Medicines and Healthcare Products Regulatory Agency (MHRA) Report 24

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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, hospital transfusion laboratories 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 in this report are correct as of 22 January 2018.

Key message

- Assessment of some serious adverse blood reactions and events (SABRE) reports support anecdotal evidence from reporters at regional meetings, SHOT Symposia and other conferences that staffing, workload and skill-mix problems are affecting laboratories' performance in meeting the requirements of the Blood Safety and Quality Regulations (BSQR). This also reflects the findings of the UK Transfusion Laboratory Collaborative (UKTLC) surveys. However, it is not always evident from the root-cause analyses that the error reported is linked to staffing, workload and skill-mix problems in the laboratory. Reporters are encouraged to continue to thoroughly investigate serious adverse events (SAE) and serious adverse reactions (SAR) and report not just how an error occurred, but to report why it occurred. Reporters must aim to address all root causes and contributory factors to allow the Medicines and Healthcare Products Regulatory Agency (MHRA) and SHOT to gather as much information as possible related to the apparent staffing and workload problems experienced by laboratories

Summary

In the second full year of MHRA and SHOT viewing all reports and deciding which meet the individual organisation's reporting requirements, more SAE and SAR have been reported in 2017 than in 2016. The European Commission recognises that high numbers of reports may indicate a healthy reporting culture in a member state compared with a member state that does not report any at all (EU 2016). More detailed analysis shows the rate of increase in SAR is greater than the increase in the numbers of SAE and that the increase in SAE comes mainly from Blood Establishments rather than hospital reports.

Many SAE reports indicated the pressures that laboratories are under related to staffing, workload and skill-mix problems. MHRA inspection data indicate that more hospital blood compliance reports (BCR) were assessed as 'high risk' in 2016/17 and one of the main findings at inspections was related to resource failings by Hospital Trust/Health Board senior management (not laboratory management).

The total number of SAE received from hospitals (i.e. excluding blood establishment SAE) remains similar to previous years, although there are differences in the reporting patterns in some categories. There has been anecdotal evidence from reporters that they are being discouraged from reporting, or are not able to report at all. While this may be true in some cases, it would appear that most reporters are able to actively engage in UK haemovigilance. This is evidenced by the increase in total number of reports received and the fact that all except 31 SABRE accounts have made at least one report since January 2017 (see Figure 2.1 in Chapter 2, Participation in UK Haemovigilance).

A question therefore arises, why has the level of hospital transfusion laboratory SAE reporting not increased to reflect the evidence of staffing, workload, skill-mix and resource problems? Are reporters prevented from reporting due to time or senior management pressure, or have quality management systems (QMS) been made robust enough to prevent adverse events from becoming serious, or resolved at the time they occurred?

Denominator data

Comparing SAE data to a previous year's data can be very complex. It is not as simple as, say, comparing the number of reactions to the number of donations transfused since one component can only cause one reaction. SAE can occur at any step in the vein-to-vein processes and it is not possible to calculate a finite number of steps where an error can occur. Therefore, there is no relationship in the number of SAE to any kind of denominator data.

Furthermore, the perception of what might make an event 'serious' can be subjective, and changes to a reporting organisation's personnel can therefore have an effect on the numbers of SAE reported.

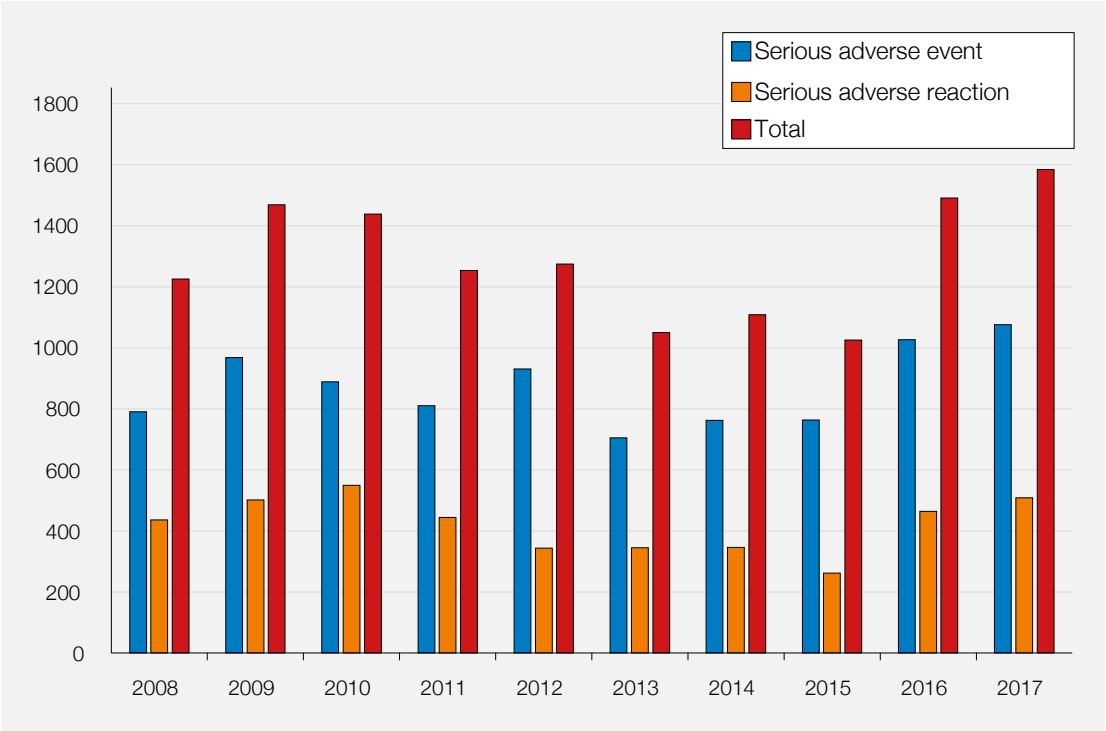
SABRE report data

Table 24.1 and Figure 24.1 display the total number of SABRE confirmation reports that were submitted and satisfy the European Commission reporting criteria for SAR and SAE since 2008. Since even old data are live, and subject to amendment. Table 24.1 has been updated to reflect changes to historic reports.

Table 24.1: Submitted SABRE confirmation reports 2008–2017

	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
SAE	790	968	889	810	931	705	762	764	1027	1076
SAR	436	501	549	444	343	345	346	262	464	508
Total	**1226**	**1469**	**1438**	**1254**	**1274**	**1050**	**1108**	**1026**	**1491**	**1584**

Figure 24.1: Submitted SABRE confirmation reports 2008-2017



This is the second full year that data have been available to both organisations following changes to the UK Haemovigilance system made in October 2015. Although comparisons can be made between 2016 data and 2017 data it is not possible to identify any trends.

The total number of reports has increased by about 6% compared to last year, however that is a result of an increase in SAR by about 9% and SAE by about 5% meaning most of the increase in reports has come from SAR reporting. In fact, further assessment of SAE figures shows that the majority of the increase in SAE (49) reports has come from blood establishments, SAE reports n=66 in 2016 and n=109 in 2017, +43.

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.

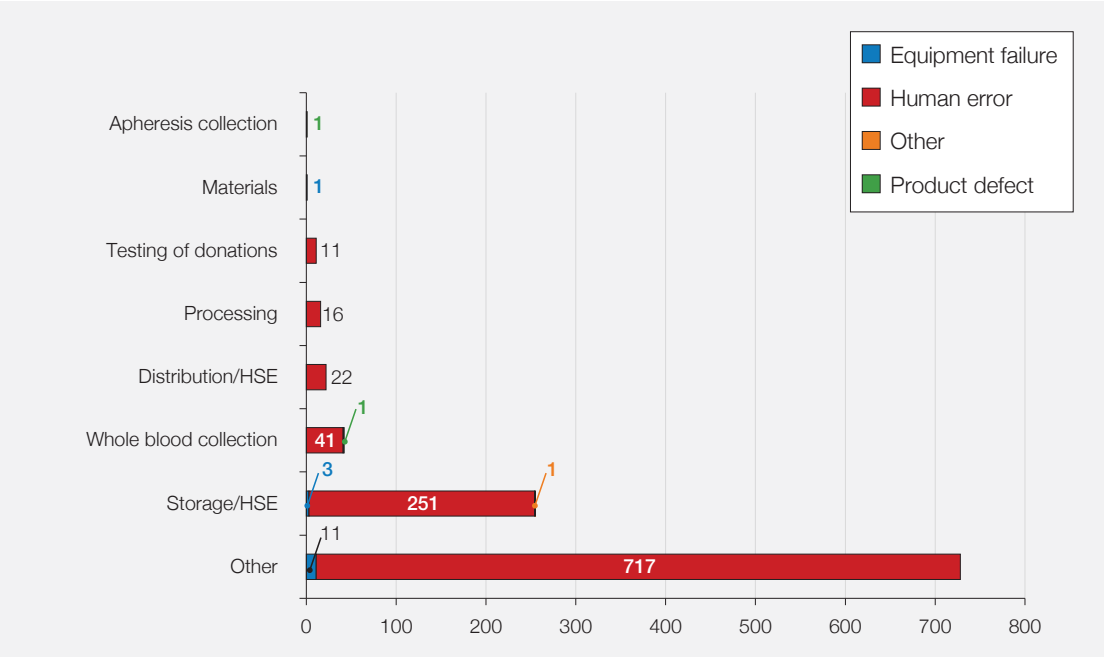


Figure 24.2: 2017 SAE confirmation reports by deviation and specification

HSE=handling and storage errors

Similar to previous years there is no real change in the proportions of each category of reported SAE. 'Other' and 'storage' categories contain the most reports, and human error remains the main root cause.

Storage data n=255 (+20)

Storage remains the second largest individual error category and includes all BSQR reportable storage SAE in both the 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 Errors (Chapter 7) and HSE (Chapter 9) chapters. The MHRA has subclassified 'storage' reports further to try and identify specific error subtypes, Table 24.2. For a description of the subcategories used, see Appendix 24.1.

Table 24.2: SAE storage error subclassification 2017

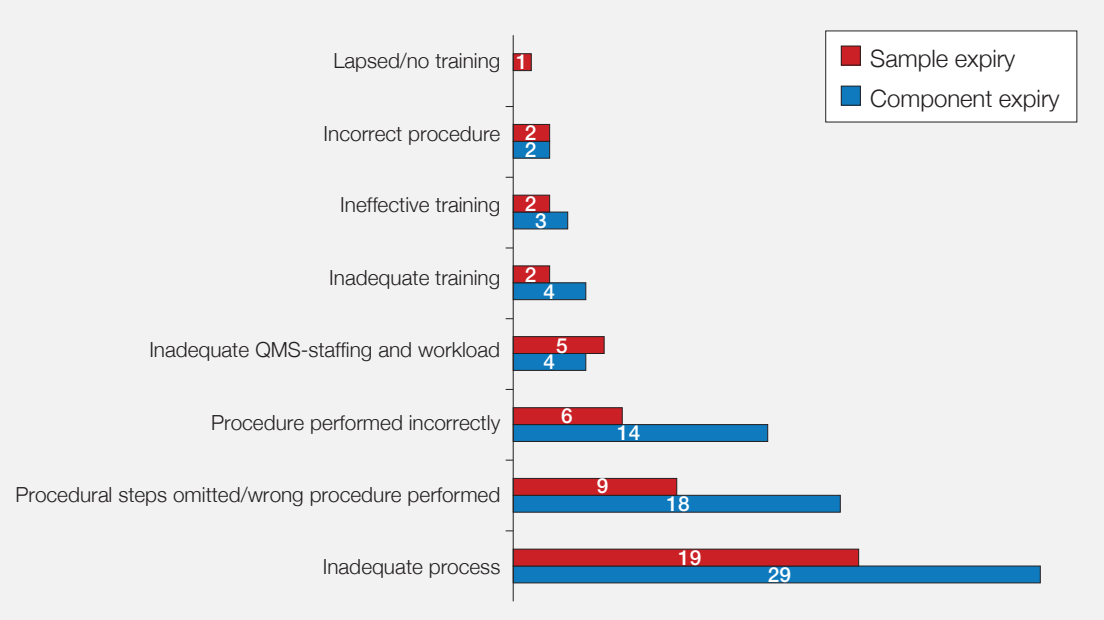
Storage subclassification	2017 (+/-2016)		2016 position
Component expiry	74	(+8)	2
Incorrect storage of component	68	(-17)	1
Sample expiry	46	(+14)	3
Return to stock error	19	(+4)	4
Failure to action alarm	19	(+12)	7
Storage temperature deviation	8	(-4)	5
Security	8	(+3)	8
30-minute rule	7	(-1)	6
Miscellaneous	6	(+1)	9
Total	**255**	**(+20)**	**x**

Despite still being the second most commonly reported storage SAE, reports of incorrect storage of component have decreased since last year. These errors can occur when any component is placed in an incorrect storage location whether in the laboratory or in clinical areas.

Failure to action alarm has seen an increase in number of reports from 7 to 19 and 11/19 were found to be due to inadequate processes. Factors involved in these reports included equipment not adequate for the task e.g. the temperature monitoring computer logging out, processes not being adequately designed to fully describe what actions to take and processes not being designed to be sufficiently robust to work out-of-hours when fewer laboratory and clinical staff are available to take the required actions.

The first and third most common storage SAE are related to component and sample expiry. These are SAE where components have time-expired and have not been removed from the supply chain in a timely manner or where the component is still in date but the patient sample has expired. Although different errors, the systems in place to manage these situations are often linked and so have been assessed in greater detail below. Collectively these errors account for n=120/1076, 11.2% of all SAE reported.

Figure 24.3: Sample and component expiry by specification 2017



QMS=quality management system

Last year the most common cause for these errors was inadequate processes and it remains the case this year. There are several measures that laboratories can take to manage expiring components and samples which include:

- Checks at various times of the day depending on staffing levels and workload
- Physical checks of storage locations where practical
- Interrogation of the laboratory information management system (LIMS) to produce lists of expiring components
- Removal of close-to-expiry components from clinical areas to allow a final check by laboratory staff if the component is required

Whatever methods are used, it is imperative that the process is properly designed to identify expiring components and to prevent them from being transfused. The design of the process must take into account whether staff are able to perform the task in a timely manner when there might be competing pressures from other tasks, and procedures must be written to include detailed instructions as to what checks to perform and how to perform them to facilitate training of new staff.

Case 24.1: Red cell units left in refrigerator long after their de-reservation date

A number of units of red cells were left in the blood refrigerator at an off-site private hospital beyond their de-reservation dates. Two of those units were left for more than a week beyond their de-reservation date and therefore could have been transfused when the sample was no longer valid. The patient for whom those two units had been issued had known blood group antibodies.

The investigation identified multiple factors that resulted in an inadequate process for managing the use of off-site refrigerators. The paperwork did not alert staff to when units had reached their de-reservation dates and the need to be removed. Training had been left to medical laboratory assistants (MLA) who had not used the standard operating procedures (SOP) as training material, relying on 'word-of-mouth', and vital aspects of the process had been forgotten and not relayed. The corrective measures included re-design of the paperwork and re-education of staff involved in both the process and noted the importance of adequate training.

Other n=726 (+8)

Since 'other' is the largest category of SAE reports, the MHRA haemovigilance team has created subcategories to further analyse this type of error, Table 24.3. For a description of subcategories, see Appendix 24.2.

Other subcategory	2017 (+/- 2016)		2016 position
Incorrect blood component issued (IBCI)	175	(-17)	1
Sample processing error (SPE)	123	(-11)	2
Component labelling error (CLE)	114	(+8)	4
Pre-transfusion testing error (PTTE)	104	(-6)	3
Component collection error (CCE)	94	(+16)	5
Data entry error (DEE)	71	(+13)	6
Failed recall (FR)	18	(+1)	7
Unspecified (UNSPEC)	9	(+7)	10=
Component available for transfusion past de- reservation (CATPD)	5	(+2)	9
Expired component available for transfusion (ECAT)	5	(+3)	10=
Incorrect blood component ordered (IBCO)	5	(-9)	8
Handling damage (HD)	2	(0)	12
Incorrect blood component accepted (IBCA)	1	(+1)	13
Total	**726**	**(+8)**	**x**

Table 24.3: SABRE reports, subcategory 'other' 2017

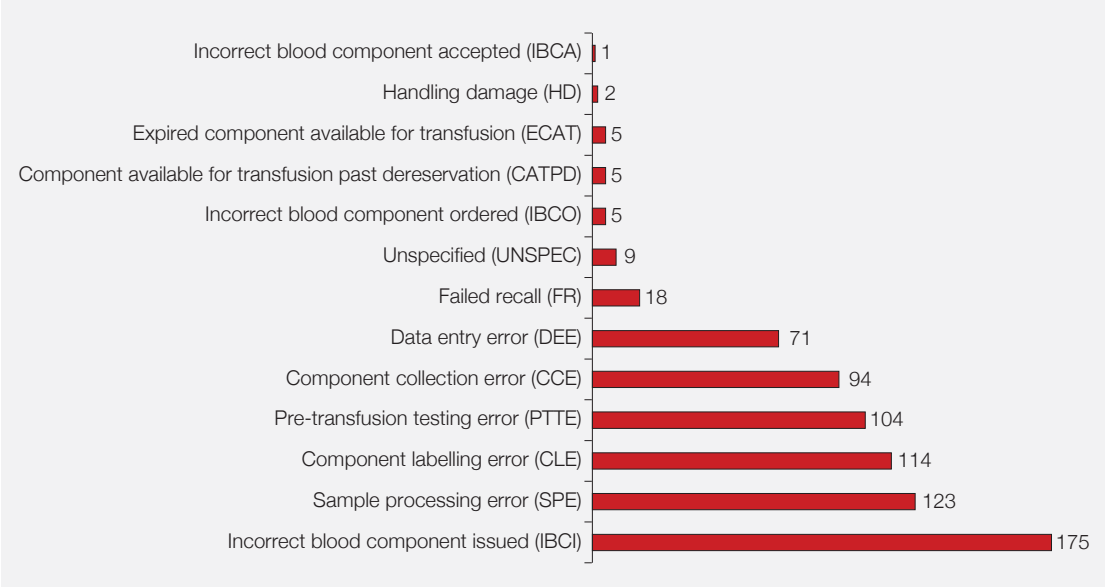


Figure 24.4: SABRE reports subcategory 'other' 2017

The total number of reports that fall into the 'other' category is similar to last year and the relative proportions of incidents in each subcategory also remains similar. However, there are some marked differences in reporting patterns. There have been reductions in the number of reports associated with incorrect blood components issued (IBCI) and pre-transfusion testing errors (PTTE). These are processes which, although they involve manual steps and human factors, can be controlled by LIMS, equipment, education and training. A reduction in these SAE could be a result of:

- Better controls in LIMS
- Improvements in processes and procedures
- Improved understanding of the processes and procedures
- Changes to the provision of HEV-screened blood (i.e. no longer reported as all cellular components are HEV-screened)

Increases have been seen in component labelling errors (CLE) and data entry errors (DEE). These are processes which are not easily controlled by equipment and electronic processes, and rely more heavily on manual steps and concentration. Conversely, there is a reduction in sample processing errors (SPE), which rely heavily on laboratory staff noticing discrepancies in labelling, forms and LIMS. Reduction in these incidents could be a result of:

- Improved sample collection processes
- Improvements to laboratory environments and reduction of distractions
- Highlighting the importance of thorough checking and concentration

There has also been an increase in component collection errors (CCE). These can occur when laboratory staff hand over components at collection, but typically involve clinical staff and porters collecting components from storage locations. Often these are the result of lapses of concentration, but analysis also suggests that staff are often poorly trained in collection processes, whether they involve electronic systems or not, and system bars and warnings are ignored or over-ridden.

Human error category and human factors

Human factors are all the things which can influence how a human behaves. These will either lead to an action being successful, or it will lead to human error and can be organisational, job-related or related to the individual concerned.

To better understand human error, the SABRE team has developed subcategories which can be applied to the report narratives to help understand the human factors involved. For a description of these categories, see Appendix 24.3. Table 24.4 shows the breakdown of reports in the human error subcategories.

Table 24.4: SABRE reports, human error subcategory 2017

Human error subcategory	Total	(+/- 2016)
Procedure performed incorrectly	291	(+22)
Procedural steps omitted/wrong procedure performed	237	(+54)
Inadequate process	211	(+16)
Ineffective training	119	(+1)
Inadequate QMS – staffing and workload	80	(-23)
Inadequate training	46	(0)
Incorrect procedure	40	(-9)
Lapsed/no training	25	(+4)
Inadequate supervision	9	(-13)
Total	**1058**	**(+52)**

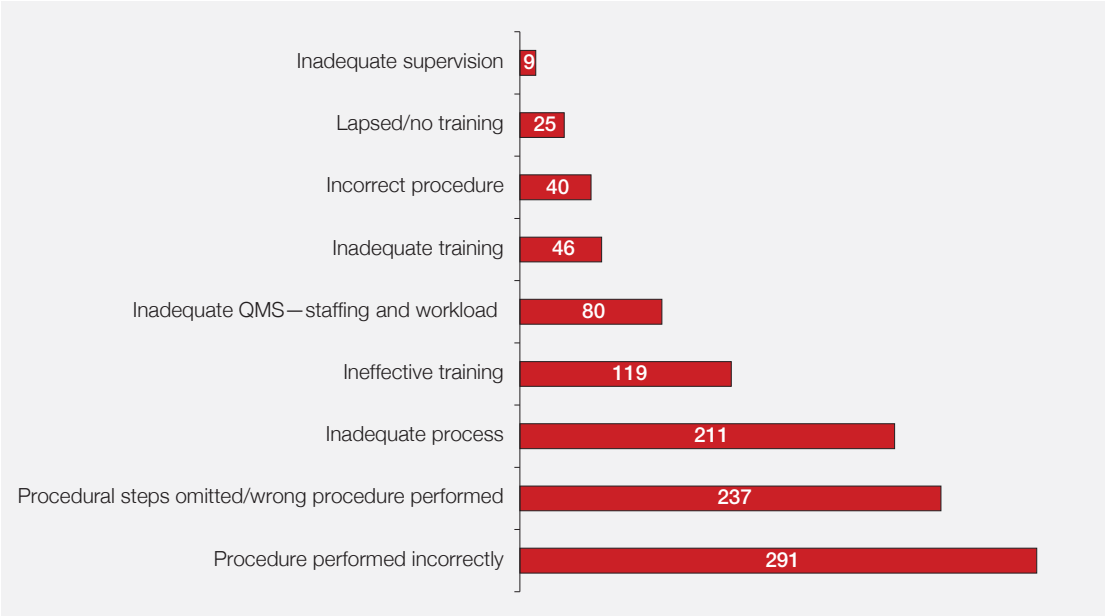


Figure 24.5: SABRE reports, human error subcategory, 2017

QMS=quality management system

NOTE: 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 distribution of categories remains similar to last year. Procedures performed incorrectly, missed steps, or wrong procedures followed account for the most of all SAE attributed to human error. These are typically errors resulting from slips or lapses of concentration by individuals after other aspects of the quality system have been ruled out.

Staff should be able to cope with a certain pressure of workload and distractions, and simply being busy should not be used as an excuse for errors. The quality of work is the responsibility of individual staff and they should take time to ensure they 'get it right first time'. Staff should be encouraged to prioritise their workload and use the support mechanisms available when they need to, such as delaying non-urgent work, or calling staff for extra support from other laboratories.

It would be wrong to suggest that over half of the SAE are the result of poor concentration. Staff are reported to be under pressure from poor staffing levels, inadequate skill mixes and high workloads. Distractions can also affect concentration and can come from interruptions by other staff, telephone calls, equipment breaking down or not being available and multitasking. Quality systems should be designed to be robust and help prevent staff from falling victim to slips and lapses. This will include, but is not limited to:

- Adequate working environment (e.g. lighting, space, equipment, logical design)
- Adequate staffing and skill mix
- Appropriate workloads
- Robust processes
- Accurate procedures
- Adequate training
- Access to information and expertise
- Leadership and supervision

Many report narratives hold staff solely responsible for the errors made. While in some cases this may be true, poor quality investigations and reports overlook the systems factors that led to staff behaving and acting in a way that resulted in error. The MHRA will often contact reporters to clarify details of their SABRE reports and discuss improvements to quality systems which may help prevent errors, but this cannot be done for every single report. It is possible that many of the SAE reports which fall into the 'procedure performed incorrectly' and the 'procedural steps omitted/wrong procedure performed' categories could be assigned to different subcategories with a more detailed SAE report.

Reports that indicate staff error as the primary cause of the SAE without a thorough investigation may account for fewer reports being assigned the category 'quality system – staffing and workload'. Fewer reports in this category compared to last year should not be seen as an improvement in staffing and workload problems. The 80 reports indicated above were assessed to directly result from staffing and workload problems, however, many of the SAE reports that occurred in the other subcategories may have been indirectly related to staffing and workload problems. For example, a sample and form were sent to the laboratory with a different address to the one recorded on the LIMS. This sample was sent towards the end of the day during a busy time and the discrepancy was not noticed due to rushing the checking process. There was no valid reason for rushing the process, despite being busy; however, rearranging the workflow at this busy time could alleviate the pressure on the staff and their perception that they need to rush to complete the work.

Top 5 SAE

'Procedure performed incorrectly' and 'procedural steps omitted/wrong procedure performed' account for over half the SAE reported and can affect any type of SAE. Since managing these types of error has been discussed above, the top 5 types of error have been assessed considering the remaining root cause types only.

Table 24.5: Top 5 SAE with human error subcategory

SAE deviation subcategory	Specification subcategory
Incorrect blood component issued (IBCI)	Inadequate process
Pre-transfusion testing error (PTTE)	Inadequate process
Sample processing error (SPE)	Inadequate process - staffing and workload
Component collection error (CCE)	Ineffective training
Incorrect blood component issued (IBCI)	Ineffective training

The following cases are included to illustrate what might be considered by way of corrective and preventive action (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.

Case 24.1: Incorrect blood component issued (IBCI) – inadequate process (Case 10.8 in Incorrect Blood Component Transfused (IBCT), Chapter 10)

Five units of group O fresh frozen plasma (FFP) were issued and transfused to a group A patient. A telephone request was taken and the correct patient's name and hospital number were written down. The investigation revealed that the wrong hospital number was copied and pasted from a different patient record and used to populate the LIMS and the wrong blood group and sample accession number obtained. These incorrect details were then transcribed to the telephone request form. Units of the incorrect group were thawed and issued to the patient. This error could have been discovered sooner when the porter came to collect the units because the porter recognised that the patient details on the label did not match the details on the collection form. The discrepancy was not thoroughly investigated and the units were re-issued to the correct patient without noticing the discrepant group.

When the units arrived at the bedside, although checks were made, it was assumed that group O FFP was compatible with the patient whose blood group was A. A further request for cryoprecipitate was processed by a different biomedical scientist (BMS) and it was only at this point that the mistake was noticed.

The hospital transfusion team could have concluded the root cause of the SAE to be a lapse in concentration that occurred when the wrong details were selected and transcribed, however they conducted a thorough investigation and wrote a comprehensive investigation report which highlighted numerous QMS failures. More importantly, however, they were able to identify CAPA which targeted exactly the root causes and make significant improvements to their QMS.

Contributory factors identified included:

- The current version of the LIMS was old and did not allow staff to move easily between programmes. A project to implement a new LIMS had stalled a number of times
- The telephone request form did not include a verification step to ensure the correct information had been recorded
- Although there were instructions in the SOP to use each programme in the LIMS the SOP did not detail how to enter the hospital number, and more importantly to verify that the correct hospital number and other details had been used
- The blood component issue SOP did not detail that verification checks of the manual information on the telephone request form matched the details entered on the LIMS
- There was no SOP to detail the return of incorrectly issued components and their re-issue
- When re-issuing the FFP, it was assumed that the correct blood group had been issued to the wrong patient, and there was no check that the component issued was suitable for the correct patient
- When the FFP was issued to the correct patient, warnings that the incorrect group had been issued were not heeded and the LIMS did not prevent their issue
- There was a knowledge gap regarding compatibility of FFP groups by the administrator
- There were procedural steps omitted by operators and missed by the laboratory supervisor

The investigating team also considered staffing/workload and skill-mix factors, but concluded that these were not factors in the event.

In addressing these factors and other issues arising from the investigation, the hospital transfusion laboratory staff were able to:

- Re-state their need for a new LIMS and revive the project to implement the new one
- Re-evaluate their processes and re-design them
- Re-write SOP to include missing instructions and steps
- Re-assess competence of staff and re-train where necessary
- Review new-starter and trainee BMS capacity proportional to number of appropriately trained staff available to undertake supervision
- Review adequate staffing levels and develop procedures for escalating unmanageable workloads

In all, 28 recommendations were identified to improve the QMS.

Case 24.2: Pre-transfusion testing error (PTTE) – inadequate process

A sample used for crossmatch and issue of red cells was 8 days old. The investigation revealed that old samples were not being discarded early enough in the day.

The CAPA to resolve this error was simply to change the process to discard old samples earlier and to update the LIMS system to recognise and not process samples that are too old.

Case 24.3: Sample processing error (SPE) - inadequate process - staffing and workload

A crossmatch sample was received with an incorrectly spelt last name and used to issue 2 units of red cells before the discrepancy was noticed. This was also reported to be a repeat error for the laboratory.

As discussed above, SPE are often a result of slips and lapses of concentration. However, there is much evidence in SABRE reports to indicate that staffing and workload pressure are directly affecting the ability of staff to work safely, causing them to rush and either skip steps in a procedure or not identify often slight discrepancies. In this particular report, the reporter identified that a recent increase in workload, as a result of severe staff shortages, was affecting staff morale by increasing stress in the laboratory. The reporter also indicated that these staff shortages had led to a delay in being able to thoroughly investigate the error.

More worryingly the reporter stated that often staff were being encouraged NOT to report SAE to SABRE. Anecdotal evidence given to the MHRA during meetings and other discussions have also indicated that laboratory managers are being encouraged to give false information on the BCR. If any SABRE reporter finds themselves in this position they should remind them of their legal responsibilities under the BSQR. Also, the MHRA will assess any information provided by whistleblower, https://www.gov.uk/guidance/contact-mhra#whistleblower-referrals.

Case 24.4: Component collection error (CCE) – ineffective training

A patient had platelets and plasma allocated. The patient required plasma, but the porter incorrectly collected the platelets, failing to perform the correct checks other than the patient name. Although the porter had been trained, it was the first time they had collected anything other than red cells and they had got confused between the two components. Instead of stopping and contacting the laboratory for advice, they continued to collect the wrong component.

When delivering training, not only must it cover all aspects of the task, but must also cover what to do if things do not go to plan. Often staff may not perform tasks regularly, and the training may have been delivered some time before they need to carry out a procedure. It is not unreasonable to assume that staff may have forgotten some of the aspects of that training. It may seem like common sense that someone should ask for help or advice when stuck, but staff must be reminded of this when they are being trained. Also, if staff having forgotten some of their training this may be an indication that training needs to be delivered more frequently for some tasks and for some staff groups.

Case 24.5: Incorrect blood component issued (IBCI) – ineffective training

A patient born after 1 January 1996 was issued and transfused with 8 units of FFP instead of Octaplas® (solvent-detergent FFP). The member of staff thought they were following the correct protocol as they incorrectly thought Octaplas® (or methylene blue-treated FFP) should be issued to patients under the age of 16.

As a result of this, a specific requirements flag was added to the patient's record. Report narratives suggest that some LIMS do not prevent staff from overriding flags and warnings and components have been issued with incorrect specific requirements. The addition of flags is important, but should not be considered in isolation as effective CAPA to prevent IBCI errors.

Figure 24.6 shows the 'other' subcategory and root cause for all SAE other than procedural steps omitted/wrong procedure performed and procedure performed incorrectly.

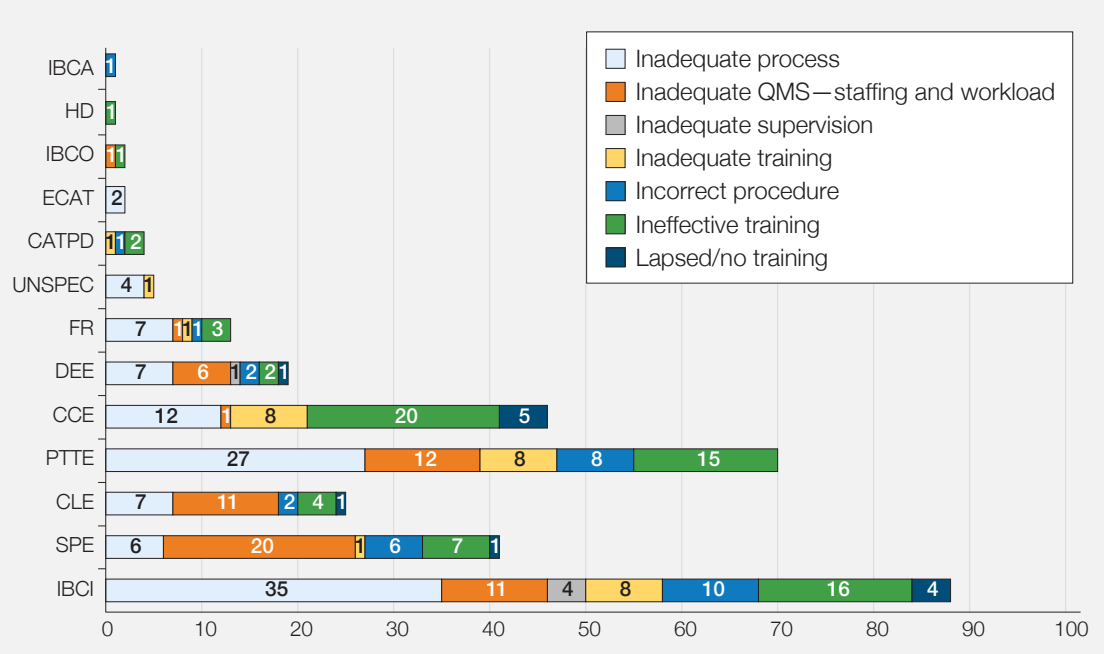


Figure 24.6: 'Other' subcategory root causes

See Figure 24.4 for key to category abbreviations

Blood establishment reporting n=109 (+43)

The majority of SAE reports originate from hospital transfusion laboratories. Although reports from blood establishments are included in the main analysis, the specific nature of the SAE reports from blood establishments are lost in the greater numbers of reported hospital transfusion laboratory SAE. Figure 24.7 displays the reported blood establishment SAE in 2017.

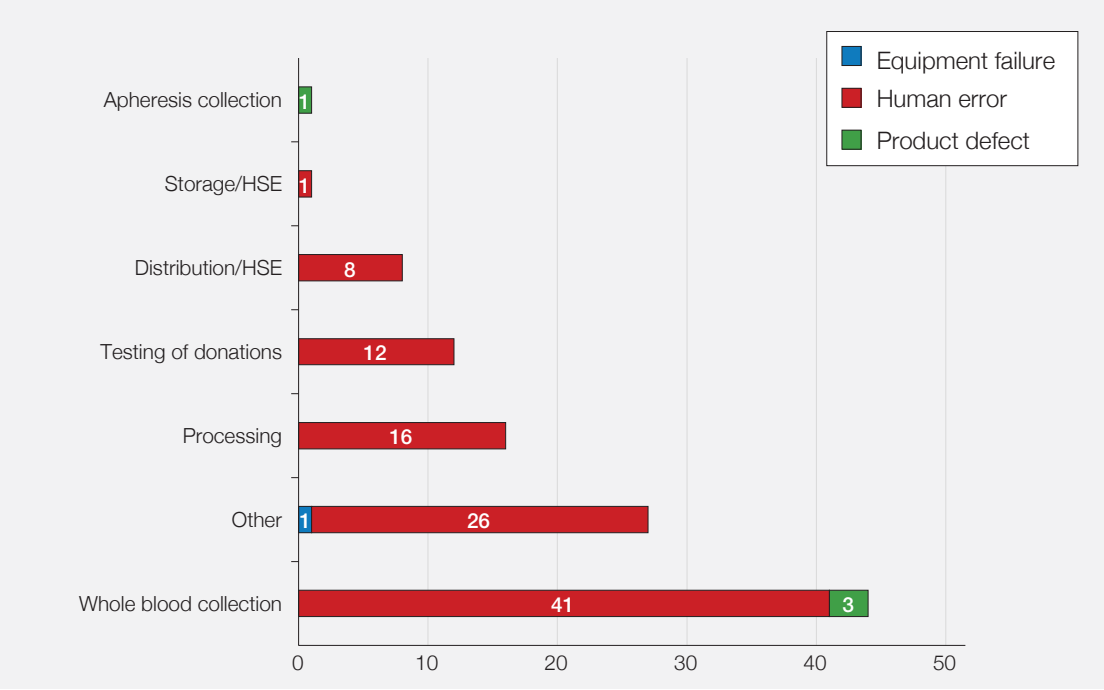


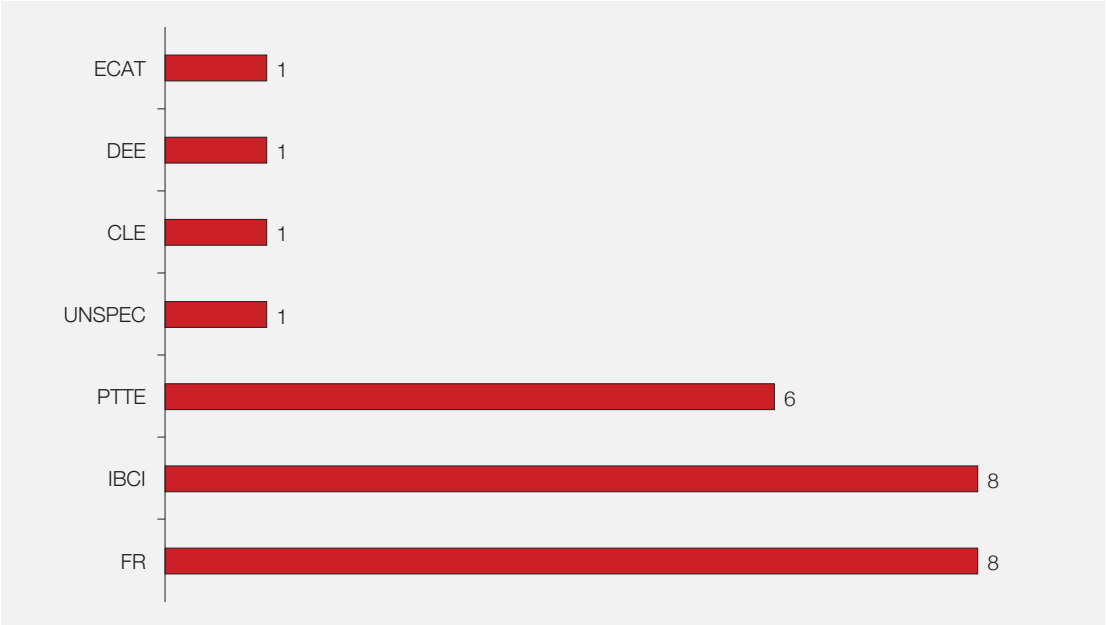
Figure 24.7: Blood establishment SAE category by specification

HSE=handling and storage errors

The SAE reported from blood establishments demonstrate an almost identical pattern to last year, except that they have reported in much greater numbers, with errors at donation remaining the single biggest category. The reason for the sharp rise in the number of SAE reports from blood establishments is unclear, but could simply be greater awareness of what should be reported.

Assessment of the 'other' category, Figure 24.8, once again shows that failed recalls are the main error. SAE in the 'incorrect blood component issued' and 'pre-transfusion testing errors' demonstrate that blood establishment laboratories are liable to making similar errors to hospital laboratories,

Figure 24.8: Blood establishment SAE 'other', 'human error' by subcategory



See Figure 24.4 for key to category abbreviations

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®, 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

To avoid any confusion the MHRA will only supply, in this Annual SHOT Report, total SAR numbers reported to Europe, Table 24.6.

Table 24.6: SAR reports, by imputability, reported to SABRE in 2017 n=508

	Imputability score				
	NA	**0**	**1**	**2**	**3**
SAR reports by imputability score	7	76	185	181	59

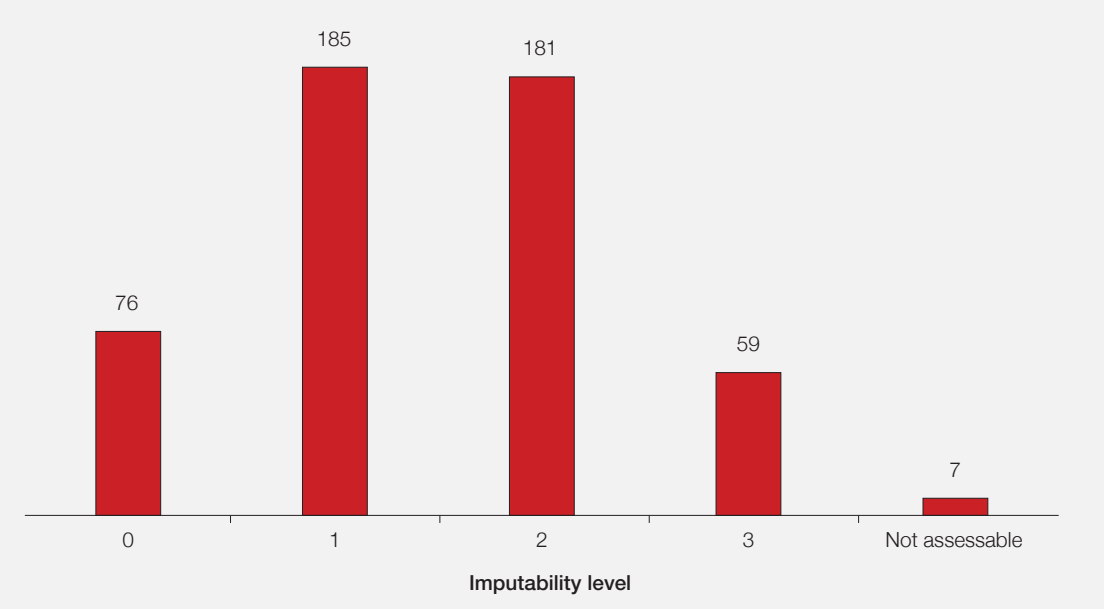


Figure 24.9: SAR reports, by imputability, reported to SABRE in 2017

MHRA inspection activity on hospital blood banks 2016-2017

Author: Graham Carroll

A total of 299 blood compliance reports (BCR) were submitted for review for the reporting period 01 April 2016 to 31 March 2017. Twenty-seven hospital blood banks (HBB) including 6 control sites were selected for inspection; this included sites under the oversight of the Inspection Action Group (IAG) and Compliance Management Team (CMT) following previous inspections.

Inspection outcomes

Inspections for the reporting period 01 April 2016 to 31 March 2017 are performed in the following year, i.e. from 01 April 2017 to 31 March 2018. At the time of writing, a total of 19 inspections had been performed at 18 sites, and the numbers of deficiencies are as follows:

Critical	Major	Other
0	42	76

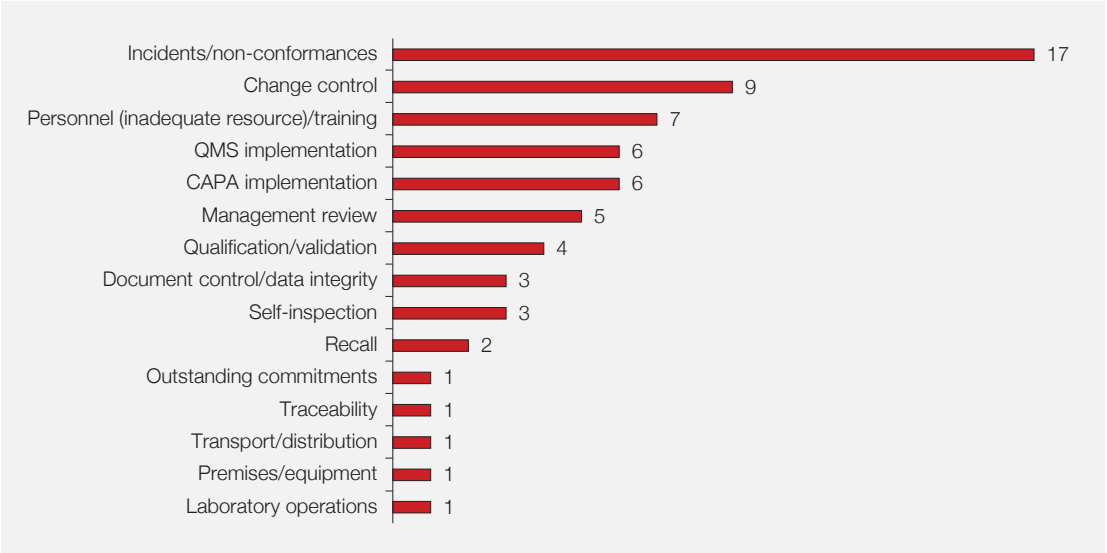
Table 24.7: MHRA inspection deficiencies

Five HBB had significant deficiency findings related to their operations and were escalated to the CMT. This is a significant increase over the previous year. Common deficiency groups identified from these inspections included:

- Senior management not fulfilling their responsibilities
- Non-conformances/incidents/events and CAPA implementation
- Change control management
- Self-inspection
- Resourcing and training
- Failure to complete previous commitments
- Data integrity failures

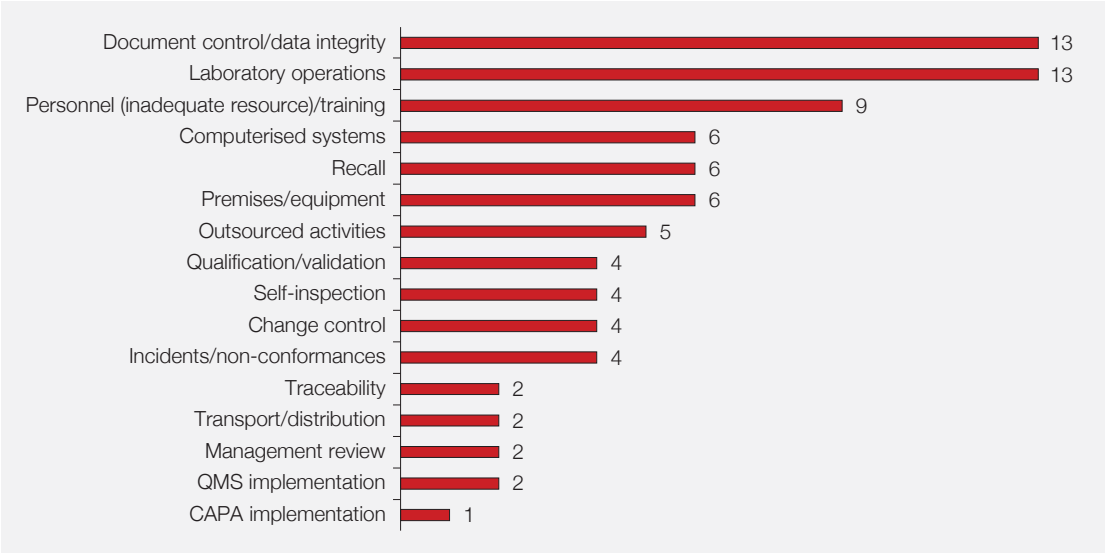
An overview of the compliance management escalation processes used by the good manufacturing practice (GMP) inspectorate, including information on the IAG and CMT referral processes, is available from the MHRA inspectorate blog: https://mhrainspectorate.blog.gov.uk/2017/02/06/overview-of-compliance-management-escalation-processes-used-by-the-gmp-inspectorate/.

Figure 24.10: Categories of major deficiencies found



QMS=quality management system; CAPA=corrective and preventive actions

Figure 24.11: Categories of other deficiencies found



QMS=quality management system; CAPA=corrective and preventive actions

Summary of significant issues identified at inspected sites

Senior management responsibilities

Senior management has the ultimate responsibility to ensure an effective quality system is in place, that it is adequately resourced and that roles, responsibilities, and authorities are defined, communicated and implemented throughout the organisation. In a number of cases, senior management was not adequately monitoring the performance of the QMS to ensure that it was effective and adequately resourced. Examples of this included:

- Management meetings were not performed at the specified frequency
- Reports reviewed by senior management lacked appropriate metrics to detect that the QMS was not functioning correctly
- Meeting minutes were not prepared, or did not identify actions to be taken (including timelines and responsibilities) to address poor performance of the QMS

In some inspections, the number of systems found to be deficient indicated that there were insufficient resources to maintain an effective QMS at the same time as ensuring service delivery. Further investigation identified failings such as:

- A quality manager who was available for less than 0.1 whole time equivalent (WTE) for transfusion
- A laboratory manager with overall responsibility for quality but insufficient time to fulfil this responsibility due to required time on the bench
- No resource plan to define the required resource levels to support operational delivery and the quality system

Non-conformances/incidents/events and CAPA implementation

Incident investigations continue to be an area of concern. Example deficiencies include:

- No defined timeframes for raising, assessing, investigating, and closing incidents
- Failing to record incidents in the QMS
- Poor risk-management practices, such as not considering potential harm or detectability when determining the risk level, and not having an immediate criticality assessment when an incident occurs
- Late, incomplete or missing investigation of the root cause(s) of an incident
- Attributing incidents to human error without a documented assessment of potential process, procedural and system causes

The lack of effective investigation of incidents has a knock-on effect on CAPA implementation. An effective investigation process should ensure that CAPA are appropriate and address the root cause(s) of the incident; the CAPA process should also ensure that actions taken are effective. Issues with CAPA processes included:

- Significant numbers of overdue CAPA
- No tracking of the number of CAPA currently open, and progress towards completion
- Lack of effectiveness checks

Change-control management

Given the criticality of the testing performed by transfusion laboratories, it is concerning that issues with the control of changes continue to be cited in a high number of major deficiencies. Examples of system weaknesses included:

- Change controls not raised for significant changes, such as new equipment, new processes, software version changes for critical systems, and headcount reduction
- Lack of effective tracking and oversight of ongoing change controls
- Risks that had been identified were not addressed before implementation of changes
- Failures and deviations during execution of validation testing were not assessed or addressed before implementation of changes
- No review after implementation of changes to determine whether the change had been effective, and also to confirm that the change had not adversely impacted on other activities

Self-inspection

Self-inspection is an important mechanism to identify weaknesses and implement improvements. Inspections have identified issues with audits not being performed and non-conformances not being recorded promptly. Where audits are not performed in accordance with the pre-determined programme, this should be documented in the quality system so that an investigation can be performed to assess the impact and determine the root cause.

Resourcing 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 the QMS. Where a shortfall is identified, senior management should take action to ensure sufficient resource will be made available. Job descriptions and organisation diagrams should be in place and made available to all staff.

It is expected that staff are trained in their duties, the QMS, and good practice. The effectiveness of training should be periodically assessed. Inspections identified overdue reassessment of laboratory staff as well as porters collecting and transporting blood components. An example was also noted of cleaners who were given unsupervised access to laboratory areas but who had not received GMP training. GMP awareness training for contract service providers including contract cleaners and transport providers is required as their work can have an impact on patient safety and component quality.

Failure to complete previous commitments

MHRA inspections are closed on the basis of the commitments given to address any deficiencies identified. Closure indicates that the inspector (or CMT/IAG if applicable) have accepted the commitments given; any delay or change to these commitments should be proactively communicated to the MHRA. Examples identified at inspection included significant delays to projects, failure to complete document reviews, and removing additional resources once the inspection was closed.

Failure to adhere to commitments given, or to proactively communicate changes to the MHRA, is seen as a high-risk factor as it can be indicative of a poor-quality culture in the organisation. In a number of cases this failure has led to the direct involvement of Chief Executive Officers (CEO) and an escalation to compliance management processes within the MHRA.

Data integrity

Poor documentation practice and data integrity was the most cited ‘other’ deficiency but was also cited in major deficiencies in a number of inspections. Examples included:

- False and misleading information was presented to the inspector, including falsified dates, images of signatures which had been applied by another party, and modification of screenshots. It should be noted that depending on the impact of the data, provision of false and misleading information can result in critical deficiencies being cited
- Poor documentation practices such as uncontrolled deletions, obliteration and overwriting in documents reviewed during the inspection, impeding the ability to reconstruct an activity from the available records
- No mechanism to ensure that staff were aware of changes in procedures at the time they became effective
- Legacy procedures still in place with no overall clarifying index or document to demonstrate which local QMS documents were regarded as live for the transfusion area
- Emergency login details for electronic systems were openly available

It is important to apply the basic ALCOA principle to all data, whether written or electronic. ALCOA means that data are Attributable, Legible, Contemporaneous, Original and Accurate.

Traceability

The expectation is that the fate of every unit of blood or blood component is known and documented. The traceability of blood components remains a concern, with a major deficiency cited for significant failures to ensure that the fate of all blood components was confirmed. Specific concerns included:

- Poor overall traceability compliance
- No clear plans or actions taken to address poor compliance
- Failure to escalate risks to the appropriate level in the organisation
- Ineffective systems to monitor traceability compliance, such as groups not meeting at the specified frequency
- Traceability compliance deteriorating during the implementation of an electronic traceability system

The final point above is an important reminder that introducing an electronic system cannot, in itself, solve issues with traceability compliance. The traceability system relies on adequate and timely resources, effective training, robust record keeping and an effective system for reporting and investigating non-compliance.

Security of blood components

Storage areas should provide properly secure and segregated storage. Examples of deficiencies in security included:

- Security bypass mechanisms being open for all users
- Electronic systems not being maintained to ensure that access rights were removed for users who had left the organisation, changed roles or were no longer up to date with their training

Laboratory operations

At a number of inspections, deviations were cited for operations in the laboratory which were not consistent with good practice. Examples included:

- No formal justification available for the sample preparation centrifuge speed adopted; in addition, procedures still referenced the previous speed
- Prepared solutions within the laboratory were ineffectively labelled to identify the contents, details of preparation, and expiry
- Cause of internal quality control (IQC) failures were not consistently documented

Changes for 2017–2018

Inspections for the reporting period 01 April 2017 to 31 March 2018 will be performed in the following year, i.e. from 01 April 2018 to 31 March 2019. In response to the compliance trends identified during 2016–2017, the MHRA have notified HBB of changes to the BCR and inspection programme.

Following the adoption of the Good Practice Guidelines for blood establishments into UK law, from 01 April 2018 the MHRA will inspect blood establishments and hospital blood banks against these guidelines. All deficiencies identified at inspections (including other deficiencies) will be referenced to these guidelines, and references to EU GMP will no longer be required.

Information and guidance

For further information on the 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.

Appendices

Appendix 24.1: Storage subcategories

Component expiry	A component has time expired and not been removed from the storage location according to laboratory procedures
Incorrect storage of component	A component has not been stored in the correct location
Sample expiry	A sample has expired and the component has not been removed from the supply chain for the original patient
Return to stock error	A component has been returned to the supply chain in error instead of being quarantined or discarded
Failure to action alarm	A storage location alarm has been activated but not actioned according to the procedure
Storage temperature deviation	The storage temperature has gone out of specification without an alarm being activated
Security	A storage location is accessible to staff or public who are not authorised to do so
30-minute rule	Red cells are returned to a refrigerator after 30 minutes have elapsed contrary to local procedures for return of unused red cells
Miscellaneous	Any other storage event affecting the quality and safety of blood or blood components

Appendix 24.2: Other subcategories

Incorrect blood component issued (IBCI)	Blood issued which does not meet the patient's specific requirements
Sample processing error (SPE)	Sample incorrectly receipted into the laboratory that should have been rejected
Component labelling error (CLE)	Typically, transposition of labels
Pre-transfusion testing error (PTTE)	Any error in the process of testing patient samples and the interpretation of results
Component collection error (CCE)	Any error in the collection of components from storage locations, or the handover of components on collection from the laboratory
Data entry error (DEE)	Transcription errors of data, including both electronic and hand-written data
Failed recall (FR)	Failure to recall components in a timely manner
Unspecified (UNSPEC)	Any error affecting the quality and safety of components not specified elsewhere
Component available for transfusion past de-reservation (CATPD)	Expired components which were incorrectly collected, prior to their scheduled re-stock by the laboratory
Expired component available for transfusion (ECAT)	Any component issued for a patient, where the component expires prior to the planned transfusion
Incorrect blood component ordered (IBCO)	Components ordered from a blood establishment that do not meet the patient's specific requirements
Handling damage (HD)	Damage to a component affecting its quality and safety
Incorrect blood component accepted (IBCA)	Blood accepted into a laboratory for a specific patient where the specific requirements have not been matched

Appendix 24.3: Human error subcategories	
Procedure performed incorrectly	Failure to carry out a step(s) correctly
Procedural steps omitted/wrong procedure performed	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	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
Inadequate supervision	Errors have been made by trainees or inexperienced members of staff and should have been noticed by adequate supervision

References

BSQR. Blood Safety and Quality Regulations. (SI 2005/50, as amended) http://www.legislation.gov.uk/uksi/2005/50/contents/made [accessed 3 April 2018].

EU: Summary of the 2016 annual reporting of serious adverse reactions and events for blood and blood components (page 12) https://ec.europa.eu/health/sites/health/files/blood_tissues_organs/docs/2016_sare_blood_summary_en.pdf [accessed 3 April 2018].

Good Practice Guidelines for blood establishments https://www.edqm.eu/en/good-practice-guidelines-blood-establishments [accessed 3 April 2018].