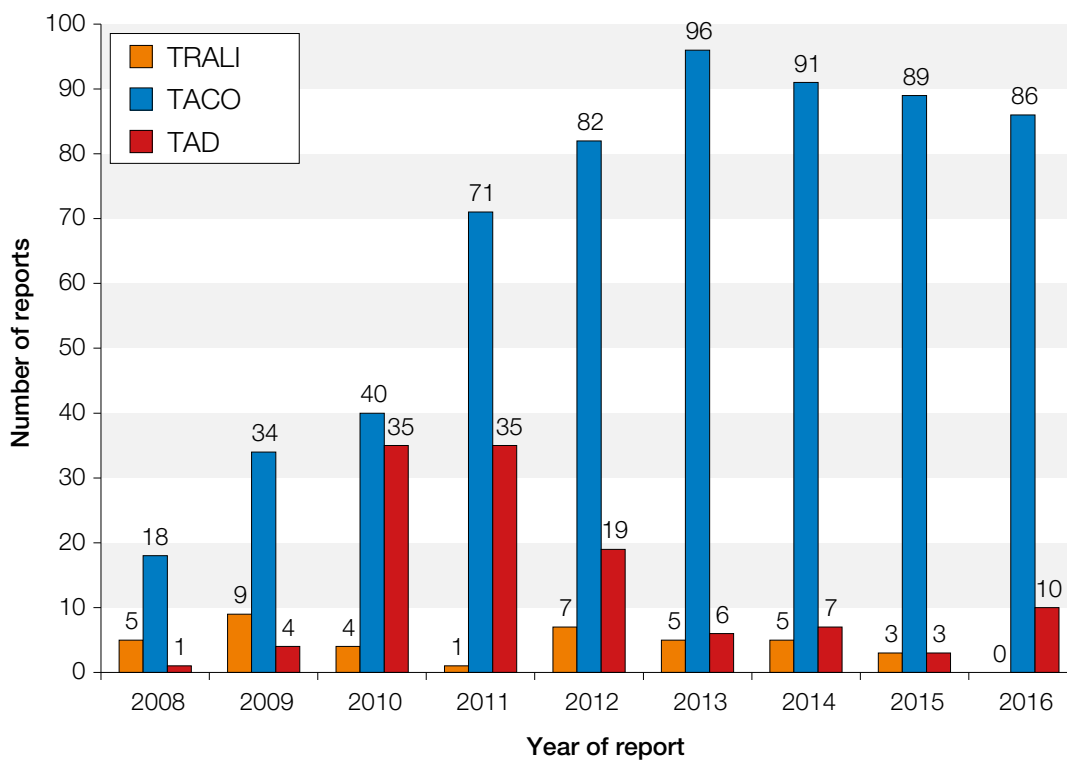
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# Pulmonary Complications

# 18

Pulmonary complications of transfusion are responsible for the majority of deaths and major morbidity from transfusion (61/115, 53.0%, deaths 2010 to 2016, Figure 3.2). During 2016 several discussions have taken place with international collaboration (haemovigilance working party of the International Society of Blood Transfusion (ISBT), the International Haemovigilance Network (IHN) and members of the American Association of Blood Banks (AABB)) about the criteria for diagnosis of transfusion-associated circulatory overload (TACO), and these are summarised in Chapter 18b that follows. Reviewing SHOT data for several years it is apparent that the number of confirmed cases of transfusion-related acute lung injury (TRALI) have reduced, and that further clarity was required about which cases to include. There are therefore changes in the TRALI definition summarised in Chapter 18a. Cases that are not assessed as at least possible TRALI have been moved to the category of transfusion-associated dyspnoea (TAD) (Chapter 18c), and the numbers in the cumulative summary graphs updated to reflect this.



**Figure 18.1:**  
Reports of pulmonary complications by year 2008-2016 (revised to reflect updated TRALI definition)



# 18a Transfusion-Related Acute Lung Injury (TRALI) n=0

Author: Tom Latham

## Definition:

**Transfusion-related acute lung injury (TRALI) is defined as acute dyspnoea with hypoxia and bilateral pulmonary infiltrates during or within 6 hours of transfusion, in the absence of circulatory overload or other likely causes, or in the presence of human leucocyte antigen (HLA) or human neutrophil antigen (HNA) antibodies cognate with the recipient.**

There were no confirmed cases of TRALI this year. Six cases were reported as suspected TRALI; 4/6 cases were transferred to transfusion-associated dyspnoea (TAD), 1/6 case to unclassifiable complications of transfusion (UCT) and one was withdrawn.

Figure 18a.1:  
Number of suspected TRALI cases and deaths at least possibly related to TRALI by year of report: using revised criteria

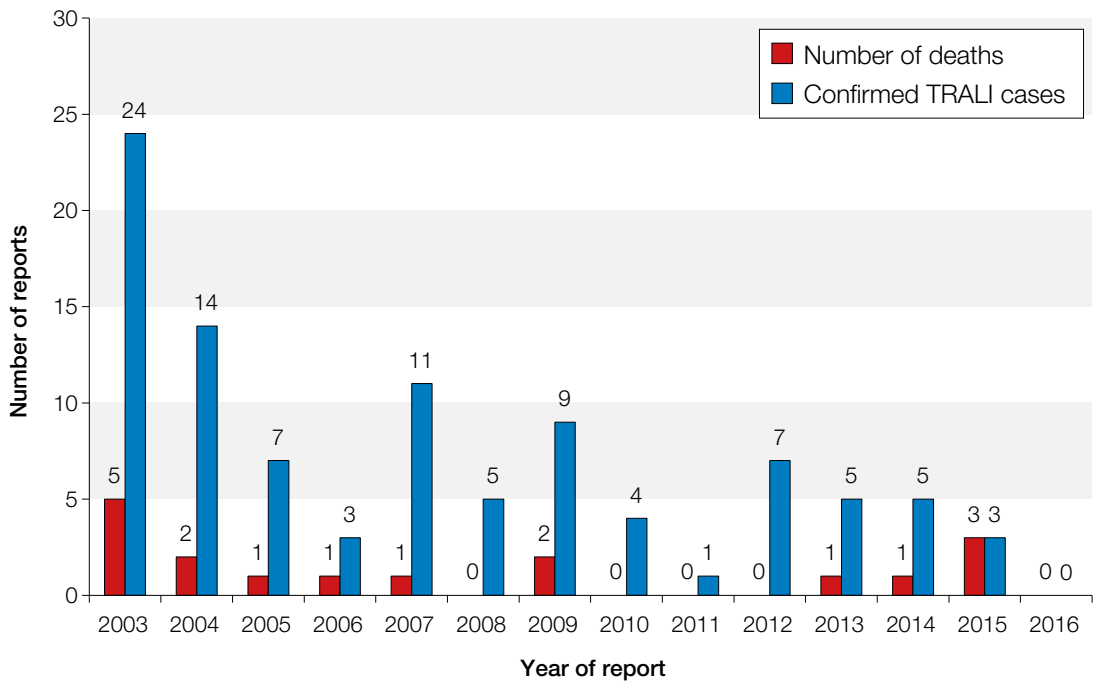


Figure 18a.1 shows TRALI cases from 2003-2016 reclassified using the new criteria. The use of male donors only for fresh frozen plasma (FFP) was implemented in 2003. Cases are recorded as deaths if death was at least 'possibly' related to transfusion (imputability 1 or greater).

## Assessment of TRALI

In this year’s report revised criteria for classifying TRALI are used. These give greater emphasis to the finding of leucocyte antibodies and use the presence of alternative explanations for respiratory compromise to determine imputability. The ‘possible TRALI’ (pTRALI) category is divided in to two categories, clarifying whether the uncertainty in diagnosis is due to the existence of alternative explanations or due to the absence of antibodies. Cases with negative serology and a dubious clinical history for TRALI have been transferred to the TAD category.

The revised criteria are outlined in Table 18a.1 below. Mapping showing how the revised criteria compare to the widely-used Canadian Consensus definitions (CCD) for TRALI is given in Table 18a.1 in order to help international comparison and Table 18a.3 shows how the 6 cases reported in 2016 would be classified by CCD.

Table 18a.4 compares the classification of historical and current cases between the two SHOT classification systems. This shows good concordance. The main difference relates to the handling of cases thought unlikely to be TRALI. It also shows that cases of ‘antibody-negative TRALI’ with a clear clinical history are rare.

Classification	Definition	Mapping to previous SHOT classification	Mapping to Canadian Consensus definition
Highly likely	Cases with a convincing clinical picture and positive serology	Highly likely	TRALI +positive serology
Probable	Cases with positive serology but other coexisting morbidity which could independently cause acute lung injury or fluid overload	Probable with positive serology	pTRALI +positive serology
Equivocal	Cases with positive serology in the clear presence of lung injury due to other causes or fluid overload	Possible with positive serology	not TRALI [excluded because of other morbidity but meets positive criteria] +positive serology
Antibody-negative TRALI	Cases with a convincing clinical picture where serology is not available or negative	Probable/possible with negative/absent serology	TRALI + absent or negative serology
Unlikely-reclassify as TAD	Cases where the picture and serology was not supportive of the diagnosis. These cases are transferred to TAD	Unlikely	pTRALI or not TRALI + negative or absent serology

**Table 18a.1:**  
Revised SHOT criteria for assessment of TRALI cases

Probability	Number of cases
Highly likely	0
Probable	0
Equivocal	0
Antibody negative	0
Unlikely (transferred or withdrawn)	6

**Table 18a.2:**  
TRALI case probability (SHOT criteria) for cases reported in 2016

Canadian Consensus classification	Number of cases
TRALI	0
Possible TRALI	2
Not TRALI	4

**Table 18a.3:**  
Classification using Canadian Consensus definitions

Table 18a.4:  
Comparison of  
previous and revised  
classification: TRALI  
cases 2012-2016

Revised classification	Previous SHOT classification			
	Highly likely	Probable	Possible	Unlikely
Highly likely	3			
Probable		12		
Equivocal			2	
Antibody negative			3	
Unlikely				17

### Illustrative case histories

In order to illustrate the revised classification, and compare assignment with the previous classification, some case histories from previous SHOT reports and this year's submissions are presented.

#### Case 18a.1: Highly likely (from the 2014 Annual SHOT Report)

*A healthy 22-year-old woman had a 3L postpartum haemorrhage (PPH) after an elective caesarean section. She was transfused with four units of red blood cells in optimal additive solution (RBCOA), four FFP and two cryoprecipitate pools. Within 10 minutes of starting the cryoprecipitate transfusion she developed difficulty breathing and became cyanosed. Her oxygen saturation was 64%, respiratory rate 30 breaths per minute, pulse 125 beats per minute and her blood pressure (BP) increased. She was treated with 80mg furosemide and had a 2L diuresis but her condition worsened. Her chest X-ray showed patchy consolidation throughout both lungs. On the next day her respiratory function deteriorated further and she required intubation. She was ventilated for one day and then made a full recovery. Laboratory investigation identified multiple HLA antibody matches between donors and this patient: three female cryoprecipitate donors had concordant antibodies and one female RBCOA donor had concordant antibodies.*

This case was classified as 'highly likely' and this remains unchanged - there is a classical history and multiple concordant antibodies.

#### Case 18a.2: Probable (from the 2015 Annual SHOT Report)

*This patient was already on oxygen for pneumonia post autologous haemopoietic stem cell transplant (HSCT) but deteriorated rapidly 20 minutes after transfusion of two units of red cells and died of respiratory failure seven days later. Serology showed HLA class I antibodies cognate with the recipient.*

This case was originally classified as probable TRALI. In the current classification this would also be classed as probable TRALI: there was severe deterioration with clear temporal relationship to transfusion and cognate antibodies, but it was not possible to rule out a coincidental worsening of the underlying pneumonia.

#### Case 18a.3: Equivocal - due to comorbidity (from the 2015 Annual SHOT Report)

*This patient developed breathlessness 40 minutes following six units of red cells, four units of FFP and one pool of cryoprecipitate for a variceal bleed. There was pre-existing fluid overload before transfusion and a chest X-ray before transfusion suggested pneumonia. However antibodies cognate with the recipient were present in one red cell unit and two donors to the cryoprecipitate pool.*

This case was originally classified as 'possible TRALI'. This case would be classed as 'equivocal TRALI' in the revised classification because there is large volume transfusion in the clear presence of pre-existing fluid overload and pneumonia, however the presence of antibodies cognate with the recipient cannot be ruled out as contributing to the respiratory deterioration.

#### Case 18a.4: Antibody-negative TRALI (from the 2012 Annual SHOT Report)

*A 3-year-old boy undergoing vinblastine chemotherapy for astrocytoma became pyrexial, tachypnoeic and hypoxic 1 hour into transfusion after 140mL of a unit of RBCOA. Chest X-ray showed bilateral ground glass shadowing. He required admission for oxygen and made a full recovery after 2 days. The red cell donor was male with no antibodies on testing.*

This case was originally classified as ‘possible TRALI’ in view of the clinical history and lack of other explanations but considering the absence of antibodies.

**Case 18a.5: Unlikely - transfer to TAD (2016)**

*A 70-year-old woman with pre-existing evidence of infection on chest X-ray, and echocardiographic evidence of pulmonary hypertension and left atrial enlargement became hypoxic 5 hours after transfusion of a single pool of apheresis platelets. Bilateral interstitial disease was shown on computerised tomography (CT) scan of her lungs. She recovered with oxygen therapy and there was some improvement after diuretics. Serology was negative.*

This case was transferred to TAD due to the negative serology and existence of multiple alternative explanations for her hypoxia, although the timing of the event would be compatible with TRALI.

**Cumulative serological data**

Since 1996, 204 of 324 (63.0%) reported cases have had full laboratory investigation for TRALI. Concordant antibodies were identified in 116/204 (56.9%) of these. The most frequently identified antibody specificities (either alone or in combination with other concordant antibodies) have been HLA-DR4 (22/116 cases, 19.0%), HLA-DR52 (17/116, 14.7%) and HLA-A2 (18/116, 15.5%). All other HLA antibody specificities have been identified in less than 10% of cases. Concordant HNA specific antibodies, alone or in combination, have been found as follows: HNA-1a (9/116 cases, 7.8%); HNA-2 (2/116, 1.7%); HNA-3a (2/116, 1.7%).

Analysis of reports of 184 complete TRALI investigations between 2001 and 2016 inclusive has shown that the specificities of concordant antibodies were as follows:

Concordant donor antibodies 2001 to 2016 inclusive				
HLA class I alone	HLA class II alone	Both HLA class I and HLA class II	Granulocyte-specific antibody (+/- HLA antibodies)	None identified
20/184 (10.9%)	36/184 (19.5%)	27/184 (14.7%)	18/184 (9.8%)	83/184 (45.1%)

**Table 18a.5:**  
Concordant donor antibodies 2001 to 2016 inclusive

**Commentary**

The definition of TRALI used by SHOT has been unchanged since 1995, and 12 years have passed since the Canadian Consensus definition was agreed (Kleinman et al. 2004). We consider that a revised definition is now appropriate in order to serve haemovigilance needs better, and to clarify the classification of pulmonary complications of transfusion. While the classical definition of ‘hypoxia and chest X-ray abnormalities within 6 hours not due to other causes’ is still valid, the difficulty from a classification point of view is that it is not possible to prove causation. The revised definition is a working definition which avoids the need to make a judgement on whether the event is caused by any morbidity present. Table 18a.4 shows that there is good consensus between current and previous classifications.

The association between leucocyte antibodies and TRALI is well established both in animal models and human studies, although there remain questions regarding pathogenetic mechanisms (Peters et al. 2015a). Most importantly, the success of TRALI prevention strategies, such as the use of male donor-only plasma, aimed at reducing the risk of transfusion of leucocyte antibodies supports a causative relationship (Müller et al. 2015). Antibody-mediated TRALI should therefore now be considered as a potentially preventable complication of transfusion. From a haemovigilance point of view, the practical need is to monitor antibody-associated cases in order to assess the effectiveness of prevention strategies. From this perspective, a purely clinical definition, where the presence of comorbidity excludes TRALI is unsatisfactory: there is no reason, for example, why fluid overload should offer protection from antibody-mediated damage.

In contrast, the nature of antibody-negative TRALI remains poorly understood (Peters et al. 2015b). While acute lung injury can be produced by manipulation of blood components in animal models, the relevance of these artificial models to lung injury in humans is unclear. Similarly, biological mediators

such as bioactive lipids which can cause lung injury in animal models have not, so far, been definitively demonstrated in human cases of TRALI. The practical need for these cases is for further research to identify possible mechanisms and preventive strategies. Given that there is no diagnostic test it is most helpful at this stage to restrict diagnosis of antibody-negative TRALI to cases which have a typical clinical history.

What is clear however, is that respiratory deterioration following transfusion is not uncommon. Many of the cases are multifactorial with several contributory factors coexisting; it is difficult in many cases to establish whether there was a causative relationship with transfusion at all. This is an important area for ongoing research but it is unhelpful for the monitoring of antibody-mediated TRALI to count cases thought unlikely to be TRALI in the TRALI statistics. Reassigning these 'unlikely TRALI' cases to the TAD classification will allow a broader approach to be taken to respiratory deterioration associated with transfusion.

There are certainly difficulties with defining TRALI based on antibody detection, and it is certainly not proposed that the demonstration of antibodies can yet be considered either a necessary or sufficient definition for TRALI. No serological test is completely sensitive and indeed assays such as Luminex bead assays are able to detect antibodies at lower levels than may have been possible in earlier reports. In addition, the difficulty of obtaining samples from both the recipient and all implicated donors means that some cases will not have complete serological investigation. It is certainly possible that some of the cases of 'antibody-negative TRALI' in fact relate to cases where antibodies are responsible but below limits of detection. Continuing to monitor the incidence of 'antibody-negative TRALI' may help to investigate this possibility, as the incidence would be expected to respond to preventive measures in parallel with the antibody-mediated cases.

Conversely, it is clear that the majority of donations with leucocyte antibodies do not cause TRALI. The risk of finding an antibody by chance increases with the number of donations received and thus the likelihood ratio of antibody testing for diagnosing TRALI decreases with the number of units transfused. In practice this will not affect the validity of classification, as patients with major haemorrhage are unwell almost by definition, thus having alternative explanations for respiratory deterioration and being assigned to lower imputability categories.

A final difficulty with revising the classification relates to international and historical comparison. As shown in the mapping above, it is fairly straightforward to translate between different classifications. The terminology 'equivocal TRALI' has thus been chosen for cases with positive antibodies but unclear history to avoid confusion with the 'possible TRALI' category in the Canadian Consensus classification.

In summary, we propose that the revised classification based on serology provides better separation between the haemovigilance need to monitor preventable antibody-associated cases and the investigative need to identify how to prevent pulmonary complications of transfusion. We also propose that the use of a pathologically-defined classification of TRALI gives a more objective basis for international comparison.

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# Transfusion-Associated Circulatory Overload (TACO) n=86

# 18b

Authors: Sharran Grey and Paula Bolton-Maggs

Last year's analysis of SHOT data made a significant contribution to progress toward internationally agreed surveillance reporting criteria for TACO. The revision group representing the International Society of Blood Transfusion (ISBT) working party on haemovigilance in collaboration with the International Haemovigilance Network (IHN) produced new draft haemovigilance reporting criteria in 2016. The reports that have contributed to the 2016 data for this year's Annual SHOT Report played a key role in validating the new draft reporting criteria for TACO.

While there is still no single agreed reporting definition, SHOT continues to emphasise the importance of reporting all suspected cases of TACO.

## Key SHOT message

- TACO must be suspected when there is respiratory distress with other signs, including pulmonary oedema, unanticipated cardiovascular system changes, and evidence of fluid overload (including improvement after diuretic, morphine or nitrate treatment), during or up to 24 hours after transfusion

## Recommendation

- A formal pre-transfusion risk assessment for transfusion-associated circulatory overload (TACO) should be performed whenever possible as TACO is the most commonly reported cause of transfusion-related death and major morbidity. An example is shown in Figure 18b.1

**Action: Trust/Health Board Chief Executive Officers and Medical Directors responsible for all clinical staff**




TACO Checklist	Red cell transfusion for non-bleeding patients	If 'yes' to any of these questions
	Does the patient have a diagnosis of 'heart failure' congestive cardiac failure (CCF), severe aortic stenosis, or moderate to severe left ventricular dysfunction? Is the patient on a regular diuretic?	<ol style="list-style-type: none"> <li>1 Review the need for transfusion (do the benefits outweigh the risks)?</li> <li>2 Can the transfusion be safely deferred until the issue can be investigated, treated or resolved?</li> <li>3 Consider body weight dosing for red cells (especially if low body weight) Transfuse one unit (red cells) and review symptoms of anaemia Measure the fluid balance Consider giving a prophylactic diuretic Monitor the vital signs closely, including oxygen saturation</li> </ol>
	Is the patient known to have pulmonary oedema? Does the patient have respiratory symptoms of undiagnosed cause?	
	Is the fluid balance clinically significantly positive? Is the patient on concomitant fluids (or has been in the past 24 hours)? Is there any peripheral oedema? Does the patient have hypoalbuminaemia? Does the patient have significant renal impairment?	

Figure 18b.1: Revised TACO pre-transfusion checklist

**Due to the differences in adult and neonatal physiology, babies may have a different risk for TACO. Calculate the dose by weight and observe the notes above.**



## Draft ISBT reporting criteria 2016

### 1. Acute onset or worsening respiratory distress during or up to 12 hours after transfusion

### 2. Two or more of the following:

- Evidence of acute or worsening pulmonary oedema (by physical examination or chest imaging)
- Evidence of unanticipated cardiovascular system changes (tachycardia, hypertension, jugular venous distension, peripheral oedema)
- Evidence of fluid overload (positive fluid balance, response to diuretic therapy with clinical improvement, change in the patient's weight in the peri-transfusion period)
- Elevation in natriuretic peptide (NP) levels (e.g. brain-natriuretic peptide (BNP), N-terminal (NT)-pro BNP) to greater than 1.5 times the pre-transfusion value

In 2016, 86 cases were accepted as TACO which is similar to the previous year.

## Deaths n=14

There were 14 deaths where the transfusion was considered to be contributory, 1 definitely related, 5 probably related and 8 possibly related.

## Major morbidity n=18

There were 18 cases of major morbidity where transfusion was judged to be contributory. Ten cases of major morbidity (e.g. requirement for high level of care) resulted in major (e.g. invasive interventions to treat the TACO) or minor sequelae (non-invasive interventions) for the patient.

## Demographic overview of cases

Table18b.1:  
Demographic  
overview of cases

Demographic	Number of reports
Deaths (imputability 3)	1
Deaths (imputability 2)	5
Deaths (imputability 1)	8
Major morbidity (serious sequelae)	5
Major morbidity (minor sequelae)	5
Major morbidity (signs and symptoms with risk to life with full resolution/unknown outcome)	8
Age	0 days to 94 years Median 74 years
Medical specialties (where data were provided)	Haematology 29.1% (25/86) Other medical specialties 44.2% (38/86) Surgical specialties/ anaesthetics 16.3% (14/86) Paediatrics/neonatal/other 5.8% (5/86)
Bleeding patients (indication code R1 or 'massive bleeding' indicated)	6
Non-bleeding patients (other indication codes or not stated)	80
Cases receiving red cells only (no other blood components)	90.7% (78/86)
Red cells alone (without other intravenous (IV) fluids)	66.7% (52/78)

Age analysis continues to show that TACO affects all age groups and is especially prevalent amongst the elderly because of the frequency of co-morbidities that predispose the patient to volume intolerance. This underlines the need to perform a pre-transfusion risk assessment on patients to identify those at risk, and take mitigating actions where appropriate. Haematology was the single medical specialty with the greatest number of patients developing TACO. This is because haematology patients are among the



most intensively transfused patients, many of whom are also elderly. The majority of cases occurred in non-bleeding patients requiring red cell transfusion indicating that there was probably opportunity to risk-assess the patient prior to transfusion and take mitigating actions. Concomitant IV fluids can complicate the assessment of the degree to which blood contributed to circulatory overload. The analysis shows that around a third of patients receiving red cell transfusion were also receiving non-blood fluids. If a patient develops signs of circulatory overload during or after transfusion and was also receiving fluids at the same time, or in the preceding 24 hours, it is important to report these cases to SHOT. This does not affect a diagnosis of TACO but may reduce the imputability assessment.

### Surveillance diagnosis of TACO: towards internationally-agreed criteria

In order to support the advance of this collaborative work, the 2016 TACO data were analysed by three sets of criteria, two of which were used last year: clinical prioritisation of key features (CPKF); the draft ISBT 2014 criteria (DISBT 2014); and the additional new 2016 draft ISBT criteria (DISBT 2016). Multiple analyses were performed for cases reported in last year's report which highlighted several important issues that led to potential over or under-attribution of TACO. Those issues were used to revise the DISBT (2014) criteria. The purpose of this year's multiple analyses was to validate the revised DISBT (2016) criteria to ensure that valid cases were identified, providing confidence in an agreed set of reporting criteria for future use, or identifying further areas for revision.

### CPKF reporting criteria

Cases accepted with symptoms and signs occurring within 24 hours of transfusion:

- Acute/worsening respiratory distress (in the absence of other specific causes)
- Acute/worsening of pulmonary oedema on imaging
- Evidence of a positive fluid balance
- Evidence of volume intolerance (response to treatment for circulatory overload or evidence of pulmonary oedema on clinical examination)

TACO was considered to be 'highly likely' with three or more features, or acute respiratory distress with pulmonary oedema on imaging; 'probable' with acute respiratory distress and clinical improvement with diuretic therapy (volume intolerance); and 'possible' with acute respiratory distress with evidence of a positive fluid balance.

### DISBT (2014) reporting criteria

Acute or worsening respiratory distress within 6 hours of transfusion (some cases may occur up to 12 hours).

#### Primary features

- Evidence of acute or worsening pulmonary oedema with bilateral infiltrates
- Enlarged cardiac silhouette on imaging – enlarged heart contour should always be present if looked for
- Evidence of fluid overload – could be a positive fluid balance or a response to diuretic therapy combined with clinical improvement

#### Supporting features

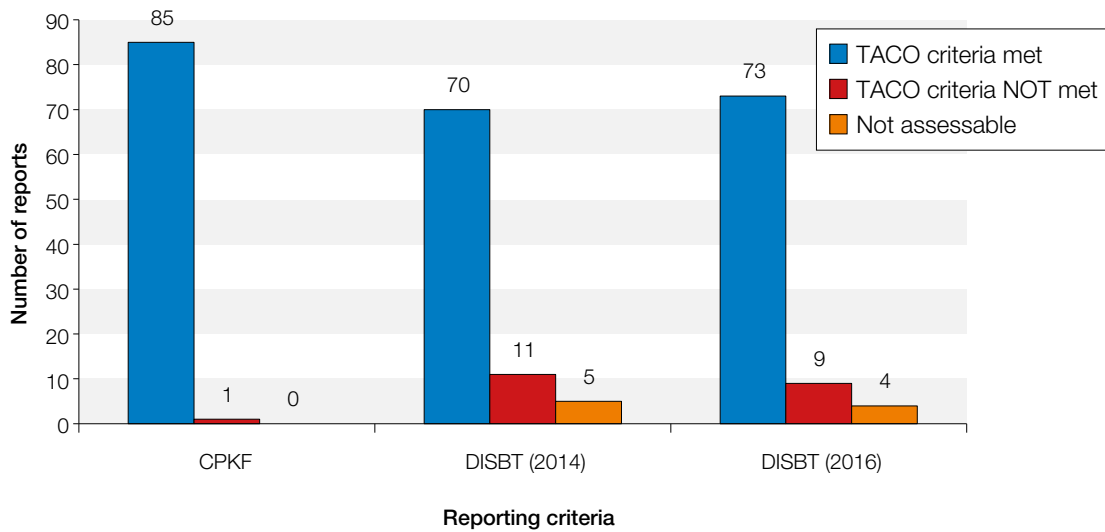
- Elevated BNP or NT-pro BNP to more than five times the pre-transfusion value (if available)
- Increased mean arterial pressure (MAP).  $MAP = DBP + 1/3 (SBP - DBP)$  or, increased pulmonary wedge pressure. The MAP is typically raised, often with a widened pulse pressure. There may be hypotension in acute cardiac collapse. (DBP=diastolic blood pressure and SBP=systolic blood pressure)

'Definite' cases must have at least two primary features, or one primary and two supporting features. Cases with only one primary feature (e.g. without chest imaging) may be considered 'probable' or 'possible' depending on the presence of other supporting features.

### Comparison of reporting criteria

This year 86 cases were analysed after withdrawals and transfer of some cases to other categories. Figure 18b.2 below compares each set of reporting criteria for cases which met the standards for TACO. CPKF and DISBT (2014) both employ a graded likelihood assessment (highly likely/definite, probable or possible), but the DISBT (2016) criteria only require the case to meet the minimum criteria without reference to likelihood. In order to standardise the comparison any cases with a positive degree of likelihood for CPKF or DISBT (2014) were considered to meet the criteria for TACO.

**Figure 18b.2:**  
TACO assessment  
by three sets of  
reporting criteria



There were 81.4% (70/86) of cases that met the criteria for TACO across all three reporting criteria. The 18.6% of cases (16/86) which did not agree provided useful data to further evaluate reasons for discrepancy, as detailed below.

### TACO reporting criteria met for CPKF but not for DISBT (2014) and DISBT (2016) n=7

This related to timing of symptoms and signs occurring after 12 hours (n=2), and when there was only one other feature in addition to acute/worsening respiratory distress (n=5). Of the latter, this related to clinical improvement after diuretic only (n=3), and acute/worsening pulmonary oedema only (n=2). The significance of this could be argued two ways. Either the CPKF set of reporting criteria is over-sensitive, or that the DISBT (2014 and 2016) sets of reporting criteria may be too exclusive. This is compounded by BNP not being performed or available in the UK, meaning that there are fewer additional criteria usually available for assessment (only one case had a BNP performed in this reporting year). However five of the cases were assessed as 'probable' or 'possible' (i.e. lower likelihood descriptors) by the CPKF set of reporting criteria suggesting some lack of confidence in certainty. The remaining two cases were assessed as 'highly likely' but this was only based on acute/worsening respiratory distress and acute/worsening pulmonary oedema alone which may be insufficient for a confident surveillance diagnosis.

### **TACO reporting criteria met for CPKF and DISBT (2014) but not for DISBT (2016) n=1**

This related to enlarged cardiac silhouette not being represented separately in the DISBT (2016) set of criteria and therefore not meeting the required minimum of two additional features. This was a neonate in whom there was pulmonary oedema but no other features. The baby had normal mean arterial pressure and heart rate for age. Enlarged cardiac silhouette is described in the pulmonary oedema criterion of the DISBT (2016) reporting criteria. If enlarged cardiac silhouette counted as a positive feature for unanticipated cardiovascular system changes, then this case would have met the DISBT 2016 set of criteria for TACO.

### **TACO reporting criteria met for CPKF and DISBT (2016) but not for DISBT (2014) n=4**

Tachycardia was added to the DISBT (2016) set of criteria for unanticipated cardiovascular system changes. Cases where there was only one additional feature (pulmonary oedema or evidence of fluid overload) without changes to the blood pressure and where BNP was not performed, meant that the presence of tachycardia provided further positive evidence for TACO where previously the case would have been assessed as 'unlikely'.

### **TACO reporting criteria met for CPKF but not assessable by DISBT (2014) and DISBT (2016) n=4**

Cases where there was only acute/worsening respiratory distress and acute/worsening pulmonary oedema are assessed as 'highly likely' by the CPKF set of reporting criteria, as no other diagnostic features are required. However, if the reporter has been unable to provide details of vital sign observations, response to diuretics, fluid balance etc., these cases are un-assessable by DISBT (2014) and DISBT (2016) sets of reporting criteria. Comprehensive case data provided by the reporter are important in ensuring robustness of the assessment.

### **Observations to inform further revision of the DISBT (2016) reporting criteria**

- It may be useful to include cases where symptoms and signs occur up to 24 hours after transfusion. SHOT data show that there were 26 cases of TACO reported as occurring within 12-24 hours of transfusion 2010-2016 inclusive
- Enlarged cardiac silhouette should be included in the criteria for unanticipated cardiovascular system changes (not in the pulmonary oedema criteria regarding radiographic imaging)
- The introduction of tachycardia into the DISBT (2016) reporting criteria regarding unanticipated cardiovascular system changes has increased inclusivity of cases
- The CPKF reporting criteria may perhaps over-attribute TACO, especially where there is only pulmonary oedema as an additional feature and/or when there may be important data missing for a comprehensive and robust assessment

### **Validation of the TACO checklist**

A TACO risk assessment in the form of a checklist was a recommendation in last year's report. This year's data were audited against the checklist and showed that 79.1% (68/86) of cases showed at least one positive feature on the checklist. Although this does not imply that TACO could have been prevented, it does endorse the sensitivity of the checklist for identifying risk factors and co-morbidities in patients who are at risk of TACO, allowing opportunity for intervention. Some transfusions will need to proceed despite risks for TACO being present but this should be conducted as a risk-balanced decision with mitigations put in place as far as possible, such as ensuring the appropriate dose of red cells to achieve the target haemoglobin level, prophylactic diuretics and close monitoring.

### Case 18b.1: Urgent transfusion in the presence of risk factors for TACO

*A patient with renal failure weighing 37kg with pre-existing fluid overload required red cell transfusion for severe symptomatic anaemia, haemoglobin (Hb) 50g/L). The patient had clinical signs of pulmonary oedema (raised jugular venous pressure, dyspnoea and frothy sputum). The patient also had a pericardial effusion and had required multiple resuscitations. One unit of red cells was prescribed and within an hour of starting the transfusion the patient began to complain of chest pain with increased work breathing, pyrexia, hypertension and tachycardia. The chest X-ray showed features of pulmonary oedema. The transfusion was stopped and the patient was given oxygen and underwent urgent haemodialysis with improvement in the symptoms.*

Although the reporter did not explain why the transfusion could not be given at the same time as haemodialysis for optimum fluid management in this renal patient, it was clear that the patient required urgent transfusion. The patient had multiple risk factors for circulatory overload in addition to being overloaded prior to transfusion. Urgent transfusions are required even in the presence of risk factors for circulatory overload and this must be undertaken as a risk-balanced decision.

Mitigations and control measures are sometimes difficult to perform in time-limited situations, and especially challenging in renal failure where prophylactic diuretics may be contraindicated. There were many other examples in the reports where risks were present and where transfusion could have been deferred, treated or investigated prior to transfusion, highlighting cases of TACO that could potentially have been prevented.

### Case 18b.2: Multiple positive features on the TACO checklist where TACO could probably have been prevented

*An elderly patient weighing 51kg with pre-existing congestive cardiac failure (CCF) (ejection fraction 30%) and aortic stenosis received regular transfusions due to non-Hodgkin lymphoma. She was admitted with worsening dyspnoea and epigastric/chest pain. Two hours into the transfusion of a red cell unit she developed tachypnoea. The chest X-ray was suggestive of some infective consolidation but also pulmonary oedema/progressive heart failure compared to the previous image. She improved after diuretic treatment. The post-transfusion Hb was 98g/L.*

Interestingly, this case was submitted as transfusion-associated dyspnoea (TAD) on the basis that there was no change in blood pressure or heart rate in this patient. The presence of pulmonary oedema and clinical response to diuretic treatment is good evidence of TACO by all reporting criteria discussed in this chapter. This patient had multiple risks as defined by the TACO checklist: CCF, aortic stenosis, and dyspnoea of undiagnosed cause (which may have been developing pulmonary oedema secondary to her pre-existing CCF). The reporter did not include the pre-transfusion Hb, but the post-transfusion Hb was 98g/L suggesting that the patient did not have severe anaemia requiring transfusion at the time of admission. She had low body weight so a dose-calculated partial unit may have been appropriate if she required transfusion at all.

The 20.9% (18/86) of cases that did not register positive features on the TACO checklist were evaluated for factors that could otherwise have potentially indicated that the patient was at risk of circulatory overload. These were grouped into those that could, or could not be prospectively identified.

### Could not be prospectively identified n=12

- No obvious pre-disposing risk factors (but the patient's full past medical history was not available to SHOT to fully assess) (n=6)
- A condition that pre-disposed the patient to circulatory overload that was subsequently diagnosed as a result of the patient developing TACO (acute renal failure, cardiac dysfunction, cardiac compression) (n=3)
- Possible alternative cause for pulmonary oedema (acute coronary syndrome) but TACO equally likely with no other pre-disposing risk factors for circulatory overload (n=2)
- Pulmonary oedema possibly developing before transfusion but respiratory symptoms attributed to the patient's underlying condition (e.g. asthma) (n=1)

### Potentially could be prospectively identified n=6

- Neonate with severe anaemia (n=1)
- Low serum albumin in the absence of other risk factors (n=1)
- Renal failure in the absence of other risk factors (n=4)

This provides further evidence for updating the TACO pre-transfusion checklist as shown in the revised infographic (Figure 18b.1), and SHOT makes this recommendation again for this reporting year.

### Persistent poor practice in common clinical scenarios

Disappointingly, there were a number of cases where inappropriate transfusion led to TACO, and this has been repeated year-on-year. The inappropriate use of fresh frozen plasma (FFP) to reverse warfarin and overtransfusion of patients with haematinic deficiency is still occurring.

#### Case 18b.3: FFP used instead of prothrombin complex concentrate (PCC) due to incorrect anticoagulant management rationale

*A 75-year-old patient was admitted with suspected lower limb ischaemia. He was already anticoagulated with warfarin for a metallic mitral heart valve. He had a 'poor chest' making him unsuitable for general anaesthetic and therefore required regional anaesthesia. The consultant haematologist was asked to give advice regarding his perioperative anticoagulant management. The consultant advised that the patient was not suitable for PCC because he/she believed there was greater risk of valve-related thrombosis and so suggested FFP and vitamin K instead. Two units of FFP were given on the ward and a further two were to be given in theatre. On arrival in theatre his respiratory status had deteriorated with tachypnoea, reduced oxygen saturation and increased oxygen requirement. Pulmonary oedema was diagnosed. He was treated with nitrates and diuretics and recovered.*

Patients with mechanical heart valves require careful perioperative anticoagulant management to prevent valve thrombosis, and also to prevent bleeding caused by the surgical procedure itself. Warfarin should be fully reversed preoperatively with PCC and vitamin K. Anticoagulation is then alternatively managed with unfractionated heparin to allow maximum control by keeping the un-anticoagulated period during surgery to a minimum. Warfarin can be resumed postoperatively. There is no advantage to using FFP over PCC to minimise the risk of thrombosis. Both provide vitamin K dependent clotting factors but PCC has the advantage of having complete and rapid reversal due to the much greater concentration of factors and is both more reliable than FFP, and gives a smaller IV volume. This was critical in this case where the larger volume of FFP caused circulatory overload and pulmonary oedema in this patient who required emergency surgery.

#### Case 18b.4: Bleeding on direct oral anticoagulants

*A 69-year-old patient with a history of CCF had persistent bleeding while anticoagulated with a direct oral anticoagulant (anti-Xa inhibitor) for atrial fibrillation. His prothrombin time (PT) and activated partial thromboplastin time (APTT) were slightly prolonged. He was given four units of FFP to treat the bleeding. He became hypertensive and developed tachypnoea and hypoxia. Pulmonary oedema was diagnosed. The patient was treated with diuretics and recovered.*

The anti-Xa inhibitor the patient was taking is known to cause prolongation of the PT and APTT. These agents are not reversible with FFP. This patient was particularly vulnerable to circulatory overload posed by the relatively large volume of the FFP dose due to his pre-existing CCF. These drugs have a relatively short half-life and therefore omission of the drug is often sufficient to restore normal haemostasis if the patient does not have renal impairment. In the presence of major bleeding, specific reversal agents should be administered where licensed and available (e.g. for dabigatran, an anti-IIa agent, see literature review in Chapter 11d, Incidents Related to Prothrombin Complex Concentrates). Omission of the drug may have been appropriate for this patient and the presence of the drug can be evaluated by drug-calibrated anti-Xa assays (where available) if there is doubt about its clearance. There are few data for the use of PCC but it may be considered if the bleeding cannot be controlled with other measures such as tranexamic acid, and if the specific reversal agent is not available.

**Case 18b.5: Red cell overtransfusion in chronic megaloblastic anaemia leading to TACO**

*A 90-year-old patient was admitted with severe megaloblastic anaemia (Hb 41g/L) and worsening peripheral oedema due to CCF. The consultant haematologist recommended six units of red cells but the ward staff decided to administer three. The patient developed dyspnoea, hypoxia and fever during the transfusion. The duty doctor diagnosed pneumonia and then eventually fluid overload. The chest X-ray showed worsening pulmonary oedema compared to the previous image performed on admission. The patient was treated with diuretics and recovered. The reporter stated that they felt that it was difficult to attribute fluid overload to transfusion because the X-ray suggested some patchy consolidation and the patient had peripheral oedema on admission.*

This elderly patient was clearly overloaded prior to transfusion due to CCF and severe anaemia, putting her at greater risk of developing TACO. Three units of red cells are excessive in this situation given the chronicity of the anaemia and the risk factors for overload, and it is fortunate the original recommendation for six units was not actioned. Severe megaloblastic anaemia causes impaired cardiac muscle function thus red cell transfusion should be avoided wherever possible because of the risk of causing potentially fatal circulatory overload. The diagnosis of TACO was complicated by the presence of fever and possible pneumonia. It is of course possible that circulatory overload and a septic condition can co-exist which may confound the diagnosis of fluid overload. It is important to recognise that a patient who has pre-transfusion fluid overload (evidenced by worsening CCF and peripheral oedema in this case) may experience exacerbation of overload by transfusion. This was a clear case of TACO caused by excessive transfusion of red cells where there were obvious risk factors for circulatory overload. A single unit or weight-based dose of red cells with a prophylactic diuretic and close monitoring, preceded by vitamin B12 therapy would have been appropriate.

**References**

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# Transfusion-Associated Dyspnoea (TAD) n=10

## 18c

Author: Paula Bolton-Maggs

### Definition:

**TAD is characterised by respiratory distress within 24 hours of transfusion that does not meet the criteria for transfusion-related acute lung injury (TRALI) or transfusion-associated circulatory overload (TACO) or allergic reaction. Respiratory distress in such cases should not be adequately explained by the patient's underlying condition (International Society of Blood Transfusion (ISBT) definition).**

### Key SHOT messages

- Most patients classified as TAD are very unwell with complicating pathology. Some of these had features suggestive of TACO but not enough reported detail to meet the SHOT criteria
- The pathophysiology of this group of complications requires further elucidation (Badami et al. 2015). There is some evidence that patients with sepsis are more at risk of respiratory complications following transfusion (Roubinian et al. 2015), a reminder that every transfusion, particularly of platelets, a rich source of biological response modifiers, (Garraud et al. 2013; Garraud et al. 2016), should be reviewed to ensure it is indicated

Ten cases are included, 2 reported as TAD, 3 transferred from TACO, 1 from acute transfusion reactions (ATR) and 4 from TRALI. Three cases were transferred from TAD to other categories, one to TACO and 2 to ATR.

### Deaths n=0

There were no deaths related to transfusion in this category.

### Major morbidity n=6

Six patients suffered major morbidity and are described in the case studies below.

### Case details

#### Case 18c.1: A sick man reacts to a platelet transfusion

*A 70-year-old man with acute myeloid leukaemia on chemotherapy with renal impairment became unwell at the end of a platelet transfusion (second pool) for epistaxis. He developed pyrexia and rigors and was considered to have possible sepsis. His respiratory rate (RR) increased from 17 to 36/min and he received oxygen (O<sub>2</sub>) and bronchodilators with improvement in his clinical condition. He had a negative blood culture. His chest X-ray (CXR) was normal.*

#### Case 18c.2: Respiratory distress with transfusion after surgery

*A 66-year-old man developed acute respiratory distress, tachycardia and raised blood pressure (200/100mmHg) during red cell transfusion following elective surgery.*

*Around 01:30 he screamed for a nurse and was holding his abdomen. Analgesics were prescribed. At the same time he became wheezy and had chest pain. The RR was 40/min, blood pressure*



202/100mm/Hg, pulse rate increased from 97 to 138 beats per minute, temperature was 37°C and oxygen saturation reduced to 90%. He was treated with oxygen and a bronchodilator and settled. A CXR showed signs of 'flash pulmonary oedema' thought to be associated with the transfusion of red cells.

**Case 18c.3: A cardiac patient developed respiratory symptoms during transfusion**

A 72-year-old man was transfused two units of red cells for a low haemoglobin (Hb) on the critical care unit (under care of cardiology). He had a history of ischaemic heart disease with three stents and a previous myocardial infarction, and was now generally unwell with diarrhoea. He had renal impairment and some evidence of heart failure. Changes to respiratory function and increased oxygen requirement were noted. A CXR showed early pulmonary oedema. Transfusion was completed at 19:00 and at 23:00 pO<sub>2</sub> dropped to 6.9. His oxygen requirement increased from 40% via facemask to 60% and then to 15L via facemask. He was given 40mg intravenous (IV) furosemide x 3 and passed 1580mL urine. TRALI was considered as a possible cause for the patient's ongoing symptoms following discharge from critical care. The TRALI expert panel concluded that the respiratory failure was more likely to be explained by the presence of heart failure, sepsis and TACO but there were not sufficient criteria for this latter diagnosis.

**Case 18c.4: Influenza, septic shock and respiratory deterioration**

A 30-year-old woman who was in intensive care with bilateral pneumonia related to H1N1 influenza and group A streptococcus septic shock developed respiratory distress during a second unit of red cells. She had some evidence of left ventricular and renal dysfunction related to her sepsis. Her CXR showed 'appearance compatible with overwhelming atypical pneumonia' and was the same after the reaction. Her pulse rate increased from 100 to 160bpm, her blood pressure increased and her respiratory rate increased from 19 to 50/min. She required oxygen and support with continuous positive airway pressure (CPAP). She had a diuresis of more than a litre after furosemide and was also treated with nitrates and diamorphine.

**Case 18c.5: Unusual and unexplained respiratory deterioration after fresh frozen plasma (FFP) and cisplatin for malignancy**

A 41-year-old woman was admitted with wheeze and cough and respiratory failure requiring admission to the intensive therapy unit (ITU) two days after treatment with two units of FFP and cisplatin. She initially had been treated for tumour-related (no detail given of primary) disseminated intravascular coagulation with raised d-dimers. The cause of the respiratory symptoms was unclear. A computerised tomography (CT) scan showed diffuse ground glass appearance. She responded to non-invasive treatment with a bronchodilator, oxygen and dexamethasone.

**Case 18c.6: Respiratory complications with features of circulatory overload and infection**

A 70-year-old woman with aplastic anaemia became unwell with shortness of breath following a platelet and a two-unit blood transfusion and required nebuliser and oxygen support 4.5 hours after completing the transfusion. Her oxygen saturation deteriorated from 95 to 84% with little change in respiratory rate, pulse, or blood pressure. She had mild fever of 37.4°C. She was treated with oxygen to 2L and her saturation improved to 94%. She was in positive fluid balance (1978mL) and had a diuresis of 4700mL following furosemide. Her respiratory rate remained between 18 and 20/minute and she continued on oxygen to maintain her saturations.

The donors of red cells and platelets were investigated and the results did not support antibody-mediated TRALI. The transfusion service also reported that the patient had strong human leucocyte antigen (HLA) antibodies and platelet autoantibodies. Pre-transfusion CXR three days prior to transfusion showed shadowing of right upper lobe 'query lung infection'. Post-transfusion CXR showed widespread pulmonary infiltrates and CT scan concluded that there was interstitial disease, possibly due to infection and other causes. HLA-matched blood was recommended for the patient due to poor platelet increment. However she died, unrelated to the transfusion events, eight days later.

**Case 18c.7: A reaction to platelets probably associated with HLA antibodies**

*An elderly lady with myelodysplastic syndrome experienced breathlessness with reduced oxygen saturation 45 minutes after a platelet transfusion (pooled, in additive 70%). This necessitated admission to the ITU. There were no details of fluid balance; there was no improvement with furosemide. The donor was an untransfused male and the patient was found to have HLA antibodies which were thought to be responsible. Since this episode she has received HLA-matched platelets.*

**Case 18c.8: Respiratory deterioration after massive haemorrhage with some features of TACO**

*A 41-year-old woman developed signs of intraperitoneal haemorrhage three days following oocyte retrieval. This operation had been covered with IV heparin because she was known to have thrombophilia (factor V Leiden) and was on long term oral anticoagulation prior to surgery. The heparin was stopped on the day of haemorrhage. She experienced major haemorrhage and during resuscitation received four units of red cells, eight of FFP, a unit of platelets and 766mL of salvaged blood. In addition she received 1900mL of other fluids. She developed reduced oxygen saturation and tachypnoea within six hours and required CPAP, was transferred to the high dependency unit for seven days. CXR showed 'pneumonia in both midzones and fluid on the left indicating possible transfusion-related acute mediastinal lung injury'. TRALI investigations were negative. She was febrile without tachycardia. She improved with the IV fluids and did not receive diuretics. She improved slowly and was on CPAP for four days.*

**Case 18c.9: Respiratory deterioration after transfusion of red cells**

*A 71-year-old man (who had a hemihepatectomy for metastatic carcinoma) developed a reaction 25 minutes after starting a transfusion of red cells. At the first assessment there were no objective abnormal signs, but after restarting the transfusion further symptoms resulted in cessation of the unit. His oxygen saturation fell for several hours. A CXR showed some increased shadowing. He deteriorated despite treatment with bronchodilators and oxygen and required transfer to the ITU for two days. No further details were given.*

**Case 18c.10: Probable fluid overload in a man with severe liver disease**

*A 48-year-old man with serious alcoholic liver disease was awaiting transplant. He had refractory ascites and hydrothorax which was drained every week. Following difficulty with ascitic drainage he developed abdominal pain and was admitted the next day to the intensive care unit. He was thought to have internal bleeding. Siting of a chest drain was followed by massive haemorrhage (requiring transfusion of 12 units of red cells, 10 of FFP, three platelet doses, eight units of cryoprecipitate and additional albumin solution). The day following this fluid balance (excluding blood components) was +2.5L. Later in the day he was noted to have a low platelet count of  $55 \times 10^9/L$  and international normalised ratio (INR) of 2, so one unit of FFP and one of cryoprecipitate were administered using pressure bags. He then developed respiratory compromise. His oxygen saturation fell from 93 to 80% (on 35% FiO<sub>2</sub>), respiratory rate increased from 16 to 30 breaths per minute and his pulse rate was 130 beats per minute. A CXR afterwards showed left-sided pulmonary oedema. He had 1.5L drained via a surgical chest drain 2.5 hours before the reaction. He was put on CPAP and continuous veno-venous haemofiltration to remove fluid as he had inadequate renal function. He improved with this treatment but died 10 days later from his underlying disease. This may have been transfusion-associated circulatory overload but there was not sufficient information to classify as this at the time of reporting.*

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# 19 Haemolytic Transfusion Reactions (HTR) n=35

Authors: Clare Milkins, Tracey Tomlinson, Anicee Danaee

## Definition:

**Acute haemolytic transfusion reactions (AHTR) are defined as fever and other symptoms/signs of haemolysis within 24 hours of transfusion; confirmed by one or more of the following: a fall of haemoglobin (Hb), rise in lactate dehydrogenase (LDH), positive direct antiglobulin test (DAT), positive crossmatch.**

**Delayed haemolytic transfusion reactions (DHTR) are defined as fever and other symptoms/signs of haemolysis more than 24 hours after transfusion; confirmed by one or more of the following: a fall in Hb or failure of increment, rise in bilirubin, incompatible crossmatch not detectable pre transfusion.**

**NB - Simple serological reactions (development of antibody with or without a positive DAT but without clinical or laboratory evidence of haemolysis) are not included (alloimmunisation, and SHOT no longer collects these data).**

## Key SHOT message

- Patients with sickle cell disease are particularly vulnerable to severe haemolytic transfusion reactions. Laboratory staff should not assume that it is safe to give only Rh/K-matched blood, as antibodies are prone to evanescence and historical antibodies may no longer be detectable serologically. The laboratory should take active steps to seek a transfusion history, and an antibody history if previous transfusion has occurred. For patients in England, Sp-ICE (Specialist Services Electronic Reporting using Sunquest ICE) should also be checked before selecting appropriately phenotyped units and similar shared databases should be checked where available in devolved countries

## Number of cases

A total of 35 cases (compared with 59 last year) have been included, 17 acute and 18 delayed (including hyperhaemolysis). The number of delayed reactions is considerably lower than reported in previous years (18 compared with 28).

An additional 5 cases of haemolytic transfusion reaction occurred as the result of errors, and the numbers are included in Chapter 10, Incorrect Blood Components Transfused (IBCT).

## Age range and median

There were 5 paediatric cases this year (age range 1 to 15 years). The overall age range was 1 to 88, with a median age of 61 years.

## Deaths n=1

There were 2 deaths in total. Both patients had sickle cell disease with hyperhaemolysis following transfusion. In one case the coroner's report ruled out the transfusion as contributory, because the hyperhaemolysis had responded to treatment before the patient deteriorated. The second death was reported as being probably related to the transfusion (imputability 2).

### Case 19.1: Death probably related to hyperhaemolysis

A young male patient with sickle cell anaemia received a red cell transfusion in the intensive therapy unit (ITU) in view of hepatic sequestration. Seven days later he had a sudden reduction in his Hb from 85g/L to 45g/L and then a further drop to 31g/L. He had haemoglobinuria, chest pain and had a tachycardia. He was treated with methylprednisolone and intravenous immunoglobulin (IVIg) and further red cell transfusion. While he was being transfused with his first unit he deteriorated, developed chest infiltrates and acidosis. He died of circulatory collapse and respiratory failure some 12 hours later despite maximum support. The coroner's report is awaited.

### Major morbidity n=7

The current definition of major morbidity includes 'evidence of intravascular haemolysis, e.g. haemoglobinaemia or haemoglobinuria'; this has caused some confusion, as these signs can also occur with extravascular haemolysis, leading reporters to inappropriately assign major morbidity to HTR where only extravascular haemolysis has occurred. We have reassigned these from major to moderate morbidity and the definition was updated in early 2017 (<https://www.shotuk.org/resources/current-resources/>).

Antibody-mediated intravascular haemolysis, where antibody coated red cells rupture in the bloodstream, is only caused by antibodies that bind complement to the C9 stage, most notably anti-A and anti-B. These reactions are immediate and severe, usually occurring before completion of the unit, and may result in major morbidity or death. Extravascular haemolysis occurs where antibodies do not bind complement (e.g. anti-D) or only bind to C3 (e.g. anti-S), with most of the antibody-coated cells being removed more slowly by the reticuloendothelial system (RES); small amounts of haemoglobin may be released in the plasma, and haemoglobinuria also often occurs, probably due to the RES being overloaded.

There were 2 cases of major morbidity described below, plus an additional 5 cases of hyperhaemolysis in patients with sickle cell disease, described separately in a later section.

### Case 19.2: Severe reaction possibly due to exacerbation of autoimmune haemolytic anaemia (AIHA) (imputability 2)

A patient suffered dyspnoea, hypotension, rigors, lower back pain, a feeling of impending doom and loss of consciousness, 5-10 minutes after commencing a second unit of red cells, and was subsequently transferred to ITU. Her Hb fell post transfusion and there was a rise in bilirubin. Pre-transfusion testing showed panagglutinins detected by low ionic strength saline (LISS) indirect antiglobulin test (IAT), and a strongly positive DAT (IgG, IgM and C3d coating), but no underlying alloantibodies. The serological picture did not change post reaction and this is possibly a case of exacerbation of AIHA.

### Case 19.3: Life-threatening fall in Hb in a paediatric patient with sickle cell disease (imputability 3)

A child with sickle cell disease was admitted to ITU with acute chest crisis and received a six unit red cell exchange transfusion. Thirteen days later the patient was readmitted with jaundice, limb pain, dark urine and Hb of 32g/L, which fell further to 22g/L. Anti-M and anti-S were identified in both the plasma and eluate. The patient suffered a stroke prior to transfusion of compatible red cells, but recovered quickly following transfusion.

This at first appeared to be a case of hyperhaemolysis as the Hb fell to a much lower level than the pre-transfusion Hb. However, destruction of all transfused red cells following a large volume exchange transfusion can clearly result in the same picture.

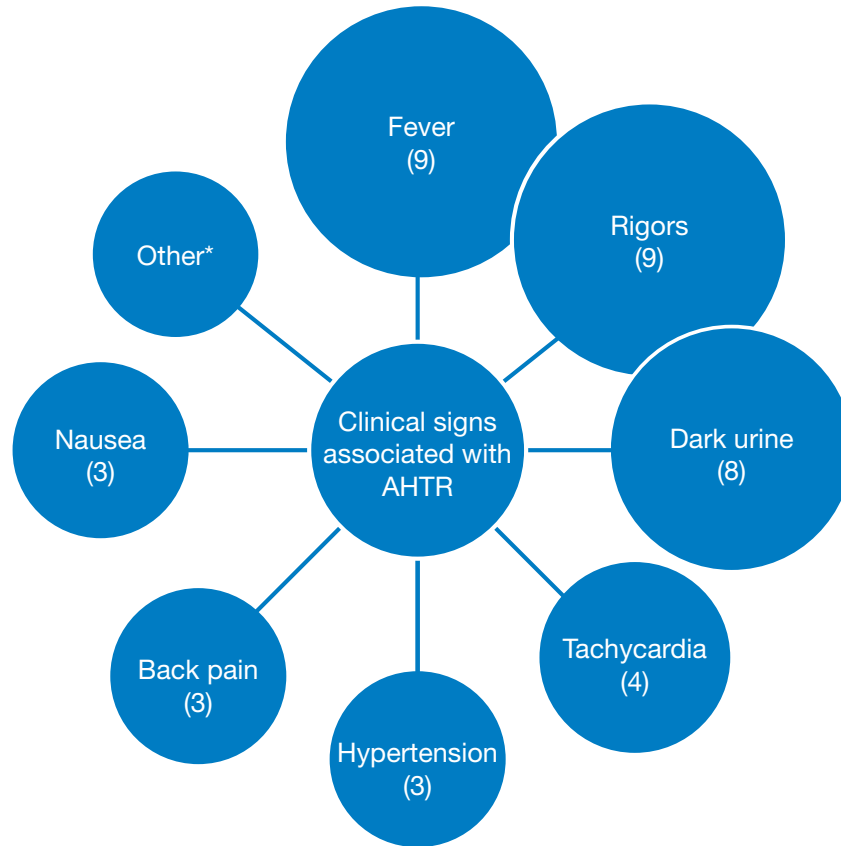
## Clinical and laboratory signs and symptoms

### Acute haemolytic transfusion reactions n=17

There appears to be no typical set of clinical symptoms associated with acute haemolytic reactions – the most commonly reported signs are shown in Figure 19.1, with the top three the same as last year.

All reports provided laboratory evidence of haemolysis, with the vast majority of patients having a raised bilirubin and a fall in Hb. There were also 6 reports of haemoglobinuria.

**Figure 19.1:**  
Clinical signs  
associated with  
AHTR



\*Other=jaundice; dyspnoea; hypotension; chest pain; elevated respirations; chills (<3 each)

### Delayed haemolytic transfusion reactions n=12 (excluding potential cases of hyperhaemolysis)

Seven patients had jaundice and/or dark urine; dyspnoea was also reported in a single case and limb pain in another. In the remaining 5/12 cases (41.7%) there were no obvious clinical symptoms associated with the DHTR, which was diagnosed by laboratory signs of haemolysis. These signs include a fall in Hb, increase in bilirubin and LDH, a positive DAT and the finding of a new antibody in the plasma and/or eluate.

### Serological findings

#### AHTR n=17

#### Antibodies to low frequency antigens where red cells were electronically issued (one certain, one probable and two possible) n=4

In one case anti-Wr<sup>a</sup> definitely caused an AHTR following electronic issue of red cells. The patient suffered fever, rigors and vomiting and had an elevated bilirubin; the IAT crossmatch was incompatible and anti-Wr<sup>a</sup> was found in the plasma and eluate. In a second case, the patient had fever, rigors, tachycardia, hypertension and a sharp rise in bilirubin; although the retrospective IAT crossmatch was incompatible, the DAT was negative and the antibody specificity was not identified. In a third case, the patient had dyspnoea and hypertension, with an increased bilirubin, and although the post-transfusion DAT became transiently positive, no further investigation was undertaken to confirm that the cause of the apparent AHTR was an antibody to a low frequency antigen. In the fourth case, the patient had fever, rigors and chest pain and passed dark urine at home a few hours post transfusion. The post-

transfusion plasma looked haemolysed, she had a rise in bilirubin and her Hb fell to the pre-transfusion level. The DAT was negative, no antibodies were found and the plasma was negative against a panel of low frequency antigens. However, the donations were not available for retrospective IAT crossmatch.

### Learning point

- If a patient has an acute haemolytic transfusion reaction with no obvious cause, unless an antibody to a low frequency antigen has been ruled out as the cause, e.g. by a retrospectively compatible indirect antiglobulin test (IAT) crossmatch, the patient's record should be flagged as unsuitable for electronic issue (EI)



#### Case 19.4: Kidd antibodies identified but relation to the reaction is unclear (1)

*A 19-year-old female patient with apparently no previous transfusions suffered chills, rigors and nausea during the third unit of red cells, which was stopped. She had a weak pan-reactive antibody and a strong positive DAT (IgG and C3d) pre transfusion, but anti-Jk<sup>a</sup> was identified in addition to the panreactivity in the post-transfusion plasma sample, and the DAT was more strongly positive. There was no evidence of alloantibody in the eluate and the units were Jk(a-). It was thought that the haemolytic episode may have been caused by cold agglutinins following transfusion of cold red cells.*

#### Case 19.5: Kidd antibodies identified but relation to the reaction is unclear (2)

*A regularly transfused patient with anti-E and anti-Ch/Rg, received two E-negative red cell units uneventfully. Twenty four days later she was admitted with acute bleeding, a Hb of 52g/L and a positive DAT (1+), and anti-C<sup>w</sup> was also identified. Transfusion was stopped after one unit when the patient became febrile, dyspnoeic and hypotensive; the LDH was raised, and spherocytes were noted on the blood film. A new sample demonstrated the same antibodies as before in the plasma but also a stronger positive DAT (3+) and anti-Jk<sup>a</sup> in the eluate. The Jk<sup>a</sup> status of the units transfused 24 days earlier was unknown but the one transfused during the current transfusion was Jk(a-). The next day, a new sample was sent to the Blood Centre reference laboratory but on this occasion the eluate was negative.*

### Learning point

- If there is evidence of a haemolytic transfusion reaction, an eluate should be tested as part of the investigation. Occasionally a new alloantibody will be detectable in the eluate but not in the plasma



#### Case 19.6: Anti-E possibly present in the pre-transfusion sample

*Towards completion of a second unit of red cells, a patient developed fever, rigors and passed red urine. He had a rise in bilirubin and no Hb increment. The DAT was negative, but anti-E was identified in the post-transfusion plasma and at least one of the red cell units was confirmed as E-positive. Retrospective testing of the pre-transfusion sample showed some weak reactions by enzyme technique that were suggestive of anti-E. The patient had also been transfused 17 days earlier, and it is probable that the anti-E was developing in response to this earlier transfusion.*

#### Case 19.7: Passive ABO antibodies

*There was one case of passive anti-A from a high-titre (HT) negative unit of group O apheresis platelets, causing an acute reaction and haemolysis in a paediatric patient (weight 22.5kg). The patient had a fall in Hb (of 22g/L) and a rise in bilirubin, with spherocytes noted on the blood film; anti-A was confirmed in the plasma and eluate. It is not known whether the HT testing was repeated.*

### Reactions probably not associated with red cell alloantibodies

There were three cases that were likely to have been exacerbation of autoimmune haemolysis, and another six where no cause was found.



### Case 19.8: Probable autohaemolysis following haemopoietic stem cell transplant (HSCT) (imputability 2)

Five months prior to this transfusion a group O D-positive child with acute lymphoblastic leukaemia (ALL) received a HSCT from a group A D-negative donor, and had developed weak anti-D. Two hours into a group O D-negative red cell transfusion, the patient developed a rash all over her abdomen, torso, face and hands; she had an increased heart rate, developed back pain and passed dark red urine. Haemolysis was confirmed by a fall in Hb and a sharp rise in bilirubin (21 to 117 micromol/L). The DAT became positive post transfusion and although the eluate was positive by IAT, no specificity was determined. The patient had similar reactions during subsequent transfusions with phenotyped matched red cells, but following treatment with IVIg tolerated further transfusions well.

**Additional cases reported as IBCT** more details are available in Chapter 10, Incorrect Blood Components Transfused (IBCT)

There were two ABO-incompatible transfusions associated with acute haemolysis: the first (due to collection and administration of the wrong unit, Case 10.5) resulted in a life-threatening AHTR; in the second case (due to wrong blood in tube, Case 10.4), the patient had mild loin pain and 'haematuria' for 24 hours.

A neonate with haemolytic disease of the fetus and newborn (HDFN) due to anti-D suffered prolonged haemolysis following exchange transfusion with D-positive red cells (Case 10.1).

A patient with known anti-S suffered a haemolytic episode following transfusion with S-positive red cells (Case 10.2).



#### Learning point

- Exacerbation of autohaemolysis is a recognised effect of transfusion, and should be taken into account when transfusing patients with autoantibodies. New autoantibodies can also be stimulated by transfusion (Young et al. 2004; Petz and Garratty 2004)

### DHTR (excluding potential hyperhaemolysis) n=12

Table 19.1:  
Specificities  
involved in the  
DHTR

Antibody	Number
Anti-Jk <sup>a</sup>	3
Mixture including Kidd	1
Other mixture	3
Anti-C, -Fy <sup>b</sup> , -c	1 each
None	2
<b>Total</b>	<b>12</b>

In addition, there was one ABO-incompatible transfusion due to wrong blood in tube that resulted in a haemolytic reaction and renal impairment, not noted until 14 days following a four unit red cell transfusion. More details can be found in Chapter 10, Incorrect Blood Components Transfused (IBCT), Case 10.3.



## Haemolytic reactions in patients with sickle cell disease n=8

HTR were reported in 8 patients with sickle cell disease, all delayed.

### Potential hyperhaemolysis n=6

This group included 6 cases with 2 deaths. Some were reported as minor morbidity and others as major morbidity. However, the reported reductions in Hb were very similar in all but one case. SHOT considers that all reported cases of probable hyperhaemolysis should be considered as major morbidity where there is a significant fall in Hb. The cases are detailed in Table 19.2.

### Classic DHTR n=2

Two severe DHTR occurred in patients with sickle cell disease. One was unavoidable and is described earlier in the section on major morbidity (Case 19.3).

The other could have been prevented as the patient had a history of red cell antibodies which were known but undetectable at the time of transfusion (Case 19.9).

#### Case 19.9: Avoidable DHTR following transfusion of antigen-positive red cells

*The patient received an eight unit red cell exchange transfusion at hospital A (prior to surgery at hospital B) with red cells matched only for Rh and K. She was admitted to hospital B 6 days later, very unwell, with fever, jaundice, black urine and a falling Hb. Hospital B had a historical record of anti-E+S+Fy<sup>a</sup>+Fy<sup>b</sup>+Fy<sup>3</sup> for this patient and confirmed that several of the units used in the exchange were antigen positive; anti-Fy<sup>a</sup>+Fy<sup>3</sup> were identified in the plasma and eluate.*

There were two opportunities for the patient history to be available to hospital A: the laboratory in hospital A could have requested the history from either hospital B or from Sp-ICE; the laboratory in hospital B could have actively informed the laboratory in hospital A as they were aware that the exchange transfusion would take place there.

Case	Serology	Clinical & laboratory signs	Morbidity	No. days post transfusion	Additional comments	Imputability of reaction to the transfusion
HH1	No antibodies; DAT positive (IgG+C3d); eluate negative	Fever; haemoglobinuria; bilirubin↑; Hb↓↓	Major: impaired renal function (creatinine 63 to 184 micromol/L) Hb fell to 41g/L	6	Treated with steroids and IVIg	Probable
HH2	Anti-E+S+c and positive DAT pre transfusion; anti-N in eluate	Fever; jaundice; pain; nausea; bilirubin↑; Hb↓↓; LDH↑	Major: Hb fell to 33g/L	6	Treated with steroids	Possible
HH3	No new antibodies; anti-C+Jk <sup>b</sup> pre transfusion; probable anti-N between transfusions	bilirubin↑; Hb↓↓	Major: Hb fell to 42g/L	2 - 14	Transfused on 3 occasions within 3 weeks; treated with steroids	Probable
HH4	Known anti-Jk <sup>b</sup> +S; no new antibodies	Chest pain; dark urine, jaundice; bilirubin↑; Hb↓↓; LDH↑↑(8180U/L)	Major: Hb fell to 41g/L	5	Treated with IVIg and steroids; death not related to transfusion	Certain
HH5	No antibodies	Tachycardia; hypoxia; haemoglobinuria;	Death probably related to HH; Hb fell to 31g/L	7	Treated with IVIg and steroids	Certain
HH6	Known anti-E+Jk <sup>b</sup> +Kp <sup>a</sup> , DAT1+; no new antibodies	Fever, jaundice, dark urine; Hb↓ LDH↑	Moderate: Hb fell to 58g/L	6	3 unit transfusion; treated with IVIg and steroids	Probable

**Table 19.2:**  
Cases of hyperhaemolysis (HH) in patients with sickle cell disease

## Timing of reactions

### Acute

The majority (9/17) of reactions occurred during the transfusion which was discontinued in all but one case, where the symptoms were not fully recognised until a fifth unit had been transfused. Four occurred within two hours of the transfusion and the remaining four within 24 hours. The suspected unit was returned to the laboratory for investigation in 12/17 cases; in 4/17 cases, the reaction occurred after completion of the transfusion (or was not recognised until after completion of the transfusion), so the empty bag had presumably been discarded. There was one case where the reaction occurred during the transfusion, and the transfusion was stopped, but the bag not returned.

### Delayed

The delayed reactions were detected between 3 and 15 days post transfusion with a median of 8 days. In some cases, the exact time period was unclear as the patients had received several transfusions over a number of days.

## References

Petz LD and Garratty G. (2004) **Blood Transfusion in AIHAs**. In Immune Haemolytic Anaemias, 2<sup>nd</sup> edition, 375-400 Churchill Livingstone, New York

Young P, Uzieblo A et al. (2004) **Autoantibody formation after alloimmunisation: are blood transfusion a risk factor for autoimmune haemolytic anaemia?** Transfusion 44, 67-72

# New or Unclassifiable Complications of Transfusion (UCT) n=9

# 20

Author: Paula Bolton-Maggs

## Definition:

**Occurrence of an adverse effect or reaction temporally related to transfusion, which cannot be classified according to an already defined transfusion event and with no risk factor other than the transfusion, and no other explanation.**

There were 11 initial reports made. Two were reports of upper body skin rashes following fresh frozen plasma (FFP) which were withdrawn as they were mild allergic reactions which are no longer reportable to SHOT. Five cases were transferred in from acute transfusion reaction (ATR) and one from transfusion-related acute lung injury (TRALI). These cases describe miscellaneous reactions to various components that do not fit SHOT definitions for other reactions.

Four additional cases related to administration of prothrombin complex concentrate (PCC) are considered with other PCC issues in Chapter 11d, Incidents Related to Prothrombin Complex Concentrates.

## Deaths n=1

There was one death that was possibly related to the transfusion, and this is detailed below in Case 20.1.

## Major morbidity n=1

In one case a neonate suffered major morbidity with bradycardia and cardiac arrest during exchange transfusion.

Type of reaction	Number
Transfusion-associated necrotising enterocolitis (TANEC)*	1
Bradycardia and cardiac arrest during exchange transfusion	1
Serious reaction to granulocyte transfusion (see below)	1
Loss of consciousness and apparent 'fit' in relation to platelets	1
Syncope in relation to red cell transfusion in a multitransfused burns patient	1
Pain at site of transfusion or elsewhere in the body	4
<b>Total</b>	<b>9</b>

\*TANEC case is unconvincing, see below

Table 20.1:  
Categorisation of  
UCT cases n=9

Unexplained pain during transfusion has been noted in previous Annual SHOT Reports usually in patients with thalassaemia. None of the patients above were reported to have haemoglobin disorders. All were elderly (74, 85 and two were 80 years of age), three episodes were related to red cell transfusions and one to platelets.

### Case 20.1: Death associated with granulocyte transfusion

*A 68-year-old man who had a previous fungal infection had received a haemopoietic stem cell transfusion (allogeneic). During the infusion he had developed atrial fibrillation (tachycardia 160-180bpm). This was controlled with digoxin. Later the same day he had a suspected transfusion reaction to granulocytes. He became very short of breath and suffered a cardiac arrest following the fourth of five proposed units, and died. This reaction was investigated for TRALI but no significant*

*antibodies were detected in any of the granulocyte or stem cell donors. Post mortem revealed an undiagnosed pheochromocytoma and the patient had evidence of preceding cardiovascular instability. The relationship of the reaction and death to the granulocyte transfusion was assessed as 'possible'.*

The case that was reported as possible TANEC is not convincing. Expert review noted that desaturations were noted prior to the transfusion. Further details are given in Chapter 22, Paediatric Summary.

**Comment:** The concept of transfusion-associated NEC continues to be debated. While some authors provide evidence for this (Stritzke et al. 2013), a more comprehensive review of the literature did not find sufficient evidence to suggest any change in feeding practice (Hay et al. 2017). We encourage continued reporting of these cases to SHOT (NEC occurring within 48 hours of transfusion), but a more formal extended study is still required.

## References

Hay S, Zupancic JA et al. (2017) **Should we believe in transfusion-associated enterocolitis? Applying a GRADE to the literature.** *Semin Perinatol* 14(1), 80-91

Stritzke A I, Smyth J et al. (2013) **Transfusion-associated necrotising enterocolitis in neonates.** *Arch Dis Child Fetal Neonatal Ed* 98(1), F10-14

# Cell Salvage (CS) n=9

# 21

Author: Dafydd Thomas

## Definition:

**Any adverse events or reactions associated with autologous transfusion methods, including intraoperative and postoperative cell salvage (washed or unwashed), acute normovolaemic haemodilution or preoperative autologous donation (PAD).**

Nine cases were reported; on review none were withdrawn, nor transferred to or from other categories. This chapter describes the main findings from 9 completed questionnaires. Although definite data about how many cell salvage procedures are undertaken within the UK is unknown, it is the author's opinion that this low number of cases reflects a degree of underreporting of adverse events.

As has been shown previously, it seems that cell salvage appears to be a very safe procedure when undertaken by trained personnel but an increased awareness of the importance of reporting adverse events to SHOT seems to be needed. As with other adverse events human factors and a lack of training about correct procedural techniques are as likely to lead to adverse events when employing cell salvage as with all other areas of transfusion practice.

## Cell salvage cases by speciality

There were 9 cases reported as shown in Table 21.1

Specialty	Number
Obstetrics	3
Vascular surgery	2
Urological surgery	1
Orthopaedic surgery	1
Neurosurgery	1
Cardiac surgery	1
<b>Total</b>	<b>9</b>

Table 21.1:  
Specialty for cell salvage reports

Emergency n=3; elective n=6  
Female n=6; male n=3

## Types of cell salvage

Intraoperative cell salvage techniques were involved in all 9 cases. There were no postoperative cases reported.

## Cell salvage adverse events and reactions

There were six adverse events of which four related to operator error. Two were machine failures.

There were three clinical reactions, two patients suffered major morbidity and later died, although the relationship to cell salvage (imputability) was not clear.

Another case had moderate morbidity but with no lasting consequence and follows the pattern previously reported of transient hypotension when administering warm cell-saved blood via a leucocyte depletion

filter. Interestingly a second obstetric case reported hypotension but no leucodepletion filter was being used. The report did however mention that the anaesthetist used a 20mL syringe and a three way in line tap to force a higher flow rate of salvaged blood into the patient. The question arises about possible release of vasoactive substances due to this technique.

Another reported case related to temporary storage of cell-saved blood in a satellite blood refrigerator as the midwife required written orders for the administration of the salvaged blood. Salvaged blood can remain at room temperature for up to 6 hours from collection and needs to remain with the patient to avoid possible administration errors. This was therefore included as operator error due to incorrect storage and not following the correct protocol; written instructions should have been left for transfusion of the cell-salvaged blood.

A third case was reported where some salvaged blood had to be discarded as the slow running intravenous infusion meant the cell-salvage blood became time expired.

This reporting year there were no reports from the use of postoperative cell salvage and this may reflect a changing trend in its use during orthopaedic procedures. One orthopaedic procedure was reported using intraoperative cell salvage for a revision hip replacement. There were black fragments noticed in the blood bag following reinfusion. This phenomenon has been reported before and is included in the miscellaneous contraindications to the use of cell salvage in titanium alloy prosthesis removal. It is recommended to discontinue cell salvage until all darkened tissue has been removed. Cell salvage can resume after thorough irrigation of the wound with 0.9% sodium chloride via an alternate suction source.

## Death n=0

Although 2 patients who suffered major morbidity described below both died, there is not enough evidence to attribute the deaths to the cell salvage.

## Major morbidity n=2

There were two patients who suffered major morbidity and both eventually died, although the imputability for cell salvage has been estimated as low.

### **Case 21.1: Cardiac arrest in a baby during cardiac surgery. Imputability 1**

*During cardiac surgery, red cells were reinfused using a cell saver. This appeared to be associated with profound hypotension and cardiac arrest. Topical haemostatic agents had been used within the surgical field, but there had been no suggestion that these caused any blockage or failure of the cell-salvage equipment or washing process.*

*The baby had a complex past medical and surgical history. Cardiac surgery had been initially undertaken two days previously to try and correct co-arcuation of the aorta and a hypoplastic aortic arch. The baby also had a complete atrio-ventricular septal defect. The initial operation two days before re-operation reported coagulation problems secondary to heparin and aspirin use and postoperatively hypotension had been a longstanding issue. Following the cardiac procedures the baby remained critically unwell developing renal failure and septicaemia eventually dying just over a month later.*

**Comment:** This sad case of a paediatric death was associated with a number of interventions. Re-do paediatric cardiac surgery following persistent hypotension carries increased risk. There is no doubt that the reporters witnessed a drop in blood pressure on one occasion associated with the reinfusion of cell-salvaged blood, but the report also mentions the use of topical haemostatic agents which have been associated with anaphylactoid responses in some patients. It might be worth stressing the importance of avoiding aspiration of these agents as there has been a case report of anaphylaxis attributed to floseal contamination of washed cell-salvage infusion (Kumar et al. 2015). This phenomenon has been reported previously and usually responds to cessation of cell-saved red cell infusion plus vasopressors. In this case, it seems that cardiac reserve was not sufficient to withstand this hypotensive challenge. A coagulopathy also seemed to be present, but again there were multiple causative factors associated with this. It needs to be remembered in such situations that only cell-salvaged red cells are being reinfused

and there may be additional need for component therapy to replace platelets, fibrinogen and clotting factors for correction of the coagulopathy.

### Case 21.2: Hypotension during re-infusion; neurosurgery. Imputability 1

*Cell-salvage blood was collected and administered during meningioma resection. Sudden cardiovascular collapse (SBP 40mmHg) occurred and the infusion limb became red. The transfusion was stopped and a dose of vasopressor and crystalloid resulted in a rapid restoration of blood pressure (BP) with a short period of tachyarrhythmia and possible atrial fibrillation followed by sinus rhythm. Transfusion of the same bag of salvaged red cells was cautiously restarted through a different cannula and site and completed without incident. A second bag of cell-saved blood was commenced approximately one hour later with repetition of cardiovascular collapse and a red limb. The infusion was stopped and the salvaged red cells discarded. Transfusion continued with crossmatched blood and products thereafter. The patient was extubated postoperatively but later admitted to the intensive therapy unit (ITU) from recovery but then developed disseminated intravascular coagulation (DIC). Two further operations were required and the patient developed a refractory coagulopathy. The patient unfortunately died and the case is under investigation with clinical teams and transfusion consultant.*

**Comment:** Meningioma resection can sometimes result in significant haemorrhage depending on vascularity of the lesion. It would be interesting to know if a double volume wash was used as this has always been the recommendation in neurosurgery because of potentially high levels of thromboplastin and other bioactive substances in brain tissue. If haemostats were used, the same comment as mentioned above may apply as this may be anaphylaxis? Cell-salvaged blood quality can be maintained by ensuring that aspiration of contaminants is minimised and appropriate wash volumes are used.

N.B. No leucodepletion filters were used in these two cases. There have been some cases reported previously where filters were not used and hypotension was still observed.

## General comments

A wealth of supporting information for the correct use of cell salvage is available on the JPAC website and is updated regularly by the UK Cell Salvage Action Group.

### Recommendations

- All cell salvage operators must undertake initial and regular update training and be assessed as competent (there should be documented evidence of competence in the form of a training record)
- All bags of cell salvage blood must be fully labelled with the patient identification and unique case number
- All hospitals where intraoperative cell salvage (ICS) and postoperative cell salvage (PCS) are undertaken should report adverse events to SHOT
- Monitoring of patients is as important for the reinfusion of red cells collected by ICS or PCS as it is for allogeneic red cells
- Practitioners need to revisit previous Annual SHOT Reports particularly related to autologous transfusion to ensure historic incidents are not repeated

**Action: Cell salvage teams**

## Reference

Kumar S, Goyal K et al. (2015) **Anaphylactic reaction after autologous blood transfusion: A case report and review of the literature.** Asian J Neurosurg 10 (2), 145-7



# 22 Paediatric Summary

Author: Helen New

## Definition:

Paediatric cases comprise all reports for patients under 18 years of age, including all paediatric cases from the other chapters in this report. Paediatric reports have been subdivided by recipient age group: neonates  $\leq 28$  days; infants  $>28$  days and  $<1$  year old; children  $\geq 1$  year to  $<16$  years and young people aged 16 to  $<18$  years.

## Key SHOT messages

- Multiple reports of laboratory errors involving neonatal pre-transfusion compatibility testing and blood group selection continue to highlight the need for a focus on education and training of laboratory staff
- There has been a higher number of paediatric reports of specific requirements not met over the last two years, in particular for 'other' categories which include laboratory errors in pre-transfusion testing and in selection of phenotyped blood
- Eleven of 21 cases of overtransfusion or undertransfusion reported to SHOT (52.4%) were in paediatric cases, consistent with the complexity of transfusion administration and prescription calculations for neonates and children
- There have been 4 reports of neonatal transfusion-associated circulatory overload (TACO) in the last 2 years
- There were 5 cases involving recipients undergoing neonatal exchange transfusion, an area of complexity for both laboratory and clinicians
- There were 3 cases where neonates were given adult O D-negative units instead of available neonatal units in emergency, in comparison with 12 similar cases in 2015

## Recommendation

- Laboratory staff should be fully trained on, and be aware of the British Society for Haematology (BSH) guidelines (BSH Milkins et al. 2013; BSH New et al. 2016) regarding pre-transfusion compatibility testing and red cell selection for neonates and infants up to 4 months old

**Action: Hospital Transfusion Teams, Hospital Transfusion Laboratories**

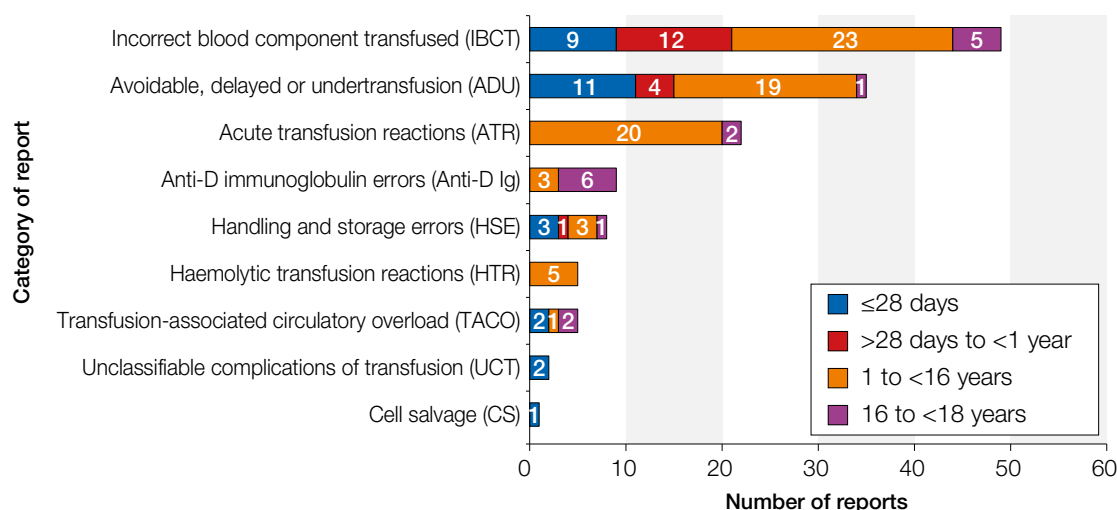


Figure 22.1: Summary of paediatric cases by category and age 2016

### Introduction

The paediatric chapter is a ‘mini-SHOT’ report within the overall report. All the paediatric cases are captured elsewhere within the individual reporting category chapters, but are discussed together here in order to give an overview of the adverse events related to transfusion in this specialised group of patients (Figure 22.1).

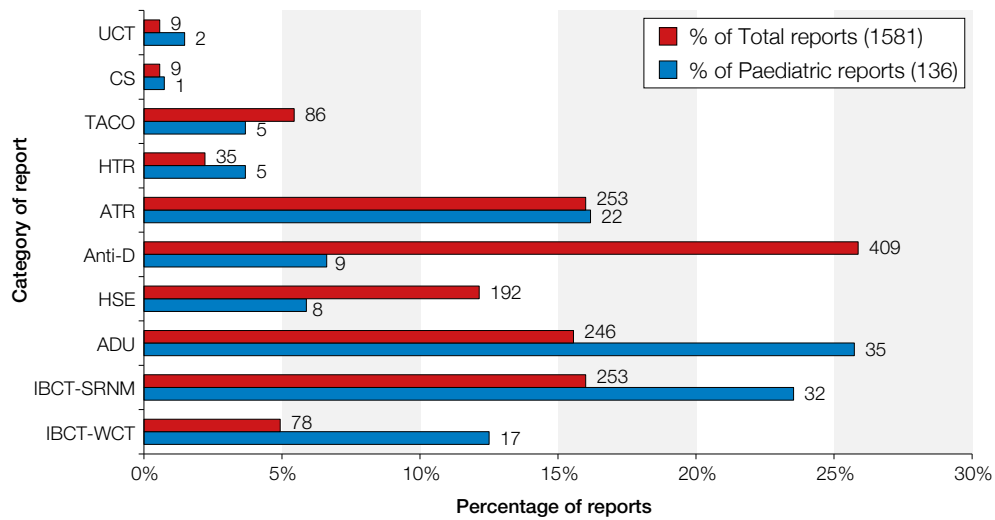
The overall number of paediatric cases including near miss (NM) and right blood right patient (RBRP) at 271 is almost the same as in 2015 (274). They contributed 136/1581 (8.6%) of total incident reports in 2016, 271/3091 (8.8%) when NM and RBRP are included.

Paediatric error-related reports (IBCT, HSE, ADU and Anti-D Ig) were 74.3% (101/136) of total paediatric reports, a higher percentage this year than previously (having ranged from 58-69% over the previous 4 years) although the actual numbers were lower than in 2015 (112). This is almost identical to the 74.5% (1178/1581) of total reports that are errors. It is striking that for certain of the error categories, paediatric cases are a relatively high percentage of total reports, e.g. for IBCT-wrong component transfused (WCT) they were 21.8% (17/78).

Laboratory errors were the primary reason behind 45.5% (46/101) of paediatric error reports (11 IBCT-WCT, 23 IBCT-specific requirements not met (SRNM), 3 HSE, 8 ADU, 1 anti-D Ig), whereas they were only 24.4% (288/1178) for total reports. Paediatric laboratory errors were also a relatively higher percentage of total reports for individual categories such as IBCT-WCT (24.4%, 11/45) and SRNM (18.4%, 23/125). There has been a notable increase in the number of paediatric SRNM cases over the last 2 years (Figure 22.3a), particularly in the ‘other’ category. This is partly due to an increase in SRNM laboratory errors, with 23 in 2016 and 22 in 2015 (ranging from 8-15 over the previous 4 years), which may be related to increased pressures on laboratory staff. Given the repeated reports of paediatric laboratory errors and the significance of them for SHOT reports as a whole, these are the focus of the SHOT paediatric recommendation for this year.

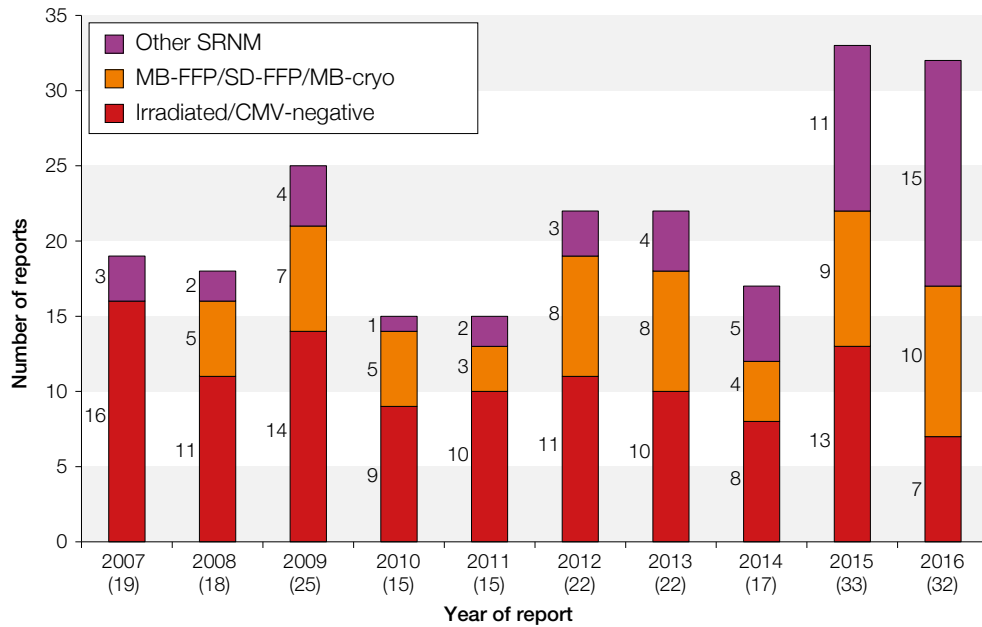
ATR showed similar numbers and pattern of component types over the last few years (apart from a temporary increase in 2014; Figure 22.3b). Paediatric reports were 22/253 (8.7%) of all ATR, in line with the overall proportion of paediatric reports. Paediatric reactions to platelets (moderate and severe allergic) predominated (Figure 22.3b). It should be noted that the majority of these reactions (12/14 identified components) were to apheresis platelets, only 2/14 pooled. This is as expected given that apheresis platelets are recommended for children where possible.

**Figure 22.2:**  
Percentages of  
paediatric and total  
reports in each  
category

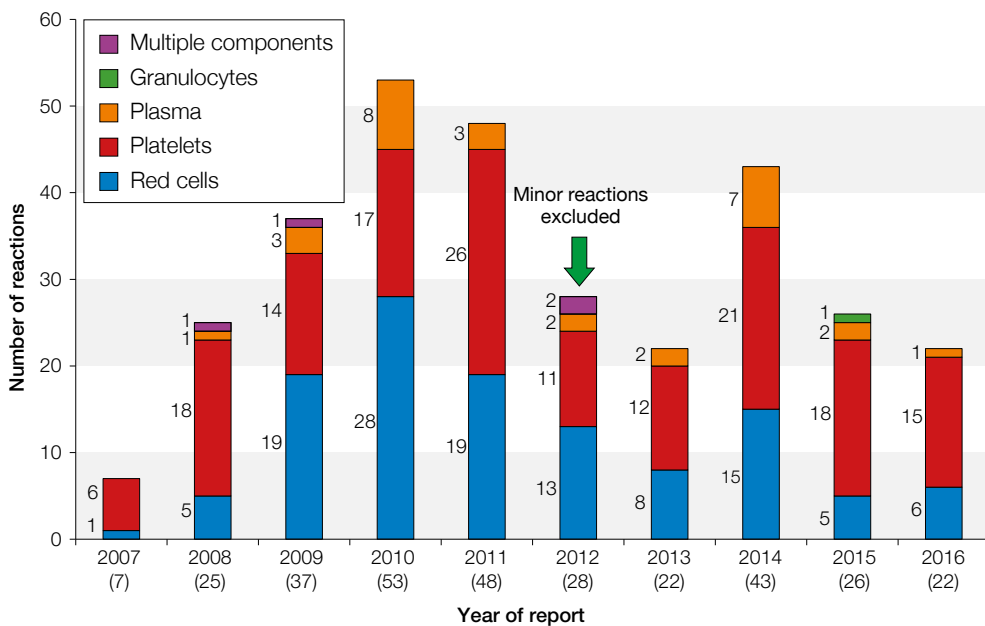


**Figure 22.3:**  
Trends in paediatric  
reports 2007-2016

a. Paediatric reports where specific requirements were not met



b. Paediatric acute transfusion reactions by component type



## Deaths due to transfusion n=0

There were 8 deaths in the 136 cases, but none were related to the transfusion.

## Major morbidity n=18

There were 18 cases of major morbidity in paediatric patients (10 ATR, 1 CS, 2 HTR, 1 IBCT-WCT Laboratory, 1 UCT, 3 TACO).

## Error-related reports n=101

## Incorrect blood component transfused (IBCT) n=49

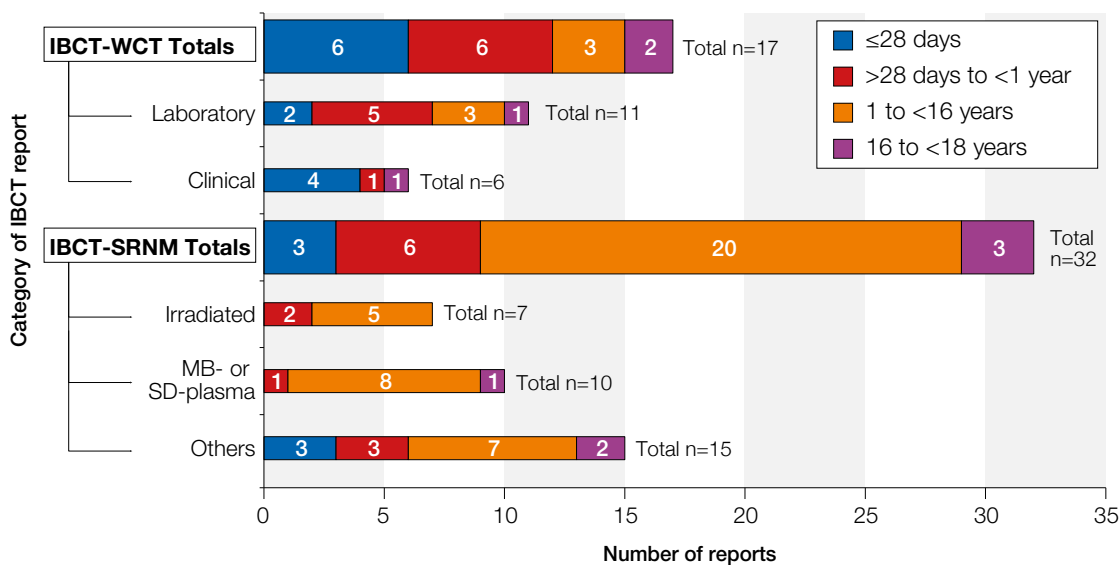


Figure 22.4: Breakdown of incorrect blood component transfusion reports

MB=methylene blue-treated; SD=solvent-detergent treated

## IBCT-wrong component transfused (WCT) n=17

### IBCT-WCT clinical error n=6

Three neonates received emergency adult O D-negative blood instead of the available neonatal red cells. In one case, despite measures taken to distinguish the adult pack from the neonatal, the wrong unit was taken.

#### Case 22.1: Preterm baby transfused with emergency adult red cells

Two emergency O D-negative units appropriate for neonates and two for adults were stored in the delivery suite blood refrigerator. Each pair of units was kept in a different clear plastic envelope with information sheets specifying the contents. A sick preterm baby (haemoglobin (Hb) 112g/L) required urgent transfusion prior to hospital transfer. Despite the information sheets, the neonatal nurse selected adult O D-negative blood for the transfusion. The hospital is now adding pictures of adults and neonates to the information sheets.

Local strategies to keep the adult and neonatal emergency red cell units separate and easily distinguishable are recommended to reduce the risk of confusion.

A fetus received an emergency intrauterine transfusion (IUT) with a non-irradiated 23-day-old paedipack as there was insufficient time to order irradiated red cells specific for IUT. This report serves as a reminder that in an emergency, it is acceptable to transfuse a neonatal paedipack (ideally less than 5 days old) as

an alternative to IUT red cells, and that maternal blood should not be used (Bolton-Maggs et al. 2013; BSH New et al. 2016).

A 5-week-old baby was grouped as O D-negative and transfused group O red cells, platelets and plasma during surgery for a bowel perforation. He was later discovered to be B D-positive: the laboratory had not been informed that he had been transfused O D-negative red cells at another site. A 16-year-old bleeding patient was transfused with O D-positive red cells that had been crossmatched for another patient and collected from the emergency refrigerator in error.

### **IBCT-WCT laboratory error n=11**

There were 4 reports of procedural errors related to neonatal and infant blood grouping/compatibility testing. A baby who had received group O IUT was grouped as O at birth. This should not have been reported as the baby's true group could not be determined due to the prior IUT. A 1-month-old baby, group A, with necrotising enterocolitis (NEC), who had received multiple transfusions with group O red cells and was grouping as O in the laboratory was given group O fresh frozen plasma (FFP) due to failure to check the historical record. An infant aged 4 months and 10 days was issued red cells using the original sample taken at birth, despite the fact that from 4 months of age compatibility testing should be undertaken as for adults.

A 3-year-old group A D-positive patient, prior to haemopoietic stem cell transplant (HSCT), was erroneously grouped as O D-positive on 7 occasions following an initial mixed field grouping result and without checking the results from the referring laboratory. A 5-year-old patient with sickle cell disease was grouped as D-positive and was transfused accordingly, but on genotyping was found to have a D variant and should have had D-negative red cells.

There were several reports of incorrect blood group selection. A 1-month-old group A D-negative baby girl was transfused with O D-positive red cells due to incorrect component selection, only discovered later at another hospital. The hospital decided to only stock D-negative neonatal red cells in the future.

A 4-day-old D-positive baby with haemolytic disease of the fetus and newborn (HDFN) due to maternal anti-D inappropriately underwent exchange transfusion with O D-positive units, resulting in prolonged haemolysis requiring further exchange transfusion (see full details in Case 10.1, Chapter 10, Incorrect Blood Components Transfused (IBCT)).

A 2-month-old baby who had received intravenous immunoglobulin (IVIg) was transfused with group A red cells, despite local protocols and the patient notes on the laboratory information management system (LIMS) indicating that they should receive group O (to mitigate any risk of anti-A in the IVIg). A 17-year-old female group B D-negative patient with sickle cell disease underwent red cell exchange transfusion with six units of O D-positive red cells due to incorrect component ordering by the laboratory, only detected 6 weeks later.

Pooled platelets were issued to a 15-year old instead of apheresis platelets. Although platelets had been requested by the ward prior to the routine platelet delivery the BMS did not check the platelets in stock and assumed that they were apheresis, discovering too late that only pooled platelets were available. Although pooled platelets may be given to children where it is not possible to provide apheresis, this was a laboratory procedural error.



### **Learning points**

- Where laboratories choose to stock both O D-negative and O D-positive paedipacks in order to optimise use of O D-negative red cells this should be highlighted to staff, given that many laboratories only stock O D-negative paedipacks
- When interpreting neonatal grouping results, laboratory staff should be aware that they need to take into account previous transfusions of group O red cells. If there is uncertainty as to whether the true neonatal group is O, group O platelets and plasma components should be avoided until the neonatal group is confirmed

**IBCT: specific requirements not met (SRNM) n=32**

Clinical cases where requirements were not communicated properly to the laboratory n=9

Laboratory primary error n=23

**Non-irradiated n=7**

There were 6 clinical cases. These included 2 infants, 1 post IUT, 1 DiGeorge – clinicians contacted the laboratory to say that the patient no longer required irradiated blood as they had a thymus, but this decision was later reversed; 2 prior to stem cell collection and 2 on treatment with fludarabine.

The final case was a laboratory error where information on the request form was missed.

An additional case where the laboratory did not select irradiated red cells for a child undergoing stem cell harvest is included in Chapter 11b, Avoidable Transfusions, Case 11b.2.

**Non-MB/SD plasma n=10**

There were 10 cases where standard plasma was provided instead of MB/SD provision by the laboratory (5 reports for FFP and 5 for cryoprecipitate).

**Others n=15**

*Inadequate pre-transfusion testing n=7*

There were 7 cases in the laboratory where there was inadequate pre-transfusion testing, several due to confusion over the requirements for compatibility testing in neonates and infants up to 4 months of age.

- 4 cases involved inadequate pre-transfusion antibody screening. A 6 day neonate was issued with red cells based on a maternal sample from 2 months before delivery. A 25 day neonate was issued with blood crossmatched against a 15-day-old sample. Another neonate was transfused red cells without antibody screening of either maternal or neonatal samples. Finally, a 14 month child was issued red cells based on the neonatal compatibility screening protocol and before the results of antibody screening were available
- There were 3 cases where maternal antibodies were not appropriately taken into account in compatibility testing: a neonate whose mother had detectable prophylactic anti-D should have had a full crossmatch but was issued blood by electronic issue; a 1-month-old infant whose mother had anti-Le<sup>a</sup> and anti-Le<sup>b</sup> antibodies correctly had blood crossmatched against the maternal sample for the first unit of donor red cells, but when a second unit from a different donor was required it was not crossmatched as necessary; a 3-month-old baby with maternal anti-C<sup>w</sup> did not have blood crossmatched on several occasions

*Failure to use phenotyped blood n=5*

- 4 for patients with haemoglobinopathies aged 2-17 years: 1 due to lack of communication from clinical staff that the patient had sickle cell disease, 1 due to incorrect phenotyping in the laboratory, 2 due to failure to follow procedures in the laboratory to provide Rh phenotyped blood for haemoglobinopathy patients (one female patient developed anti-e)
- A 7-year-old female patient on extracorporeal membrane oxygenation was transfused with K-positive blood

*Others n=3*

- Hepatitis E virus (HEV)-screened units, two cases due to lack of clinical communication with the laboratory over requirements for children with HSCT and T-acute lymphoblastic leukaemia
- Use of blood >7 days old for exchange transfusion in sickle cell disease (red cells <7 days old had been ordered but were placed into routine stock, so when requested for the exchange transfusion older red cells were issued in order to avoid delay)



## Learning point

- Procedures for pre-transfusion compatibility testing and component selection are different for recipients under 4 months of age in order to take into account maternal red cell antibodies. The maternal sample should be taken within 3 days pre delivery or collected post delivery (BSH New et al. 2016). Where antibodies are present, although crossmatching is not required for subsequent paedipacks from the same donation, it must take place each time blood from a new donor is to be transfused

## Avoidable, delayed or undertransfusion (ADU) n=35

### Avoidable transfusion n=6

There were 5 transfusions based on incorrect pre-transfusion results. Three red cell transfusions were based on erroneous Hb results, including an incorrectly transcribed Hb result on the ward (the 'mean cell volume' mistaken for Hb); cryoprecipitate was transfused to a 20-day-old neonate based on erroneous results from the coagulation laboratory (insufficient sample for accurate test); platelets were given on the basis of an unexpectedly low platelet count of  $21 \times 10^9/L$ , subsequently found to be due to platelet clumping.

#### Case 22.2: Red cell transfusion based on oxygen saturation result instead of Hb

*An 11-day-old neonate in the paediatric intensive care unit (PICU) was unnecessarily transfused on the basis of a Hb result communicated by the PICU fellow to the consultant as 87g/L. The figure was an oxygen saturation result from a blood gas sample. The true Hb result was 131g/L, and the post-transfusion Hb rose to 174g/L.*

#### Case 22.3: Hb result from shared-care hospital not taken into account

*A 2-year-old patient with a posterior fossa tumour under shared care between two hospitals had a red cell transfusion based on a Hb from one hospital (78g/L) whereas there was a more recent higher Hb result (110g/L) available from another hospital which had not been used.*

This case emphasises the need to take particular care with pre-transfusion results when a child's care is shared between two hospitals.

In an additional case, transfusion of non-irradiated components to an 11-year-old for a stem cell harvest resulted in discard of the stem cell collection and the requirement for a repeat collection with repeat transfusion (counted as avoidable, Case 11b.2 in Chapter 11).

### Delays to transfusion n=14

Four delayed transfusions to neonates and infants were due to laboratory communication or labelling issues, including a 14-day-old neonate where 'Twin' rather than 'Twin 1' was used as the forename on the compatibility label. Two were due to problems with provision of components by the Blood Service including a second exchange transfusion unit for a baby with severe hyperbilirubinaemia, and 3 were due to failure to communicate within the laboratory and order components. In one case there were problems with transmission of results from blood analysers.

There were 2 delays to 1-year-old children with major haemorrhage, either not preparing components in time, or not activating the protocol correctly.

A 15-hour delay in transfusion of a 1-month-old infant occurred due to difficulties in inserting a cannula for the transfusion. An unusual delay resulted when a paediatric patient (6 years old) needed an emergency transfusion at a hospital that had never previously transfused children. As there were no protocols in place, the transfusion was delayed while the Medicines and Healthcare Products Regulatory Agency (MHRA) and the hospital chief executive were contacted for approval.



**Overtransfusion n=9**

Five cases involved overrunning or incorrectly set volumetric pumps. Two neonates were overtransfused by a few millilitres. A 4-year old received an entire unit of red cells instead of the prescribed volume (60mL less than the volume of the whole unit) as there was no 'volume to be infused' programmed into the infusion pump, another received 56mL more than prescribed, and a 14-year old received an additional 67mL.

There were 3 cases due to incorrect prescription, 2 using a calculation of the transfusion volume on the basis of the incorrect weight of patient.

**Case 22.4: Use of an incorrect weight to calculate the transfusion volume**

*A 10-month-old infant weighing 14kg was overtransfused due to incorrect weight (23kg) being used to calculate red cell volume. The infant received 350mL red cells instead of the correct 200mL. The pre-transfusion Hb was 86g/L, post-transfusion Hb 167g/L.*

Incorrect calculation of transfusion volume for children is repeatedly reported, and in this case resulted in a significant increase in transfusion volume.

**Case 22.5: Prescription of platelets in 'units' not 'mL' resulted in overtransfusion**

*A 2-year-old child, 9.5kg, with an ependymoma was given a prophylactic platelet transfusion with 300mL platelets prescribed as 'unit' not in mL over 30 minutes (i.e. 32mL/kg, given at 64mL/kg/hour). There was no adverse outcome. The recommended volume is 10-20mL/kg for children <15kg.*

Although on this occasion there were no adverse sequelae, prescription of blood components in units for small children can lead to circulatory overload with serious clinical consequences.

**Case 22.6: Excess volume of cryoprecipitate transfused**

*A 14.5kg 2-year-old child with hypofibrinogenaemia and liver disease was prescribed 65mL of cryoprecipitate but the laboratory had insufficient small volume packs and provided a large volume pack. The nurse did not refer to the prescription volume and the entire 296mL was transfused. The child required urgent administration of furosemide.*

This case emphasises the care that needs to be taken with transfusing small recipients who may require only a small proportion of the component volume provided. The recommended volume for cryoprecipitate is 5-10mL/kg at this age.

**Learning point**

- Paediatric transfusion volumes should be meticulously calculated. In order to prevent overtransfusion of blood components, it is recommended that they should be prescribed in mL and not units (BSH New et al. 2016), unless there are risk-assessed protocols for prescribing in units for older children. Previous SHOT reports have highlighted similar cases, and have recommended that paediatric transfusion prescribing should be the focus of ongoing education in hospitals

**Undertransfusion n=2**

A neonate requiring exchange transfusion was supplied by the Blood Centre with a unit incorrectly labelled with the original whole blood volume rather than the final manufactured component volume.

A 1-month-old infant was prescribed 33mL red cells over 3 hours but the pump was set at 0.33mL/hour so the baby was undertransfused.

**Avoidable and wrong use of O D-negative n=1**

An anaemic newborn baby was given emergency O D-negative blood but should have had crossmatched D-positive blood due to maternal anti-c. D-negative blood is incompatible with anti-c (Case 11b.5).

### Unnecessary transfusion n=3

A 2-year-old child with pyruvate kinase deficiency was transfused prior to an adenotonsillectomy but the operation was cancelled.

Two transfusions were deemed to have been unnecessary by consultants on review, emphasising the importance of senior input in transfusion decisions. One of these was a second platelet transfusion within 4 hours for a 9-year-old child with acute lymphoblastic leukaemia and the other was a postoperative red cell transfusion for a 14-year-old patient with a Hb of 76g/L.

### Handling and storage errors (HSE) n=8

#### Cold chain errors n=3

Platelets and red cells were transfused after being too long out of temperature control (one transfusion of red cells out of temperature control for 7 hours).

#### Transfusion of 'expired' components n=2

SD-FFP was transfused 1 hour and 45 minutes beyond the expiry time to a neonate because ward staff looked at the expiry date on the pack, not the post-thaw expiry time.

A unit of red cells was left in a satellite refrigerator beyond sample validity and was subsequently transfused. The new sample revealed that the patient had a positive antibody screen.

#### Excessive transfusion time n=3

There were three reports of excessive red cell transfusion times in recipients up to 1 year of age, of between 5 hours and 5.5 hours.

### Anti-D Ig n=9

All cases related to problems with anti-D Ig administration in pregnancy, following sensitising events or delivery, the youngest 13 years of age. See Chapter 14, Adverse Events Related to Anti-D Immunoglobulin (Ig) for further details.

## Transfusion reactions n=35

### Acute transfusion reactions (ATR) n=22

There were fewer overall reports than in 2015 (26), but similar proportions of the different components implicated, with two thirds of ATR reports to platelets (Figure 22.5). The percentages of paediatric ATR to components were: red cells 6/22 27.3%, platelets 15/22 68.2%, plasma (MB-cryoprecipitate) 1/22 4.5%. There were 7 severe reactions to platelets, 2 to red cells (requiring admission), and 1 to MB-cryoprecipitate. No ATR were reported in infants or neonates.

- **Red cells:** There were two allergic reactions, classified as severe as they required admission to the ward. The rest were febrile reactions
- **Platelets:** The platelet reports were all of allergic reactions of variable severity. 11 were from apheresis, 2 pooled, 1 human leucocyte antigen (HLA)-matched, 1 of unknown type of platelets
- **Plasma components:** A 15-year-old patient undergoing scoliosis surgery developed tachycardia and hypotension following a transfusion with MB-cryoprecipitate, but with no respiratory compromise. The reaction was classified as allergic due to a significantly raised mast cell tryptase result. However, the patient was bleeding in theatre and it is uncertain whether the overall change in clinical condition was due to the cryoprecipitate

a. Comparison of proportions of adult and paediatric ATR related to different components

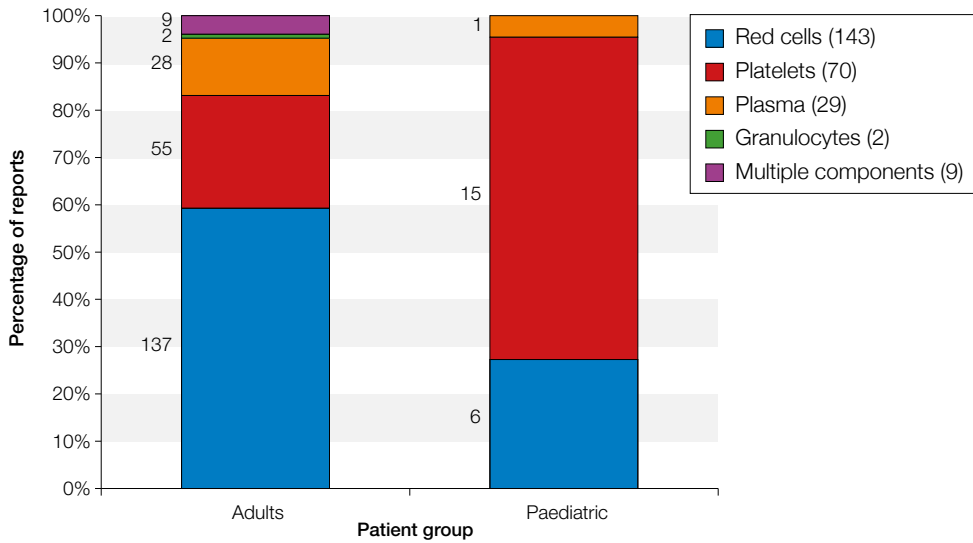
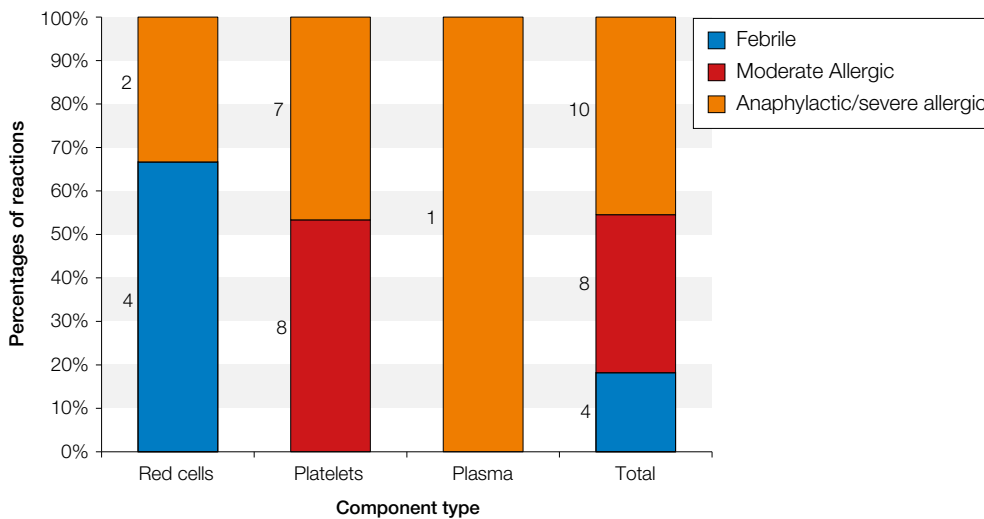


Figure 22.5: Paediatric ATR reports

b. Percentages of reaction types for each component for paediatric reports.



### Haemolytic transfusion reactions (HTR) n=5

A 9-year-old child group A D-negative was given O D-negative high-titre antibody-negative apheresis platelets due to a shortage of A D-negative platelets and developed a fever, rigors and an increase in bilirubin. The direct antiglobulin test (DAT) became positive following the transfusion and anti-A was eluted from the red cells.



## Learning point

- For children, group O platelets are avoided for non-group O children, even though they are tested for high-titre anti-A/B haemagglutinins, in order to reduce the risk of haemolysis (BSH New et al. 2016). The risk of haemolysis may be greater for small paediatric than for adult recipients as they are often transfused with a greater volume of platelets per kg body weight. Moreover, children are usually transfused with apheresis platelets in plasma, not pooled platelets in platelet additive solution, so receive a greater plasma volume than recipients of pooled platelets

See Chapter 19, Haemolytic Transfusion Reactions (HTR) for details of other paediatric cases.

## Transfusion-associated circulatory overload (TACO) n=5

There were two reports of TACO in neonates, and three in children aged between 10 and 17 years. A preterm newborn baby had a rapid respiratory deterioration requiring intubation following a double volume exchange transfusion. The baby had been born very anaemic, with the highest cord blood Hb of 70g/L, so at risk of developing heart failure.

### Case 22.7: Symptoms of TACO developing during a neonatal top-up transfusion

*An 18-day-old preterm baby with intrauterine growth retardation and Hb 63g/L was given a top-up transfusion and developed respiratory distress 75 minutes later having received 7.8mL red cells (7.5mL/kg). He required respiratory support with oxygen and non-invasive nasal ventilation. A chest X-ray showed airspace changes compatible with pulmonary oedema or infection. The transfusion was stopped and he had symptomatic improvement following treatment with furosemide. A diagnosis of possible TACO was felt the most likely despite the small volume of red cells transfused.*

These two case reports highlight that it is important to be aware of TACO in neonates, and to consider even following small-volume top-up transfusions in babies without the conventional risk factors described in older recipients.

## Cell salvage (CS) n=1

A 15-day-old neonate undergoing emergency cardiac surgery became profoundly hypotensive and had a cardiac arrest following infusion of red cells using a cell saver. However, the baby had other comorbidities including hypotension and there were haemostatic problems during surgery so imputability was uncertain (see Chapter 21, Cell Salvage (CS) for further details).

## Unclassifiable complications of transfusion (UCT) n=2

There was one case reported as mild NEC, in a 26-day-old very preterm (24 weeks) neonate who developed a distended abdomen 14 hours after a red cell transfusion and subsequently had blood in the stool. However, the baby had started desaturating prior to commencing transfusion and the symptoms settled after conservative treatment. Expert review concluded that this was unlikely to be a case of transfusion-associated NEC.

### Case 22.8: Rapid clinical deterioration following neonatal exchange transfusion

*A 1-day-old neonate with HDFN due to anti-D, born anaemic with Hb 88g/L, had a rapid clinical deterioration two hours into an exchange transfusion. The baby developed bradycardia and hypoxia and had a cardiac arrest requiring resuscitation and intubation. No obvious cause for the deterioration was found. The red cells were negative for high-titre haemagglutinins.*

There was a similar case in the 2015 Annual SHOT Report where the 'least unlikely' cause for a baby's deterioration was felt to be high-titre anti-A antibodies in the transfused unit (1:512). These cases emphasise the vulnerability of neonates undergoing exchange transfusion procedures and the difficulty in some cases in understanding the reason for clinical deterioration.

## Near miss (NM) n=122 and right blood right patient (RBRP) n=13

There were a total of 47 NM cases of wrong blood in tube (WBIT) where there was confusion between the mother and baby identities, of potential harm to the baby, 29 of which were reported under the mother's details. There were also 5 cases of WBIT due to misidentification of twins.

### Case 22.9: Transfusion volume miscalculated by a factor of 10

*A 5-month-old infant was prescribed 447mL red cells (124mL/kg) in error as the transfusion formula used was not adjusted to take account for the change in reporting of Hb units from g/dL to g/L. The error was noted prior to administration.*

This is an important learning case as it highlights that there can still be confusion about the units of Hb in relation to calculating transfusion volumes. As a double check when prescribing, it should be noted that transfusion volumes to non-bleeding neonates would not normally exceed 20mL/kg.

See Chapter 12, Near Miss Reporting (NM) and Chapter 8, Right Blood Right Patient (RBRP) for an overview of the other cases including paediatric.

## Commentary

- There were 15 reports of laboratory errors involving neonatal and infant pre-transfusion compatibility testing and blood group selection across the different reporting categories. This striking number of reports may reflect staffing issues in hospital laboratories as has been highlighted elsewhere. Moreover, there has been an increase in the number of laboratory SRNM cases reported over the last two years. A focus on training about neonatal/infant specific requirements and pre-transfusion compatibility testing is needed
- Prescribing and administration errors leading to overtransfusion continue to constitute a risk to patients. The near miss with platelets written up as a 'unit' rather than mL for an infant is important to highlight as such errors can lead to significant overtransfusion
- The 4 reports of neonatal TACO in the last 2 years, having had only a single previous neonatal report since 2007, is likely to reflect increased clinical awareness and recognition. Neonatologists are encouraged to continue to monitor babies for signs of TACO following transfusions
- The 5 cases involving recipients undergoing neonatal exchange transfusion involved both laboratories and clinicians reflecting the special component requirements and the complexity of the clinical situation and vulnerability of the recipients
- The reduction in the number of cases in 2016 where neonates were given adult O D-negative units in emergency situations is heartening, and may reflect local strategies to reduce this risk in hospitals

## References

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BSH New HV, Berryman J et al. (2016) **Guidelines on transfusion for fetuses, neonates and older children**. *Br J Haematol* 175, 784–828

# 23 Summary of Incidents Related to Transplant Cases n=93

Authors: Alison Watt and Paula Bolton-Maggs

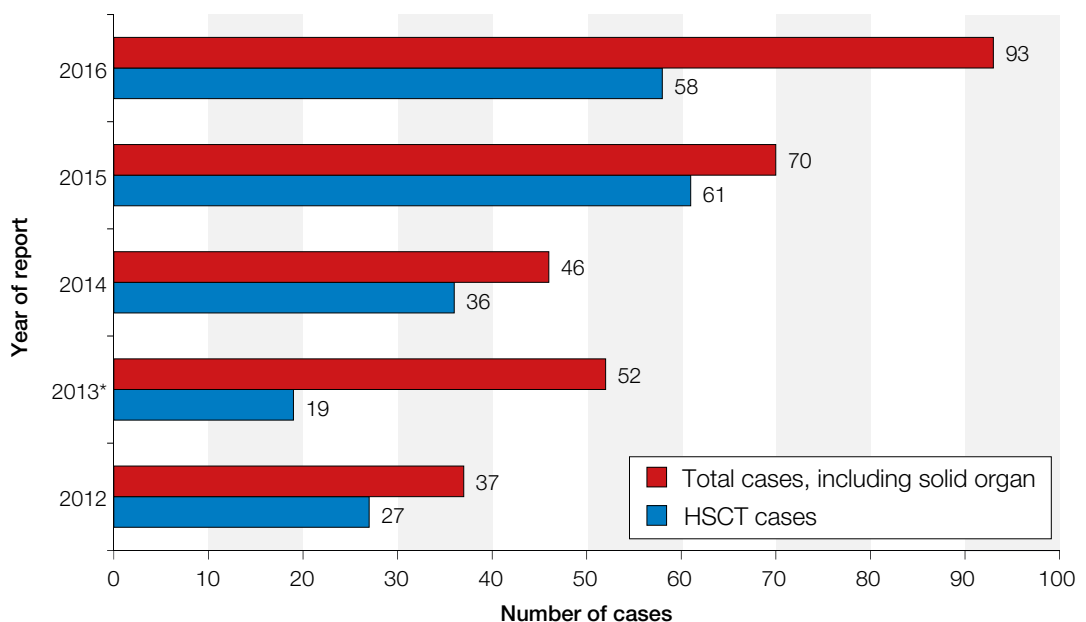
## Key SHOT messages

- It is essential to give irradiated components to haemopoietic stem cell transplant (HSCT) patients prior to stem cell harvest
- Procedures should be robust when institutions use remote access electronic issue of compatible red cells in order to ensure a current valid sample is not replaced in the system while a transfusion is in progress
- Excellent communication between clinical transplantation staff and transfusion laboratory staff is imperative to ensure transplant patients receive appropriate components
- National guidelines are needed that are suitable for both transplantation and transfusion professionals that cover the procedures necessary for managing transfusions to transplant patients

Since 2012 incidents related to transplant patients have been summarised to highlight the particular problems associated with transfusion in both HSCT and solid organ transplants. There are several difficulties with the specific requirements associated with transfusing transplant patients and there are particular complexities when the transplant is ABO-incompatible or mismatched for the D antigen.

The number of reports related to transplant cases increased again in 2016 to n=93 (n=70 in 2015).

Figure 23.1:  
Transplant  
transfusion errors  
2012-2016 n=298



\*1 patient had both HSCT and solid organ transplants

Figure 23.1 shows that the increase in 2016 results from errors related to solid organ transplants, in particular a general increase in reports where specific requirements were not met (SRNM). For comparison solid organ transplant SRNM in 2016 was n=30 and in 2015 n=5; HSCT SRNM in 2016 n=38, 2015 n=26. These increases mainly result from failures to request or supply hepatitis E virus (HEV)-screened components, n=39 in 2016. The Advisory Committee on the Safety of Blood, Tissues and Organs (SaBTO)/British Society of Blood and Marrow Transplantation (BSBMT) recommendations (SaBTO 2016) for the requirement for HEV-screened components for transplant patients became applicable in March 2016, when the Blood Services were able to supply screened components.

Type of transplant	ABO/D errors	SRNM	Other**	Total
HSCT	19	38	1	58
Solid organ	4	30	1	35
<b>Total</b>	<b>23</b>	<b>68</b>	<b>2</b>	<b>93</b>

Table 23.1: Summary of errors made in transplant cases n=93

\*\*Other=summary of 2 cases in Table 23.2

The cases analysed here are included in the data discussed in other chapters:

- Incorrect blood component transfused (IBCT)
  - wrong component transfused (WCT) n=15
  - specific requirements not met (SRNM) n=53
- Near miss WCT and SRNM n=23
- Avoidable, delayed or undertransfusion (ADU) n=2

SHOT category	Description of error	Outcome
ADU Avoidable	A child, aged 11, requiring irradiated components for stem cell harvest was transfused with red blood cells (RBC) that were not irradiated (Case 11b.2 in Chapter 11b, Avoidable Transfusions)	The stem cell collection had to be discarded and the patient needed additional G-CSF* to re-mobilise marrow for repeat collections
ADU Delay	A liver transplant was started with 18 units of RBC allocated to the patient and available from the remote issue refrigerator in theatre. After transfusion of 1 unit, there were no longer any RBC allocated for this patient, because a new sample had been booked in, invalidating the previous test results	Access to group specific RBC by remote issue suddenly became unavailable and RBC units could not be released until the new sample had valid results

Table 23.2: Non-ABO/D or SRNM transplant errors n=2

\*G-CSF=granulocyte-colony stimulating factor

### Learning points

- It is essential to give irradiated components to haemopoietic stem cell transplant (HSCT) patients prior to stem cell harvest
- Procedures should be robust when institutions use remote access electronic issue of compatible red cells to ensure a current valid sample is not replaced in the system while a transfusion is in progress, because this can lead to confusion and delays



### ABO and D errors n=23

SHOT category	ABO* error	D error	Total
IBCT	13	2	15
Near miss	6	2	8
<b>Total</b>	<b>19</b>	<b>4</b>	<b>23</b>

Table 23.3: ABO and D errors in transplant cases n=23

\*1 case was mismatched for both ABO and D



The unintentional transfusion of ABO-incompatible blood components is a never event in England (NHS England 2015) and is similarly reportable in the devolved countries, e.g. as 'red incidents' in Scotland. However, it is not known if these errors are being reported, possibly because in five years of analysing transplant-transfusion incidents there has only been 1 case of ABO-incompatible transfusion that resulted in an adverse outcome for the patient (Bolton-Maggs, 2013). Table 23.4 summarises cases that could be classifiable as never events (in England).

**Table 23.4:**  
Details of ABO-incompatible red cell transfusions to allograft HSCT patients n=6

ABO/D	Gender	Patient group	Donor group	Group transfused	Error
<b>IBCT as a result of clinical error</b>					
ABO	Female	A	B	A	protocol or communication
ABO	Female	A	B	A	protocol or communication
<b>IBCT as a result of laboratory error</b>					
ABO	Female	A	O	A	LIMS* flags not heeded or updated
ABO/D	Male	A	O+/O-**	A	LIMS flags not heeded or updated
ABO	Male	A	O	A	LIMS flags not heeded or updated
ABO	Male	A	O	A	LIMS flags not heeded or updated

\*LIMS=laboratory information management system, \*\* O+/O-=double cord groups O D-positive and O D-negative

### Specific requirements not met n=68

**Table 23.5:**  
Failure to provide components with correct specific requirements for transplant patients n=68

SHOT category	Irradiated	HEV	Irradiated and HEV	Other*	Total
<b>Errors related to HSCT</b>					
SRNM clinical error	12	5	4	1 HLA	22
SRNM laboratory error	3	2	0	1 EI	6
Near miss clinical error	1	3	0	0	4
Near miss laboratory error	5	1	0	0	6
<b>Subtotal errors HSCT</b>	<b>21</b>	<b>11</b>	<b>4</b>	<b>2</b>	<b>38</b>
<b>Errors related to solid organ transplants</b>					
SRNM clinical error	2	21	0	0	23
SRNM laboratory error	0	0	0	2 MB	2
Near miss clinical error	2	3	0	0	5
Near miss laboratory error	0	0	0	0	0
<b>Subtotal errors solid organ</b>	<b>4</b>	<b>24</b>	<b>0</b>	<b>2</b>	<b>30</b>
<b>Total</b>	<b>25</b>	<b>35</b>	<b>4</b>	<b>4</b>	<b>68</b>

\*HLA=human leucocyte antigen-matched, EI=electronic issue, MB=methylene blue-treated component

Transplant patients have complicated specific transfusion requirements, which became more complex in 2016 with the additional requirement to provide HEV-screened blood components for patients receiving solid organ transplants or allograft HSCT (SaBTO 2016a). In autumn 2016 SaBTO reviewed their guidance on the introduction of HEV-screened components and concluded that universal screening of all donations would be a more effective strategy (SaBTO 2016b). 100% HEV-screened red cells were available in England from 1<sup>st</sup> May 2017, from 3<sup>rd</sup> April 2017 in Wales, and in Scotland from 5<sup>th</sup> April 2017. Replacement of frozen components followed as stocks were used up.

In the 2015 Annual SHOT Report (Bolton-Maggs et al. 2016) it was highlighted that the need for irradiated components for some patients receiving solid organ transplants has been challenged (Hui et al. 2016) and that the guidelines are being revised by the Transfusion Task Force of the British Society for Haematology (BSH), but until then the current guidance remains in place (BSH Treleaven et al. 2011). It is essential to consider the importance of irradiated components for HSCT patients. There were two cases reported in 2016 of children who received non-irradiated components in the week before a planned stem cell harvest. Case 11b.2 is described in Chapter 11b, Avoidable Transfusions, and noted in Table 23.2.

This was an avoidable transfusion to an 11-year-old transplant patient who then needed a repeat stem cell harvest, including further stimulation with granulocyte-colony stimulating factor. Another incident is included in the SRNM data, a 4-year-old child with neuroblastoma received non-irradiated platelets three days prior to stem cell harvest. These cases show the importance of continuing to ensure HSCT patients receive irradiated components.

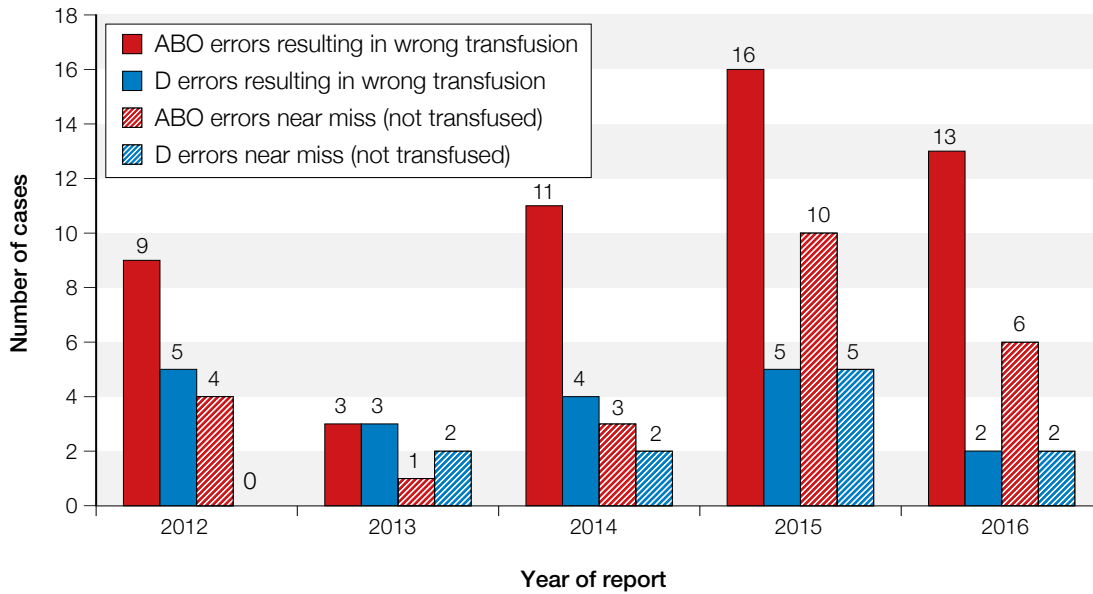


Figure 23.2: Transplant ABO and D errors 2012-2016, n=106

### Causes of error

Error made	ABO/D error	SRNM	Other	Total
<b>Errors related to HSCT</b>				
Clinical error - protocol or communication	4	22	1	27
Clinical decision making	0	3	0	3
Laboratory error - LIMS flags not heeded or updated	12	10	0	22
Laboratory error - communication	0	1	0	1
Lack of understanding in laboratory	3	1	0	4
Non-availability of HEV screened	0	1	0	1
<b>Subtotal errors HSCT</b>	<b>19</b>	<b>38</b>	<b>1</b>	<b>58</b>
<b>Errors related to solid organ transplants</b>				
Clinical error - protocol or communication	0	24	0	24
Clinical decision making	0	4	0	4
Laboratory error - LIMS flags not heeded or updated	3	2	0	5
Laboratory error - communication	0	0	1	1
Lack of understanding in laboratory	1	0	0	1
<b>Subtotal errors solid organ</b>	<b>4</b>	<b>30</b>	<b>1</b>	<b>35</b>
<b>Total</b>	<b>23</b>	<b>68</b>	<b>2</b>	<b>93</b>

Table 23.6: Causes of all transplant errors, including near misses n=93

## Commentary

In this fifth year of analysing SHOT transplant data, similar lessons have emerged, particularly the need to manage the complications associated with ABO-incompatible transplants. This has been echoed in a recent American update (Staley 2016) on ABO-incompatible (ABOi) haematopoietic progenitor cell (HPC) transplantation (HSCT) which concluded: 'ABOi HPC transplantation poses a unique challenge to the clinical transplantation unit, the HPC processing lab, and the transfusion medicine service. Thus, it is essential that these services communicate closely with each other to ensure patient safety. Additionally, it is critical for the transfusion service to have processes in place to ensure components of the correct ABO type are given to the patients, as well as for when and how to convert the recipient's ABO type to donor's ABO type.'

A recommendation was made in the 2012 Annual SHOT Report (Bolton-Maggs et al. 2013) that 'guidelines should be developed that cover the procedures, particularly communication protocols, necessary for managing transplant patients, especially where ABO/D mismatched transplants have been given.' It could be seen as a missed opportunity that the British Transplant Society Guidelines for Antibody Incompatible Transplant Third Edition (BTS 2016) does not include guidance on transfusion for ABO-incompatible solid organ recipients in the immediate post-transplant period, nor advice about communication protocols, which should include informing the transfusion laboratory of the recipient's specific requirements.

Specific national guidelines are still needed for both transplantation and transfusion professionals that cover the procedures necessary for managing transfusions to transplant patients.

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# Haemoglobin Disorders: Update

# 24

Author: Paula Bolton-Maggs

## Key SHOT messages

The management of sickle cell disease could be improved by careful communication:

- Clinicians should inform the transfusion laboratory of the diagnosis so that appropriate units of red cells can be selected
- Where patients with sickle cell disease present to hospitals who rarely see such patients, advice should be sought from the local haematologist, and the national sickle cell disease network as necessary (West Midlands Quality Review Service 2016)
- Biomedical scientists (BMS) should ensure the red cell phenotype is recorded prior to transfusion
- BMS should pay particular attention to seeking out any historical antigen sensitisations in sickle cell patients in their own laboratory records, in national databases such as Sp-ICE (Specialist Services Electronic Reporting using Sunquest ICE) in England, and by contacting other hospitals where the patient has been transfused in order that appropriate antigen-negative units can be selected for transfusion



Sickle cell disease n=160

HTR	61
SRNM	59
ATR	21
ADU	9
IBCT	6
TACO	2
TAD	1
TTI	1

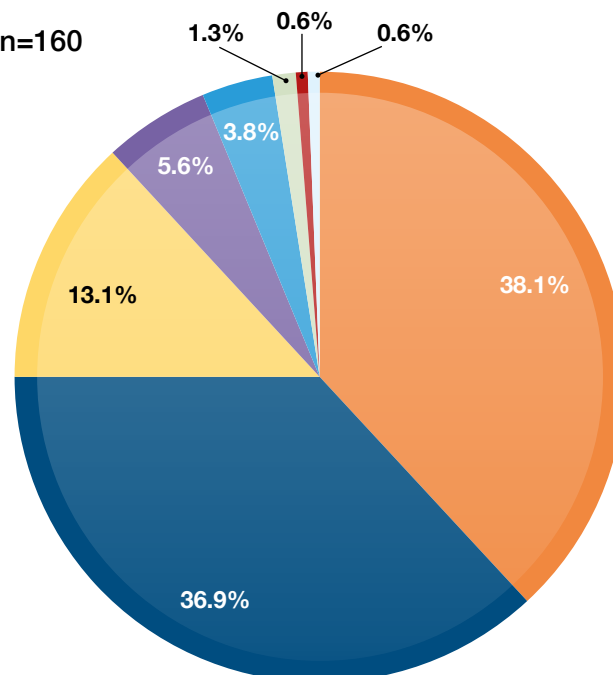
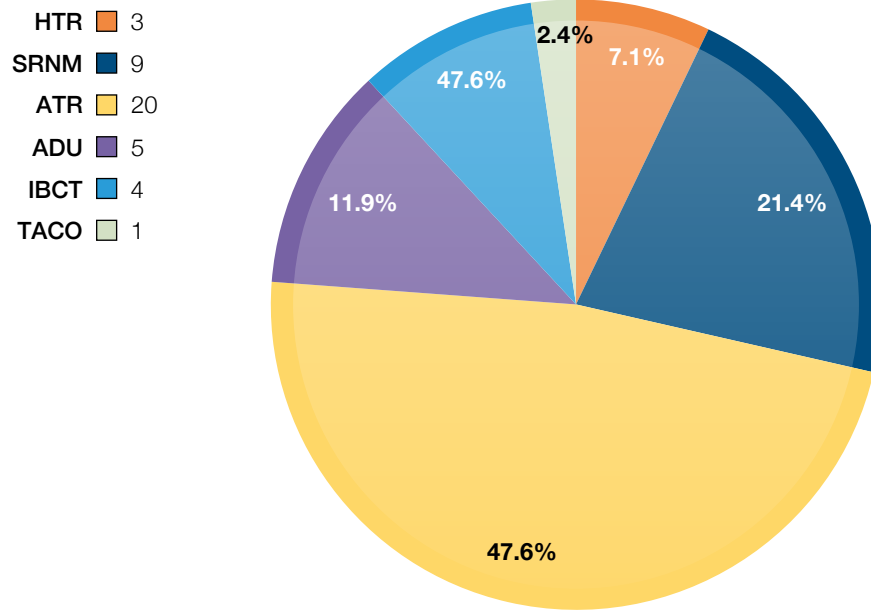


Figure 24.1: Cumulative data for adverse events in haemoglobin disorders 2010 to 2016

**Thalassaemia n=42**

*ATR=acute transfusion reaction; ADU=avoidable, delayed or under or overtransfusion; IBCT=incorrect blood component transfused; SRNM=specific requirements not met; TACO=transfusion-associated circulatory overload; TAD=transfusion-associated dyspnoea; HTR=haemolytic transfusion reaction; TTI=transfusion-transmitted infection*

As in previous years the majority of reported adverse incidents in patients with sickle cell disease (SCD) are haemolytic transfusion reactions and instances where specific requirements were not met, together 120/160 (75.0%) incidents, compared to 12/42 (28.6%) in patients with thalassaemia. Patient education may help reduce some of these incidents.

The median age of patients reported in 2016 was 32 years, range 2 to 73 (9/51 aged more than 40 years and one over 70).

### Specific requirements not met

The most striking feature from this year of reporting is the increase in cases where specific requirements were not met (n=24 compared with n=10 in 2015), particularly in patients with SCD n=21. These 24 errors occurred both in clinical (n=9) and laboratory (n=15) areas. (In one case it was not clear whether the haemoglobin disorder was SCD or thalassaemia).

Clinical errors occurred mainly because the clinical staff failed to inform the laboratory that this was a patient with haemoglobinopathy (5/9). In three cases hepatitis E virus (HEV)-screened components were not requested for patients with SCD who had undergone renal transplants. One pregnant patient (thalassaemia) did not receive cytomegalovirus (CMV)-screened red cells and 5 patients with SCD did not receive appropriate phenotypes.

Laboratory staff failed to select an appropriate phenotype in 11/14 cases of SCD (failure to notice diagnosis on request form; failure to heed historical results e.g. Case 10.10). One of these patients had been transfused fourteen units over a 2-year period with red cell units issued by four different members of staff. One 15-year old developed anti-e following transfusion when admitted in sickle crisis. Her Rh genotype had not been determined and she did not receive phenotype-selected units. The report noted staffing issues: 'Staffing levels plus new staff meant that covering night shifts was difficult'.

A thalassaemia patient who was supposed to receive R1R1 (CDe/CDe) red cells was supplied from the Blood Centre with rr (cde/cde) which was then not noticed in the transfusion laboratory prior to transfusion risking sensitisation to the c antigen.

**Case 24.1: An elderly patient develops alloantibodies**

*This 73-year-old man with SCD had not been seen since 2009 and was not transfusion dependent. He attended the emergency department (ED) in late 2015 requiring transfusion. The BMS followed historic crossmatch instructions on his record, which only stated to give Rh-compatible red cells with no additional comment indicating that genotype/Rh phenotype should be performed. All haemoglobinopathy patients since 2012 have had either a Rh/K phenotype or genotype tested as minimum prior to issuing red cells for these patients. This patient developed anti-E in response to transfusion of two units of red cells during this admission. One of these units was E-positive. His genotype showed that he should have been receiving C-negative, E-negative units. An in-house Rh/K phenotype performed on his pre-transfusion sample demonstrated a mixed field reaction with both C and E antigens implying that the patient had been transfused elsewhere within the past three months.*

**Avoidable transfusion****Case 24.2: Inappropriate transfusion due to poor knowledge**

*A pregnant woman with known SCD, who normally has a low haemoglobin (Hb), was taken to theatre. She was not actively bleeding. The doctor wanted two units of O D-negative blood for the patient, and did not want to wait for crossmatched units. Transfusion of the first unit started but was rapidly stopped by the haematology registrar after 20mL was transfused.*

This was an avoidable transfusion as the patient's Hb was normal for her and she was not actively bleeding. The use of O D-negative units for a known sickle cell patient is not optimal and could result in the development of antibodies. The patient did not require any blood following the surgery. 'Expert haematology advice must be sought before a decision is made to transfuse, unless in an emergency' (Davis et al. 2017b).

**Incorrect blood component transfused**

Three patients received wrong red cell transfusions.

A 17-year-old D-negative woman required exchange transfusion. She received six units of D-positive red cells following an error in ordering from the Blood Service which was not detected either in the laboratory or at the bedside. Fortunately testing several months later has not detected anti-D formation.

A 5-year-old child newly diagnosed with SCD was noted to be D-positive and transfused with D-positive cells, however this was a D-variant and she should have received D-negative cells.

A young man with SCD received a transfusion of a unit which was incompatible by crossmatch. This was related to mislabelling but fortunately he suffered no ill effects.

**Haemolytic transfusion reactions**

Eight were recorded, all in patients with SCD. Six were classified as hyperhaemolysis (details in Table 19.2 in Chapter 19, Haemolytic Transfusion Reactions (HTR)) of whom 2 died, one probably related to the transfusion (Chapter 19, Case 19.1) and in the other death was unrelated (Case 24.3 below). All 8 patients suffered major morbidity; two other patients had classical delayed HTR.

**Case 24.3: Death from complications of SCD in a woman who also had hyperhaemolysis**

*A pregnant woman with known sickle cell disease and alloantibodies was transfused with appropriate antigen-matched units. One week later she presented with a painful episode, fever and probable chest infection. She also had signs and symptoms of intravascular haemolysis with a low reticulocyte count but very high lactate dehydrogenase (LDH). The direct antiglobulin test (DAT) was negative throughout admission and no new alloantibodies were identified. A diagnosis of hyperhaemolysis was made and she was treated with intravenous (IV) antibiotics, IV methyl prednisolone and intravenous immunoglobulin (IVIg). The Hb continued to fall and she was transferred to the intensive therapy unit (ITU) and emergency caesarean section performed. Post section there was initial improvement and Hb stabilised at 55g/L but lactate rose. Therefore a decision was made to transfuse one unit of blood*

with further steroids and give erythropoietin, B12 and a multivitamin injection. The Hb increased to 65g/L and then remained stable. She continued to deteriorate and had cardiac arrest - three further units were transfused but unfortunately the patient died. The coroner concluded she died from complications of SCD and that the transfusion reaction did not play a role in her death as there was evidence that the haemolysis was already under control.

#### **Case 24.4: Failure to consult available historical records in SCD prior to exchange transfusion**

A 43-year-old woman was under shared care between two different hospitals. She required specialist surgery at another centre which was not her usual base. She had a history of anti-S, anti-E, anti-Fy<sup>a</sup>, anti-Fy<sup>b</sup> and anti-Fy3. She had been transfused with appropriate phenotype, and the antibodies were not detectable from 2013. She underwent preoperative exchange transfusion at the specialist centre with eight units. Her base hospital transfusion laboratory records and Sp-ICE data were not accessed for her antibody history. Four days later she presented to her own hospital unwell with haemoglobinuria and was initially thought to be in sickle crisis. However this was a delayed haemolytic transfusion reaction associated with anti-Fy<sup>a</sup> and anti-Fy3 (identified in the eluate). She made a full recovery.

This was an avoidable complication had the historical data been sought as is recommended in guidelines (Davis et al. 2017a). (Case 19.9 in Chapter 19, Haemolytic Transfusion Reactions (HTR)).

### **Literature update**

New transfusion guidelines have been published for SCD and should be consulted and adhered to in order to avoid complications (Davis et al. 2017a; Davis et al. 2017b). In particular 'a transfusion history should be obtained in all sickle cell disease patients requiring transfusion, whether elective or emergency. Close communication is essential between clinical and laboratory teams so that appropriate blood is given' (Davis et al. 2017a). There is also a series of Cochrane reviews of transfusion in SCD (Estcourt et al. 2016a; Estcourt et al. 2016b; Estcourt et al. 2016c), and a series of review articles in Lancet (Editorial 2016; Gladwin 2016; Lettre and Bauer 2016).

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# 25

# Medicines and Healthcare Products Regulatory Agency (MHRA) Report on Blood Safety and Quality Regulation in 2016

Author: Chris Robbie

## Introduction

The United Kingdom (UK) Blood Safety and Quality Regulations 2005 (as amended) (BSQR) require that serious adverse events (SAE) and serious adverse reactions (SAR) related to blood and blood components are reported by Blood Establishments (BE), hospital blood banks and facilities to the MHRA, the UK Competent Authority (CA) for blood safety. This requirement is enabled by the Serious Adverse Blood Reactions and Events (SABRE) reporting system. All data within this report are correct as of 18 January 2017.

## Key messages

- The MHRA have added a subcategory to human error 'Inadequate QMS – staffing and workload' to specifically highlight those SAE directly related to problems where low staffing levels or high workload were the main cause of an error occurring. Skill-mix is also considered to be an important factor in these cases. We have deliberately excluded reports from this category where staffing and workload were at acceptable levels and the laboratory was simply described as 'busy' which might overlook alternative root causes
- Human error accounts for 98.1% of all SAE
- Reporters are encouraged to investigate all possible causes, especially if at first it would seem the root cause is a slip or lapse by an individual. Further investigation may identify improvements to the overall quality system that could have long lasting preventive outcomes
- Changes to the way the MHRA and Serious Hazards of Transfusion (SHOT) receive reports via SABRE have increased the total number of reports received and assessed by the MHRA. Therefore it is impossible to make direct comparisons of the numbers of reports received to previous years, other than in Table 25.1. Where relevant we have compared the proportion of reports received to 2015
- Reporters are always encouraged to report SAE and SAR, not only to meet their regulatory requirements, but also to provide as much data as possible to the MHRA and SHOT haemovigilance schemes so lessons on best practice can be learnt throughout the blood transfusion community

## Summary

2016 SABRE data has been analysed by the MHRA haemovigilance team in order to identify common errors and to make recommendations for improvements to corrective and preventive action (CAPA) plans. Changes made to the reporting process in October 2015 have resulted in more SAE and SAR being reported in SABRE. With a single year of data collected and analysed under the new process, it would be unwise to draw any conclusions from the increase in number of reports received overall.

Human error remains the biggest root cause for all SAE reports. Additional subcategories have been introduced to help identify the reasons for errors occurring and identifying the appropriate human factors to address to prevent future occurrence and improve quality management systems (QMS).

Incorrect blood components issued (IBC) remains the single most common error made and laboratories are encouraged to take steps to thoroughly investigate and improve QMS to prevent this on-going problem. Examples of the top five reported SAE and their human factor subcategories have been used as examples where real incidents have been addressed by real laboratories.

Please be aware if comparing SABRE and SHOT numbers there are significant recognised differences. These differences include, but are not limited to the following:

- MHRA data are based on reports made strictly under the BSQR
- A report is only included in the annual numbers if it has been confirmed to MHRA within that reporting year
- The MHRA does not include errors in clinical practice and administration of blood e.g. wrong blood in tube (WBIT), inappropriate transfusions and errors in anti-D immunoglobulin (Ig) issue and administration
- The MHRA does not include reactions to blood products such as Octoplas® (solvent-detergent fresh frozen plasma)

Further discussion on the differences between MHRA and SHOT reporting can be found in the joint Laboratory chapter (Chapter 7).

If you require further guidance on this issue please contact the SABRE helpdesk on 020 3080 7336.

### SABRE report data

Table 25.1 below displays the total number of SABRE confirmation reports that were submitted and that satisfy the European Union (EU) reporting criteria for SAR and SAE since 2007.

	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
SAE	655	790	968	889	810	931	705	764	765	1027
SAR	264	436	500	549	444	343	345	346	262	465
<b>Total</b>	<b>919</b>	<b>1226</b>	<b>1468</b>	<b>1438</b>	<b>1254</b>	<b>1274</b>	<b>1050</b>	<b>1110</b>	<b>1027</b>	<b>1492</b>

Table 25.1: Submitted SABRE confirmation reports 2007–2016

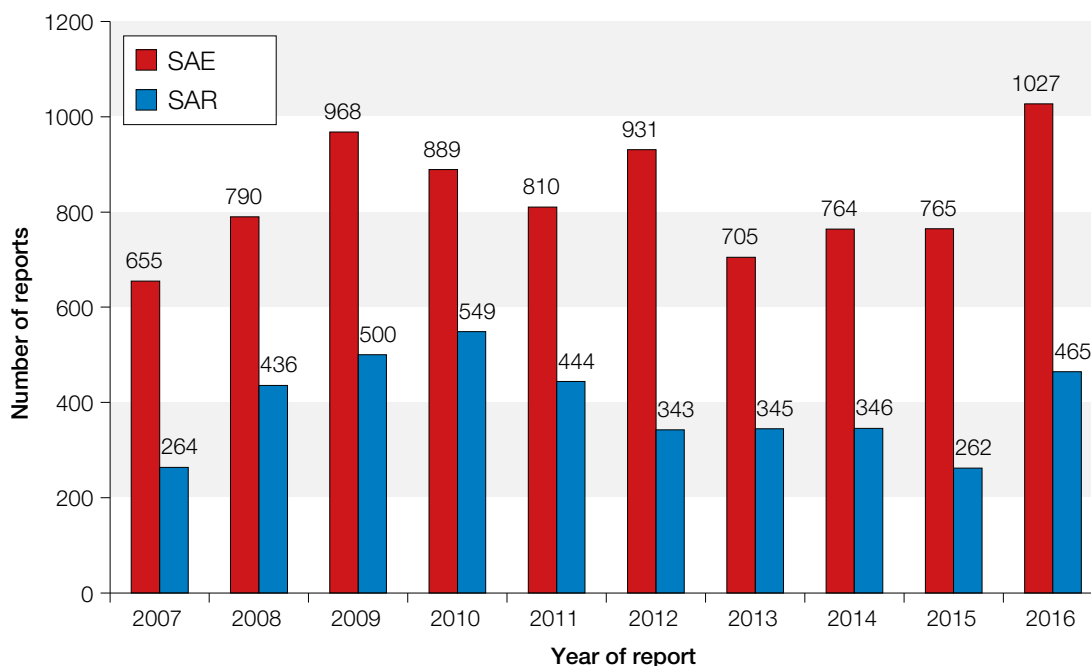


Figure 25.1: Submitted SABRE confirmation reports 2007-2016

From October 2015, all reports to SHOT and the MHRA can be viewed by both organisations. The MHRA can select any SAE that met the BSQR reporting requirements. It was expected that the number of SAE reports would increase. The increase in the numbers of SAE reports made in 2016 is likely to be due to reporters making reports that were previously thought to be 'SHOT only' reportable, either because they were not thought to be covered by the BSQR reporting requirements, or they were deemed to be low-frequency near misses and not serious enough to report to the MHRA.

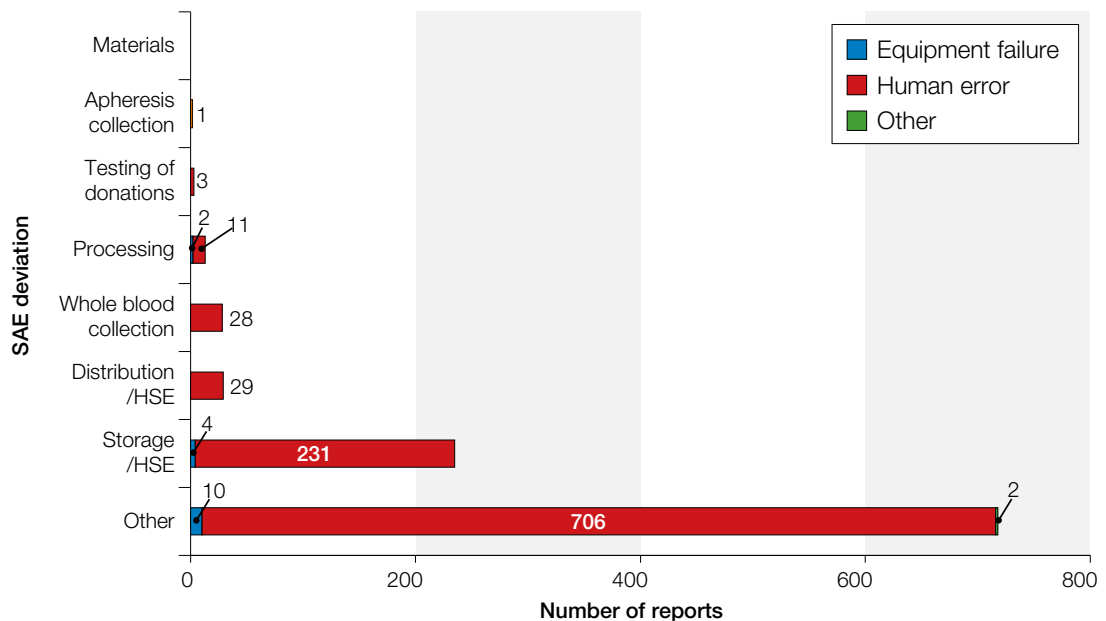
In 2015 approximately 2.7 million components were issued in the UK, with 765 SAE confirmation reports submitted to Europe. That represents 283 SAE per million components issued or 0.03%. In 2016 this has increased to 1027 SAE reports for approximately 2.5 million components issued, representing 411 SAE per million components issued or 0.04%. Analysis of next year's data will provide more scope for assessing if the increase in SAE per million components issued is related to the change in the reporting process or representative of the challenges currently being faced in haemovigilance.

## Serious adverse events

### Definition:

**Any untoward occurrence associated with the collection, testing, processing, storage and distribution, of blood or blood components that might lead to death or life-threatening, disabling or incapacitating conditions for patients or which results in, or prolongs, hospitalisation or morbidity.**

Figure 25.2:  
2016 SAE  
confirmation  
reports by  
deviation and  
specification



As previously mentioned, we are unable to compare the numbers of reports with previous years, but there is no real change in the proportions of each category of reported incident from previous years. 'Other' and 'storage' categories contain the most reports, and human error remains the main root cause.

### Storage data n=235

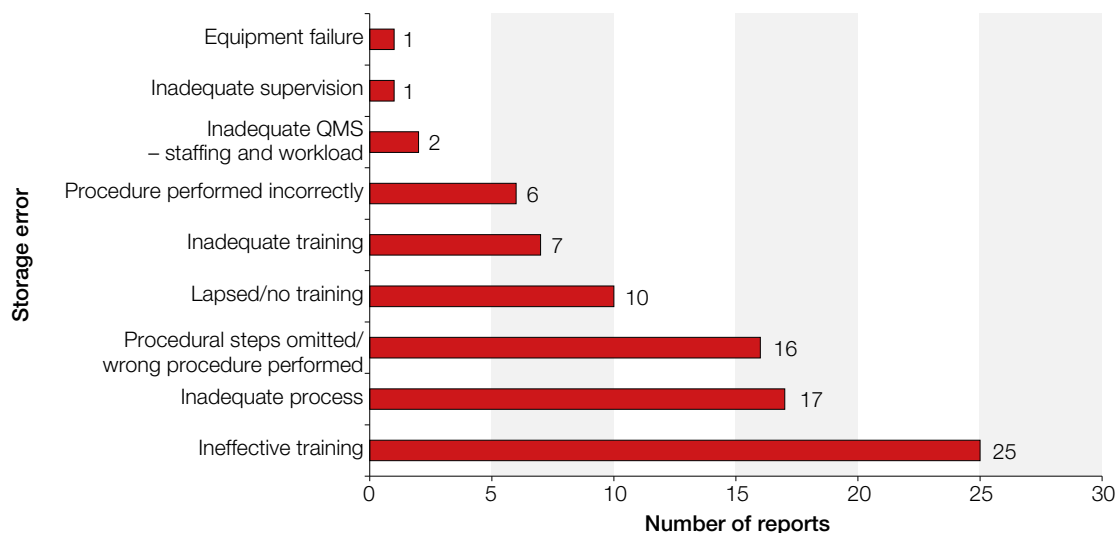
Storage remains the second largest individual error category and comprises all BSQR-reportable storage SAE in both laboratory and clinical areas. For a breakdown of handling and storage errors (HSE) in the laboratory and the clinical area, please see the relevant sections of the laboratory chapter (Chapter 7) and the HSE chapter (Chapter 9). The MHRA has broken this category down further to try and identify specific storage error subtypes, Table 25.2.

Storage subclassification	2016	2015 position
Incorrect storage of component	85	2
Component expiry	66	1
Sample expiry	32	4
Return to stock error	15	5
Storage temperature deviation	12	6=
30 minute rule	8	8
Failure to action alarm	7	3
Security	5	6=
Miscellaneous	5	9
<b>Total</b>	<b>235</b>	

**Table 25.2:**  
SAE storage error subclassification 2016

The increase in numbers of storage errors compared to SAE overall is not as great (15.8% compared with 25.5%). This may indicate that processes relating to storage have been improved and staffs' understanding of the procedures has increased. The category 'failure to action alarm' is now the 7<sup>th</sup> most common storage SAE from the 3<sup>rd</sup> most common. This would suggest that as a result of improved process design, improved standard operating procedures (SOP), training and understanding, laboratory staff are acting on alarms of storage locations. This means that blood components are less likely to be wasted or removed from the supply chain without risk of harm to patients.

The most common error is incorrect storage of component. Typically this involves the storage of a component at the wrong temperature or in an unmonitored storage device. Although these SAE can occur in laboratories and during transportation or distribution, they are most likely to occur in clinical locations.



**Figure 25.3:**  
Incorrect storage of component by specification 2016

Figure 25.3 shows that the most common cause of components being stored incorrectly was ineffective training of staff who had either not understood the process or had forgotten it due to infrequent update training for a rarely performed task. Inadequate processes were the second most common cause where there was no defined process for what to do if blood was not administered immediately or where out-of-service storage equipment was not adequately prevented from being used. Finally, failure to follow established storage procedures by adequately trained staff resulted in the 3<sup>rd</sup> most common error (procedural steps omitted/wrong procedure followed).

Expired components (component expiry/sample expiry) continue to be reported in large numbers. These are reported when either a component time-expires and remains in a storage location after it should have been removed, or the sample has expired meaning an in-date component is unsuitable for the patient it had been issued to. Around a third of all these SAE are a result of inadequate processes which do not robustly control the storage of expired components.

Laboratories are encouraged to continue to improve storage and monitoring equipment. However, clinical areas and laboratories should also be encouraged to ensure that processes and procedures relating to the storage of components, temperature monitoring and removing unsuitable units from storage locations are robust and clear and that staff are properly trained in them and are able to activate those procedures effectively, even when lone-working or during emergency situations.

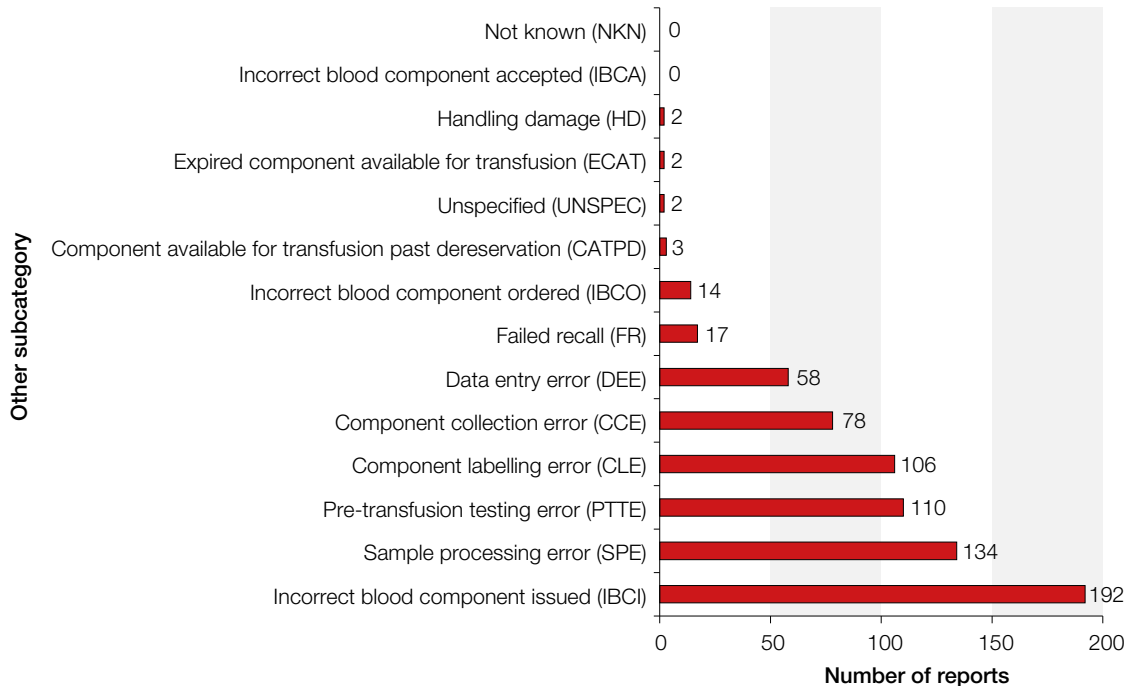
**Other n=718**

Since 'other' is the largest category of SAE reports, the MHRA haemovigilance team has created subcategories to further analyse this type of error, Table 25.3.

**Table 25.3:**  
SABRE reports,  
subcategory 'other'  
2016

Other subcategory	2016	2015 position
Incorrect blood component issued (IBCI)	192	1
Sample processing error (SPE)	134	4
Pre-transfusion testing error (PTTE)	110	3
Component labelling error (CLE)	106	2
Component collection error (CCE)	78	6
Data entry error (DEE)	58	5
Failed recall (FR)	17	7
Incorrect blood component ordered (IBCO)	14	8
Component available for transfusion past de-reservation (CATPD)	3	9=
Unspecified (UNSPEC)	2	9=
Expired component available for transfusion (ECAT)	2	11
Handling damage (HD)	2	12=
Incorrect blood component accepted (IBCA)	0	14
Not known (NKN)	0	12=
<b>Total</b>	<b>718</b>	

**Figure 25.4**  
SABRE Reports,  
subcategory  
'other', 2016



Incorrect blood component issued (IBCI) errors remain the largest 'other' subcategory of all 'other' SAE reports as it has done for a number of years. These are mainly laboratory errors where special requirements are not met. The introduction of new guidelines surrounding the use of hepatitis E (HEV)-screened components has had some impact on the incidents reported, although not in any great numbers. The reasons for HEV-screened IBCI being reported are similar to the other IBCI but also demonstrate that some incidents were the result of not having a robust process for flagging these requirements, or that the new guidance was not adequately communicated to laboratory staff with robust SOP and training. Furthermore, it is apparent that many of these reports have occurred following haemopoietic stem cell transplant (HSCT) or solid organ transplant where the appropriate ABO and D group for transfusion has changed from the patient's original group.

Sample processing errors (SPE) have become the second most common SAE overall from fourth the previous year. These are typically errors where sample/form/laboratory information management system (LIMS) discrepancies which should be spotted in the laboratory are not.

Component labelling errors (CLE) have moved from the second to fourth most common incident. Typically these are where labels are transposed at the labelling stage. Without further investigation it would not be possible to say if this represents an improvement in labelling processes or a result of fewer donations being bled and therefore fewer components being used in the UK overall. What we do not have are data on the number of times those components are labelled i.e. the number of times an individual component is labelled, returned to stock to be re-used and relabelled later. Further discussion on these categories and the reasons for them occurring is provided below.

## Human error category and human factors

Human factors are all the things which can influence how a human behaves. This will either lead to an action being successful, or it will lead to human error. These factors can be organisational, job-related or related to the individual concerned.

In order to understand human error, the SABRE team has developed subcategories which can be applied to the report narratives to help understand the human factors involved. In addition to the existing categories, two new categories have been added this year. With resources being stretched and reported problems with recruitment and retention of staff 'inadequate process – staffing and workload' has been added. All laboratories should have developed a capacity plan and set minimum staffing levels and decided on acceptable workloads which can be completed accurately and safely. Errors which occur when the laboratory cannot meet these levels should not be made the responsibility of the staff that made the errors, but the CAPA should be reviewed with the aim of improving the QMS. Inadequate supervision applies to SAE where ineffective leadership has led to staff making errors, or where errors by trainees have not been spotted.

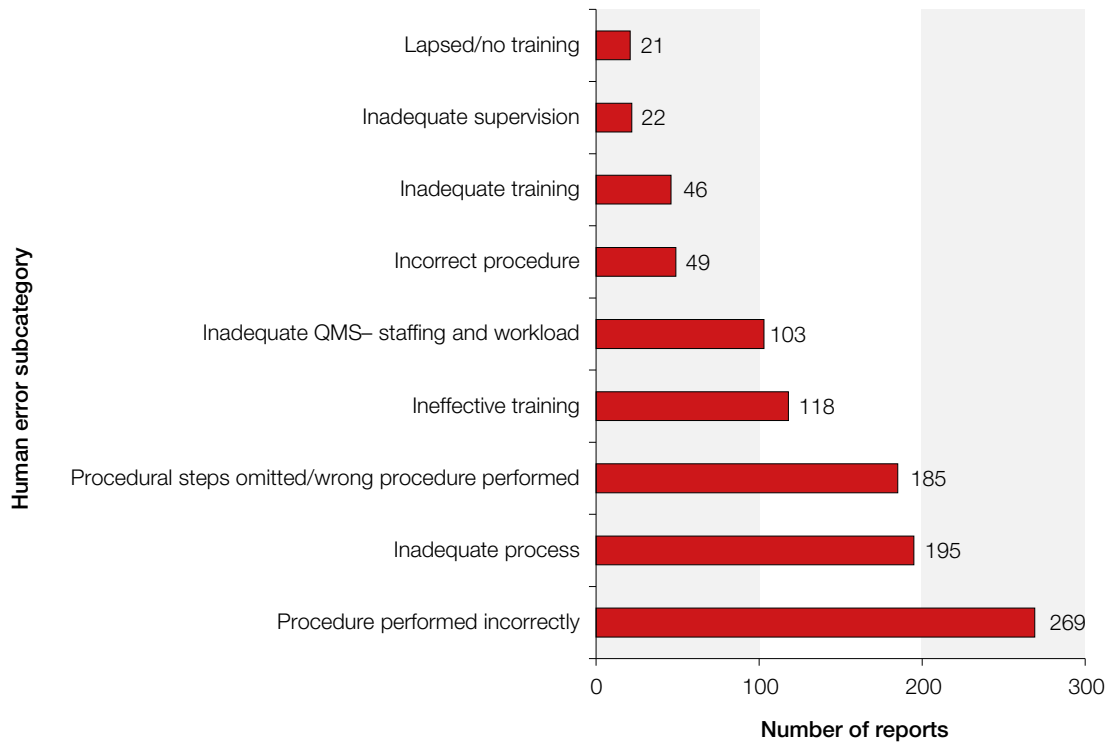
The categories are:

- Procedure performed incorrectly – failure to carry out a step(s) correctly
- Procedural steps omitted – missing a key step or not following the procedure
- Inadequate process – inadequate design of a process
- Incorrect procedure – process not properly described in the SOP
- Ineffective training – training not understood by operator
- Inadequate training – training process not fit for purpose
- Lapsed or no training – carrying out a procedure without any formal training
- Inadequate QMS – staffing and workload – where staffing levels below the minimum level, or unacceptably high workload has resulted in staff making errors. It is also important to consider an appropriate skill-mix when deciding on minimum staffing levels



Figure 25.5 shows the breakdown of reports received and categorised into the human error subcategories.

**Figure 25.5:**  
SABRE reports,  
human error  
subcategory, 2016  
n=1008



N.B.: These numbers should be used as guidance only. The quality of these data are limited by a number of factors.

- The root causes of incidents are usually the result of many contributory factors. The subcategory chosen reflects the most likely reason for the main SAE category
- The subcategory chosen is based on the information in the report. A limited investigation or a report which does not provide the MHRA with enough information may not be subcategorised appropriately

The addition of two new subcategories makes comparison with last year's data difficult. The largest category is 'procedure performed incorrectly' accounting for more than a quarter (27%) of all human error reports. These errors are ones where the operator is trained and knows what to do. They would normally follow the correct procedure and perform these tasks successfully, but for some reason a slip or lapse of concentration has led to a mistake. In these cases other root causes have been ruled out, such as an inadequately designed process, an SOP which does not clarify the procedural steps, training that does not cover the error, low staffing, high workload, etc. Common types of error where this category might be applied might be repetitive or detailed work where high levels of concentration or awareness are required such as sample process errors where discrepancies might be easy to overlook, or component labelling errors where thorough verification of the labels is not performed before attaching a label to the wrong component.

Although it is each member of staff's individual responsibility to work safely and accurately, it is recognised that sometimes slips or lapses are going to occur at times. This does not mean there are no steps that can be taken by both laboratory managers and individuals to reduce the chances of these types of incident occurring.

- Review process design and use of equipment to ensure all processes are robust
- Review SOP to ensure that the process is adequately described in logical order, ensuring staff know exactly what to do
- Ensure SOP also contain information about what to do if the task goes wrong
- Ensure training covers all critical points and competency assessment challenges them

- Minimise all distractions and ensure the design of the laboratory is logical
- Allow staff to work safely at their own pace without rushing
- Ensure there are contingency plans for when staffing levels are below minimum or there are spikes in workload
- Ensure these contingency plans are activated when required
- Staff need to follow all steps precisely and never cut corners or rush for any reason
- Never improvise. Consult SOP for the correct procedure rather than asking colleagues or working contrary to the defined process

The second most common factor affecting staff making errors is 'inadequate processes' (19%). These are errors where the process does not always ensure the correct outcome, even when followed correctly. Often a process might not include relevant steps that ensure a consistent and safe outcome, or has not even been designed and established and relies on staff performing tasks which have not been standardised.

For example, a member of the SABRE team was discussing a component labelling error with a reporter. During their investigation they realised that there was no standard way to label a component and all staff were doing it slightly differently. One member of staff had the bags upside down or face-down when labelling meaning that the accurate verification of the donation numbers was impossible. This example demonstrates that without a process being adequately designed and written in an SOP, non-standard practice can increase the risk of errors occurring.

The category 'Inadequate QMS – staffing and workload' was introduced to gain insight to the extent of staffing and workload problems with regard to the occurrence of SAE. Evidence collected in previous year's SABRE reports, MHRA inspection reports, SHOT and the UK Transfusion Laboratory Collaborative and other sources suggest that resource issues are having a serious and detrimental effect on a laboratory's ability to function safely. Previously we had not had any data to support this observation and this is an attempt to provide some.

To qualify in this category, the SABRE team tried to establish those SAE where staffing levels were below minimum levels as defined by the capacity plan or workload was high, either in the long term or short term. We assigned different subcategories where other human factors were more likely to have an impact. For example, if the SAE was assessed by the reporter to have occurred when it was 'busy', this would not normally be assigned this category unless it was busy due to a laboratory operating below its minimum staffing level or the workload was greater than would normally be expected for the available staff to manage.

This first assessment of these types of error has demonstrated that, 10% of all SAE fall into this subcategory. It is too soon to analyse this in detail. Successive years of collecting and assessing SAE reports would give a better understanding of the extent of these human factors in the occurrence of SAE and will be interesting to see how this percentage changes with time. What we can conclude is that these pressures are real and do affect the quality and safety of blood and the quality of service provided.

When resolving issues relating to staffing and workload, laboratories have been successful in using QMS data as evidence to increase resource. However, not every laboratory will be successful. It may that laboratory managers and their staff will suggest novel and innovative solutions. Some of these solutions evidence in SABRE reports include:

- Training laboratory assistant staff to perform some tasks to provide relief to biomedical scientists
- Changing shift patterns and reviewing break times to ensure greater numbers of staff are available at busier times
- Reviewing rules relating to numbers of staff on leave at the same time
- Reviewing processes to ensure they are streamlined
- Reviewing workloads to spread the work out more effectively when staff are available

## Assessing reports

The assessment of each reported SAE and SAR relies on the quality of the information reported.

Each report needs to:

- Be detailed enough to understand the problem
- Be thoroughly investigated to establish why the incident occurred and why staff acted in the way that they did
- Identify CAPA which addresses each of the root causes and human factors identified
- Include all relevant information in the SABRE report

A good quality report will be closed out and provide us with plenty of quality information to assess. It will reduce the number of follow up calls and emails and any additional investigation required on the part of the reporter.

By reporting and investigating incidents thoroughly, it is hoped then that over time reporters will be able to gain enough evidence where necessary to help ensure they have sufficient resources to address long term problems with appropriate preventive action.

## Top five SAE

Table 25.4:  
Top five SAE  
with human error  
subcategory

SAE deviation subcategory	Specification subcategory
Component labelling error (CLE)	Procedure performed incorrectly
Sample processing error (SPE)	Procedure performed incorrectly
Incorrect blood component issued (IBCI)	Procedure performed incorrectly
Incorrect blood component issued (IBCI)	Inadequate process
Incorrect blood component issued (IBCI)	Procedural steps omitted/ wrong procedure performed

Table 25.4 shows the top five SAE deviation subcategories and the subcategory of human error. Real examples are shown below to illustrate what might be considered in way of CAPA to address the root causes. They are not meant to represent actual investigation processes and CAPA for all similarly categorised incidents, but are representative of many of the reports received, and are clearly designed to focus on improvements to systems, practice and transfusion laboratories. The examples show the categorisation for MHRA SAE and the SHOT equivalent is in brackets.

### 1) CLE (SHOT category near miss (NM)): Procedure performed incorrectly

On checking a unit of red cells at the bedside with an electronic checking system, the unit was found to have an incorrect blood label attached. Labels had been transposed on units for the same patient by laboratory staff. The unit was correctly labelled before transfusion commenced.

- The biomedical scientist (BMS) labelling the units became distracted and did not check the labels once attached to the units
- The BMS was spoken to and told to follow procedures at all times. If they are becoming distracted then they must stop labelling units and place them back into the holding refrigerator until the distraction has passed. They must then label the units rechecking any labelling that has already been done
- The BMS have been told to ask anyone trying to speak to them to wait until they have completed the labelling and checking

### 2) SPE (SHOT category RBRP): Procedure performed incorrectly

On two occasions a crossmatch was completed using request forms that did not contain a date of birth. On both occasions the units were issued. The date of birth is one of the three local essential identifiers. The units were used. The identifiers were checked again on the sample and confirmed as correct.

- The correct procedure was discussed with the staff member involved and covered again by the blood bank manager
- Following further discussion with the BMS she states: 'Case 1 occurred towards the end of a very busy shift during which I had received no comfort breaks and was feeling tired. Case 2 occurred at the end of my fourth night shift in a row and again I was tired'
- This was felt to be an issue relating to ongoing staffing problems as well as this individual taking on an additional course and struggling to cope. Vacancies were advertised but not filled. According to the laboratory manager, workload was not deemed to be excessive and it was the individual's choice not to take comfort breaks rather than due to workload

### **3) IBCI (SHOT category near miss): Procedure performed incorrectly**

The staff nurse had noticed that units for a patient were not irradiated or HEV-screened as indicated on the prescription chart. The units were allocated and electronically issued for this patient ready for transfusion in the haematology clinic. The units were returned to blood bank and the units with correct special requirements were issued.

- Electronically issued units for two patients were authorised and labelled within 75 seconds of each other
- This was caused by rushing to complete the labelling of electronically issued blood, when there was no urgency to either request
- The CAPA included coaching the BMS to take his time and not to rush the issue and labelling of blood components. This will be an ongoing exercise

### **4) IBCI (SHOT category specific requirements not met (SRNM)): Inadequate process**

One unit of HEV-status unspecified red cells was issued and transfused to a patient who should receive HEV-screened components. A special requirement form stating this requirement had been received in the transfusion laboratory the day before. The LIMS had been updated accordingly with a note on the special requirement pad added. Two red cell units were issued which were not HEV labelled. One unit was transfused.

- The current version of the LIMS does not allow for a screen flag to show for HEV requirement (this is in place for other special requirements)
- The relevant information was in a special requirement pad at time of component issue but this was not heeded by the BMS
- The next version of the LIMS is due to be installed, awaiting information technology (IT) department support to progress. This is proceeding. This version has the facility of an alert flag for HEV-screened components
- As a temporary preventive measure, an HEV-screened alert has been set up that can be added to a patient's sample booking-in screen

### **5) IBCI (SHOT category NM SRNM): Procedural steps omitted/wrong procedure performed**

Two units of non-irradiated blood were issued to a patient by the BMS despite the request form indicating that the patient required irradiated blood components.

- The requirement for irradiated components was documented in the patient's notes, but not communicated to the laboratory via approved means (email to a designated email account). The BMS issuing blood did not notice that the irradiated requirement was ticked on the request form and so did not issue irradiated units as the computer did not say to do so. The omission was noted by the staff on the ward when the unit was checked prior to commencing transfusion
- The haematology team members were re-educated about the importance of emailing the email account with any special requirements

- The BMS (and all other staff in transfusion) were reminded of the importance of checking information on the form, and questioning/following up any requests made to ensure special requirements are met

### Effective CAPA

These top five categories of SAE demonstrate a number of different approaches and actions that can be applied when identifying suitable, targeted CAPA. Effective CAPA that addresses weaknesses and flaws in the QMS can prevent errors occurring in other areas of the laboratory, and not just with the actual task that failed. The focus should not necessarily be on re-training, re-competency assessment or adding extra steps in a process, unless it is absolutely necessary to do so. There are certain key principles to consider when improving your QMS and when investigating incidents. This list is not exhaustive and is meant for guidance only.

- QMS
  - Is staffing appropriate?
  - Is workload manageable?
  - Is the environment (premises and plant) fit for purpose?
  - Are tasks and processes designed to be robust?
- Procedures
  - Are there SOP to describe the tasks and processes?
  - Are they document-controlled?
  - Do they contain unambiguous instructions as opposed to a set of requirements or expectations that need to be achieved?
- Training
  - Is there a training plan?
  - Is the training material adequate and fit for purpose?
  - Has training been delivered?
  - Has training been understood and understanding assessed?
  - Does good manufacturing practice (GMP) education cover the relevant aspects of GMP?
- Personnel
  - Is there effective supervision and leadership?
  - Do supervisors watch out for and challenge bad practice?
  - Are staff aware of their responsibilities?
  - Do staff carry out their duties in accordance to GMP?
  - Are staff actively engaged in improving the QMS?

### Blood Establishment reporting n=66

The majority of SAE reports originate from hospital transfusion laboratories. Thus although reports from BEs are included in the main analysis, the specific nature of the SAE reports from BEs are lost in the greater numbers of hospital transfusion laboratory SAE reported. Figure 25.6 displays the reported BE SAE in 2016.

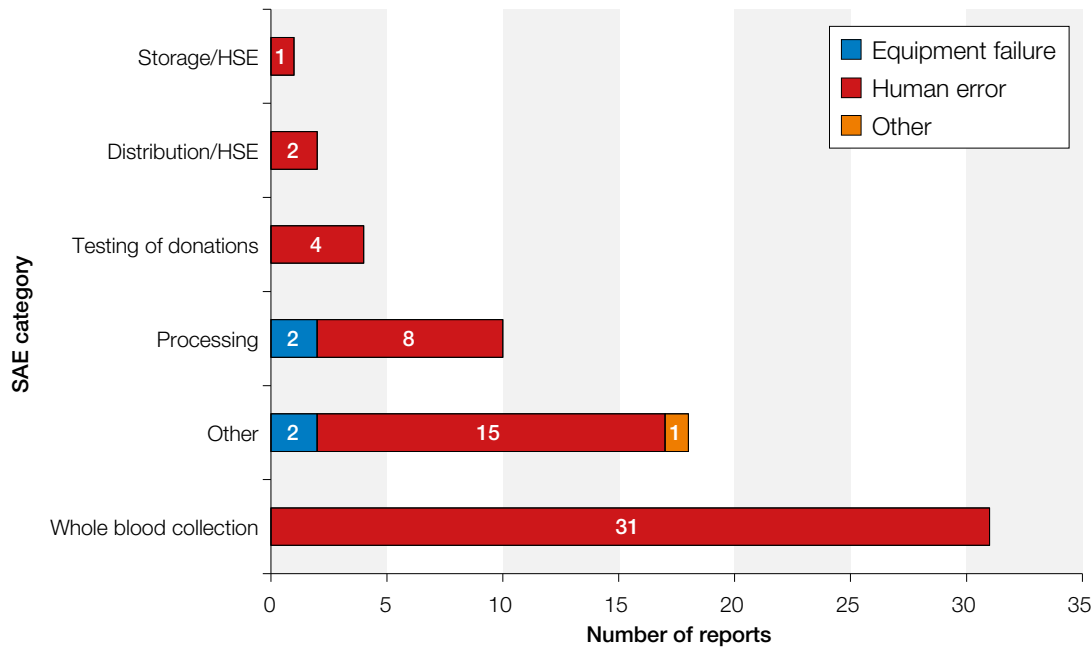


Figure 25.6: BE SAE category by specification n=66

Almost half of all BE SAE result at the donor collection stage. Typically these are slips and lapses when screening the donor where travel or life-style information is not properly acted upon.

The second largest category is 'other' and as for hospital SAE, these are similarly subcategorised. The most common SAE in this category is 'failed recall'. These are typically where the recall of components resulting from alerts from their bacterial monitoring systems, or action on late donor information is not acted upon in a timely manner. Investigation of these errors has prompted BEs to improve their recall processes and improve awareness of the correct procedures.

## Serious adverse reactions (SAR)

### Definition:

An unintended response in a donor or in a patient that is associated with the collection, or transfusion of blood or blood components that is fatal, life-threatening, disabling or incapacitating, or which results in or prolongs hospitalisation or morbidity...Blood Establishments and the person responsible for the management of a hospital blood bank shall notify the Secretary of State (Competent Authority) of any serious adverse reactions observed during or after transfusion which may be attributable to the quality or safety of blood or blood components:

- (i) Collected, tested, processed, stored or distributed by the blood establishment, or
- (ii) Issued for transfusion by the hospital blood bank

### Blood products

Adverse reactions involving blood products (i.e. licensed medicines such as anti-D Ig, Octaplas® (solvent-detergent fresh frozen plasma), or coagulation factor concentrates should be reported to the MHRA via the Yellow Card scheme (<http://yellowcard.mhra.gov.uk>).

### Summary of SAR report data

Changes to the way SAR are reported in SABRE have been in effect since October 2015. As well as being the first step towards a single, integrated reporting process, reducing duplication of effort for a reporter, these changes were also implemented to address a perception that some reporters were not meeting their regulatory requirements in reporting all SAR to the MHRA, but were reporting some reactions as 'SHOT-only' incidents. This change in process has also enabled SHOT experts to assess reaction reports to ensure that SAR reports are categorised consistently with SHOT data. SHOT will then upload the confirmation report on behalf of the original reporter.

It is still too early to tell how this change will affect the collection of SAR reports in SABRE. Analysis of this year's data has shown an increase in the number of SAR reports included in the annual summary. It is likely that MHRA will receive more SAR reports than before as there is no 'SHOT-only' button. However, the number of reports depends on SHOT being able to assess and complete the confirmation report before the end of December. This has been the first full year of the new process and it is still likely that an equilibrium will be found.

To avoid any confusion the MHRA will only supply, in this Annual SHOT Report, total SAR figures reported to Europe, see Table 25.5

Table 25.5:  
SAR reports, by  
imputability, confirmed  
on SABRE in 2016  
n=465

	Imputability score				
	NA	0	1	2	3
<b>SAR reports by imputability score</b>	7	81	162	155	60

In previous years SAR data between the two organisations have differed and caused confusion for reporters, the EU and at parliamentary level. It is hoped that the new SAR reporting arrangements will avoid this confusion and produce more accurate SAR data for the UK and Europe. For SAR type please see the relevant clinical reactions chapters in this report for more detail.

### MHRA inspection activity on hospital blood banks 2015 – 2016

A total of 303 blood compliance reports (BCR) were submitted for review for the reporting period 01 April 2015 to 31 March 2016. Following assessment, 17 hospital blood banks (HBB) including 1 control site were selected for inspection. One additional HBB was inspected following notification from the site that inaccurate information had been provided in the BCR. The risk scores for the inspected sites ranged from 3 to 47.75.



## Inspection outcomes

A total of 19 inspections were performed and the numbers of deficiencies are as follows:

Critical	Major	Other
1	43	67

**Table 25.6:**  
Deficiencies found  
in 19 inspections

1 HBB resulted in a critical deficiency finding and was referred to the Inspection Action Group (IAG).

The critical deficiency was as a result of:

- Senior management had not ensured that there were sufficient resources to support the quality system
- Management of deviations (incidents):
  - Incidents had not been raised, investigated and closed in a timely manner
  - Non-conformances were not raised for all significant deviations
  - Control of changes, and their associated validation:
    - A number of significant changes had been implemented without change control records or formal validation being completed
  - Poor document control:
    - The documentation system had not been maintained
    - Standard operating procedures had not been approved prior to use by the laboratory staff
    - Procedures lacked clarity and were ambiguous
    - Poor documentation practices
  - Staff training was deficient:
    - There was no training policy
    - GMP refresher training was not up to date
    - Competency records of staff had not been updated since their initial appointment, in some cases dating back to 2009
    - There was no evidence that staff were aware of, trained, and competent in the use of key quality system procedures that were in place
  - Self-inspection was deficient: no audits had been performed during 2016 or 2017 to date
  - Management oversight of the quality system was deficient:

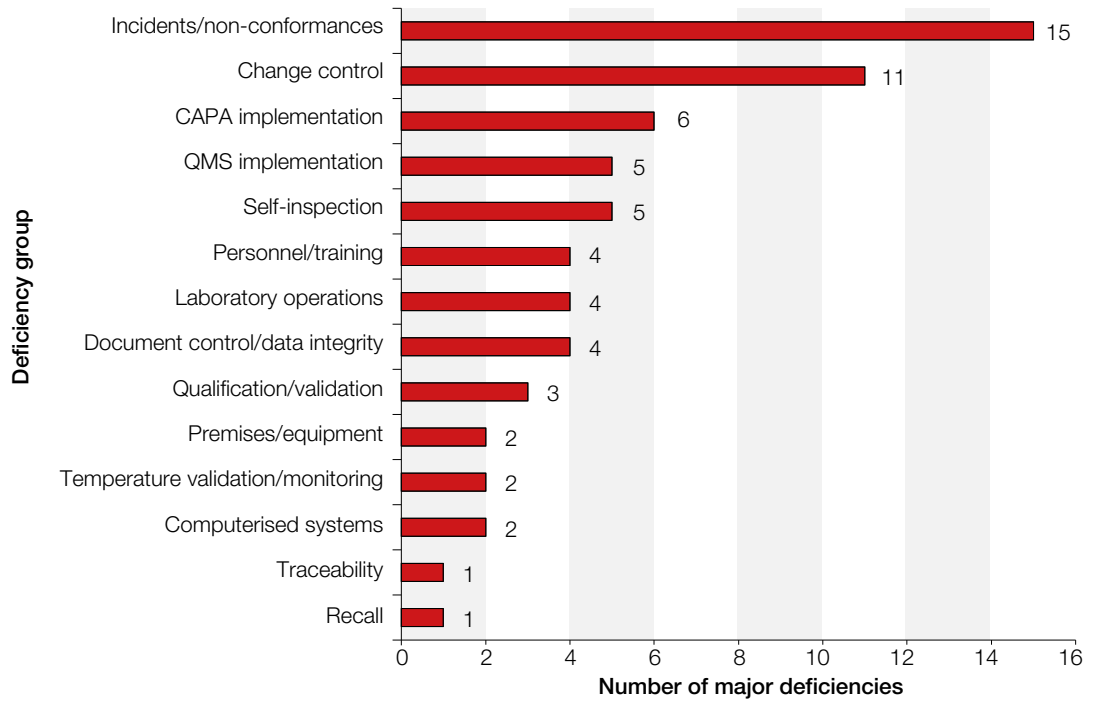
3 HBBs had serious deficiency findings related to their operations and were escalated to the Compliance Management Team (CMT). Common deficiency groups identified from these inspections included:

- 1) Incident investigation process and CAPA implementation
- 2) Change control management
- 3) Document control
- 4) Self-inspection
- 5) Training

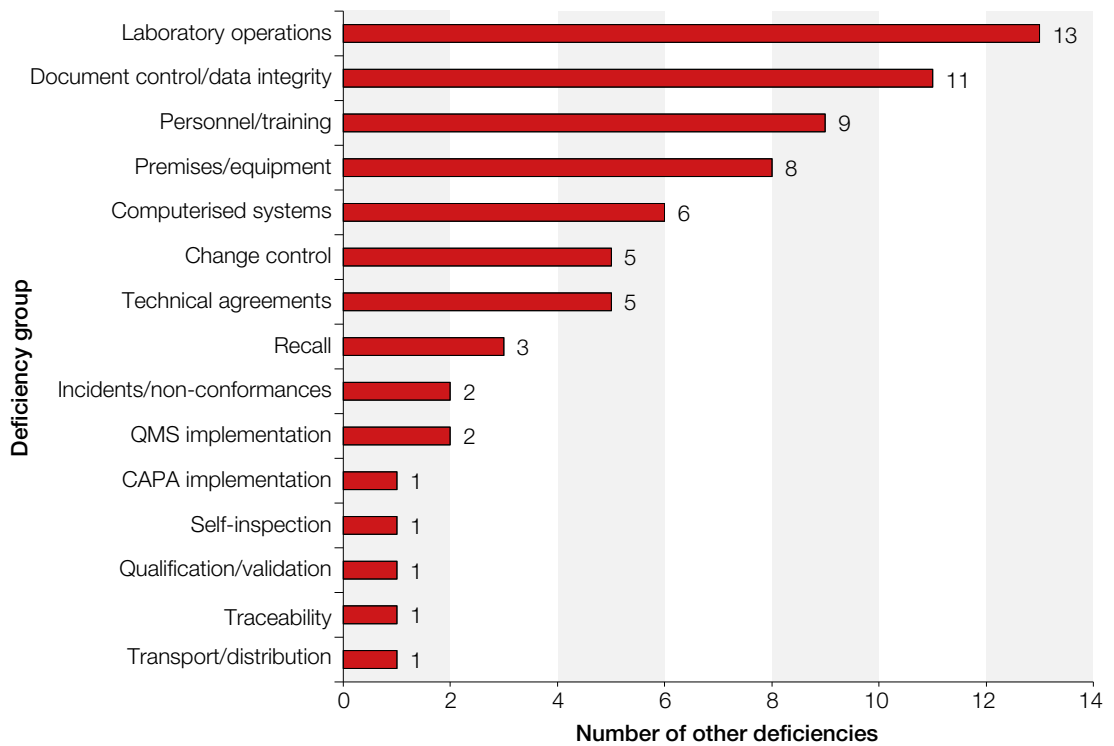
An overview of the compliance management escalation processes used by the GMP Inspectorate, including information on the CMT referral process is available from the MHRA Inspectorate Blog <https://mhrainspectorate.blog.gov.uk/2017/02/06/overview-of-compliance-management-escalation-processes-used-by-the-gmp-inspectorate/>

Deficiencies classified as 'major' and 'other' were identified in the deficiency group as below:

**Figure 25.7:**  
Major deficiency groups



**Figure 25.8:**  
Other deficiency groups



## Summary of significant issues identified at inspected sites

### Quality management systems (QMS)

Senior management has the ultimate responsibility to ensure an effective quality system is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation. However, evidence from inspections showed that senior management's leadership and active participation is lacking and periodic management review involving senior management from across the operation is not performed. The quality systems are not always trended and monitored to ensure its effective implementation.

In one example, the hospital trust had not implemented a quality system for blood banks based on the principles of good practice in compliance with the standards set out in the Annex to Commission Directive 2005/62/EC.

Many transfusion laboratories treated their QMS as the sole responsibility of the quality and transfusion managers, i.e. is treated as something the rest of the personnel do not get involved in. Sites need to invest more time in training and, by involving staff at all levels, instilling an understanding that quality systems are everybody's responsibility.

Metrics for each quality system tended to be reported as 'open' and 'closed'. Overdue items were not reported for discussion. It is crucial that all overdue quality items should be discussed and risk assessed on the impact caused by the delay in completing the agreed commitments.

### Non-conformances/incidents/events

In general, the incident investigation procedure including the conduct of investigation was lacking in detail and has led to a failure to provide staff with adequate guidance. Inspections also identified weak root cause analysis systems that did not fully identify the true root cause and therefore failed to identify appropriate CAPA. Risk assessment was not performed on the impacted components or patients.

Incidents were not always appropriately rated for risk criticality and raised in a timely manner. This is important with respect to potential recalls as, if components are not recalled in an appropriate time-frame, the chance of them being transfused is increased. If these errors were triaged and categorised as 'critical/major' the likelihood is that they would be immediately acted upon.

### Change control management

Repeated deficiencies were cited relating to change control management and its implementation, for example:

- There was no arrangement in place for the prospective evaluation of planned changes and their approval prior to implementation
- The proposed implementation date was not included on the change control form as part of the review and approval
- There was no evidence to support evaluation had been undertaken to confirm the quality objectives had been achieved after the change implementation
- There was no system to track and monitor the progress and full implementation of change controls

This lack of an appropriate change control systems had led to a lack of pre-'go live' authorisation and/ or post-implementation review. In addition, change control requests were not always raised when significant changes had taken place.

## CAPA implementation

The implementation of CAPA was generally found to be deficient with no system in place to track and monitor the progress of CAPA closure and no requirement to monitor and assess the effectiveness of implemented CAPA.

As it is important to identify real root cause for all incidents and events to allow the implementation of appropriate CAPA, it is also important that all CAPA should be completed by the agreed timeline and its effectiveness monitored to avoid any reoccurrence. Any extension in completing the CAPA should be risk assessed, justified and approved by appropriate personnel.

## Laboratory operations

Issues were identified from the sample receipt and acceptance process to suggest that the 'zero tolerance' approach could be bypassed.

Investigation of analyser quality control (QC) failure was in some cases inadequate. Little attention was given to establishing why the QC had failed before process re-runs were initiated. A single passing repeat could be used to invalidate a failed test. Investigation to identify potential causes of failure was not always evidenced.

Other typical deficiencies seen included:

- Incorrect centrifuge setting for sample preparation
- No batch acceptance being performed for received consumables
- Analyser solutions were not labelled effectively with no preparation date or expiry date
- Preparation of reagents, such as Kleihauer reagents was not recorded, hence there was no evidence to demonstrate the correct methodology had been followed
- Test cards and reagents were stored in unmonitored locations
- The control of returning equipment for use immediately following completion of work by external service providers was inadequate
- Errors in labelling of issue units
- Unsupervised overnight access to the laboratory for collection of blood from the issue refrigerator

## Document control and data integrity

Poor documentation practices were the mostly cited deficiency. Examples included: incomplete records, missing entries, overwriting, obliterations, missing sign/date on errors, ditto marks and arrows.

Procedures which lacked clarity or were ambiguous, overdue for review and superseded SOP not retrieved and taken out from use, had led to a failure to provide staff with correct instructions when performing testing or daily activities.

Records that had not been completed contemporaneously or staff signed for incorrect results, e.g. out of temperature limits for the temperature-controlled storage facilities or signed for other staff without explanation, had the potential to result in serious data integrity issues. It is important to apply the basic ALCOA principle to all data: Attribute, Legible, Contemporaneous, Original, Accurate.

## Personnel and training

A capacity plan should be put in place to demonstrate that the staffing level is sufficient to cover the workload including out-of-hours working and effective implementation of QMS. Where a shortfall is identified, senior management should ensure sufficient resource will be made available. Job descriptions and organisation diagrams should be consistent with respect to reporting lines and made available to all staff.

Evidence from inspection showed that staff were not being trained/updated following significant changes due to the lack of training policy and training matrix. Staff were not aware of, trained, and competent in the use of key quality system procedures, and this was especially an issue for staff working out-of-hours. Some training records did not reflect the correct competency assessment or the re-training was overdue. Training records were not always available for review including those for senior management.

Another area of concern related to nurses and porters who collect issued blood units from the issue refrigerator, as the re-training has not been performed in accordance with the training schedule. It was stated that the staff could not be released to complete the necessary training due to the demand on the wards. This is not acceptable practice and the senior management in the clinical area should also be made aware of the regulatory requirements.

GMP/GDP awareness training for contract service providers including contract cleaners and transport providers is required as their work can have impact to patient safety and component quality.

### Computerised systems

With the innovation and development of computerised systems and software, it is more common to see the use of electronic quality and documentation management systems, automatic analysers, patient databases, automatic issuing system, blood tracking systems and temperature monitoring systems. Special attention should be given to the control of such computerised systems and the integrity of QC data.

Some common IT errors included:

- Data quality issues – merging errors and quality control of data entry and transfer between systems
- Level of availability of technical support/knowledge – amongst laboratory users and the organisation's IT
- User requirements – not always met
- System security – appropriate access level, individual login and password
- Storage – backup
- Alternation of data – audit trail
- Contingency and failure – business continuity planning

The use of computerised systems and handling of electronic data should be in compliance with EU GMP Annex 11. The MHRA GMP Data Integrity Definitions and Guidance for Industry March 2015 also provide best practice guidance. <https://www.gov.uk/government/publications/good-manufacturing-practice-data-integrity-definitions>

### Premises and equipment

A common issue related to the poor housekeeping of storage facilities, e.g. icing in freezers or dirty storage units. Temperature mapping and monitoring was also problematic, with monitoring devices found not to be calibrated or mapped correctly. Equipment maintenance schedules were not always followed and service records were not reviewed for approval by laboratory staff prior to release for use.

### Post-inspection actions

Post-inspection actions had not always been completed in the agreed timeframes and the relevant inspector had not been made aware of a transgression at the same time as the issue became known by the site.

On repeat inspections, sites had failed to demonstrate compliance to the agreed remedial plan either in respect to the timeline committed to or the action taken. Evidence of commitments not being completed is periodically observed and sites are reminded of the requirement not to provide false and misleading information. The regulations are clear in that sites are to ensure that adequate resource, oversight and

priority is given to these commitments, to ensure that they are completed in a timely manner. In a number of cases this failure has led to the direct involvement of local chief executive officers and an escalation of compliance management processes within the MHRA.

### Summary of learning points from inspections

- Define and review all system processes regularly to ensure that they are fit for purpose
- Improve root cause analysis procedures and applications ensuring that the whole process is looked at and areas of weakness identified (including internal and external QC) so that appropriate safeguards and corrective measures can be introduced
- Critically review all incidents so the severity of risk can be appropriately categorised and assessed and so that corrective and preventive actions can be introduced in an appropriate timeframe
- Senior management should ensure an effective quality system is in place, adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation
- Monitor system performance so that failures due to resource issues can be raised to the appropriate level
- Raise change controls in an effective and timely manner to ensure that process changes have an appropriate level of validation data
- Introduce measures that ensure effective laboratory housekeeping is undertaken and maintained. This applies particularly to the care and maintenance of storage facilities
- Design and implement an achievable and effective training plan for all routine and out-of-hours staff, and ensure that this includes the QMS procedures
- Attention and special care is required for the control of data in hard copy or in electronic format
- Good documentation practices must be followed
- Post-inspection actions must be completed as agreed or notify the inspector of slippage

### Information and guidance

For further information on **MHRA and the Regulation of Blood** please refer to the MHRA website: <https://www.gov.uk/topic/medicines-medical-devices-blood/blood-regulation-safety>

The MHRA Blood forum was launched in June 2016 as a tool to help those involved in blood component collection, processing, testing and distribution to comply with the EU Blood Directives, UK Statutory Instruments and good practice requirements. It provides the ideal opportunity for extended communication between peers and allows users to put forward their comments and get 'real-life' examples of ways in which they can manage robust quality procedures that ensure compliance and which dovetail with their own business needs and resources.

<http://forums.mhra.gov.uk/forumdisplay.php?60-Blood-Forum>

### References

BSQR. **Blood Safety and Quality Regulations**. (SI 2005/50, as amended)  
<http://www.legislation.gov.uk/ukSI/2005/50/contents/made>

**Human Factors and Ergonomics**. HSE website <http://www.hse.gov.uk/humanfactors/>

**Good Practice Guidelines for elements of the Quality System**. Council of Europe website,  
[https://www.edqm.eu/medias/fichiers/good\\_practice\\_guidelines\\_dec\\_2013.pdf](https://www.edqm.eu/medias/fichiers/good_practice_guidelines_dec_2013.pdf)



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