25 Medicines and Healthcare Products Regulatory Agency (MHRA) Report on Blood Safety and Quality Regulation in 2016

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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 (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 (IBCI) 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 Octaplas® (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
Total	**919**	**1226**	**1468**	**1438**	**1254**	**1274**	**1050**	**1110**	**1027**	**1492**

Table 25.1: Submitted SABRE confirmation reports 2007–2016

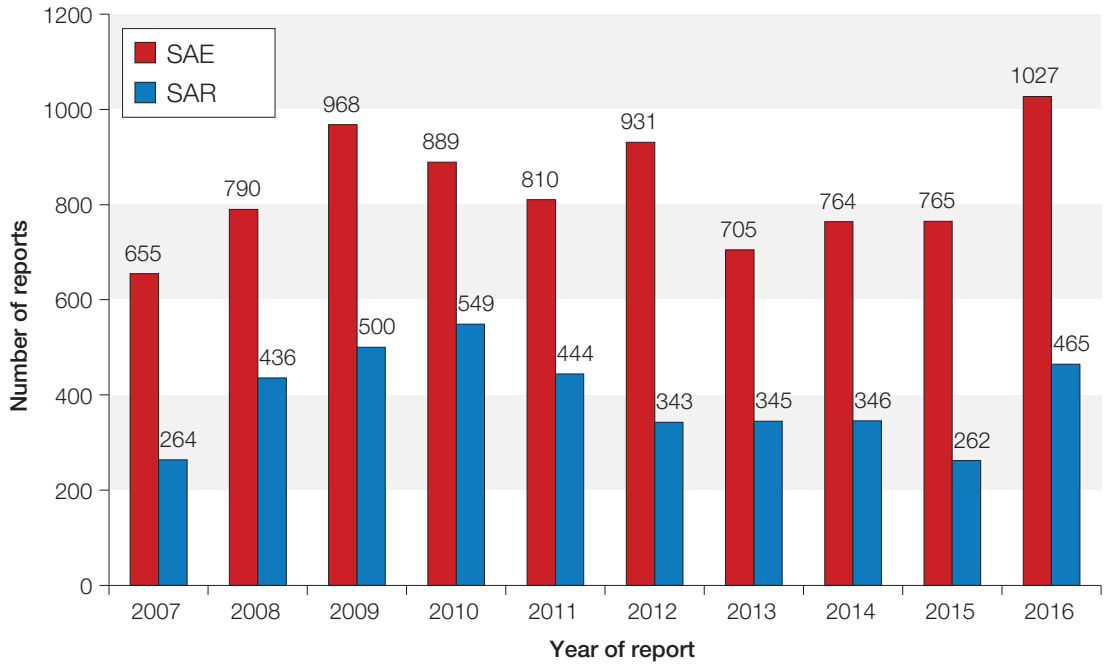


Figure 25.1: Submitted SABRE confirmation reports 2007-2016

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.

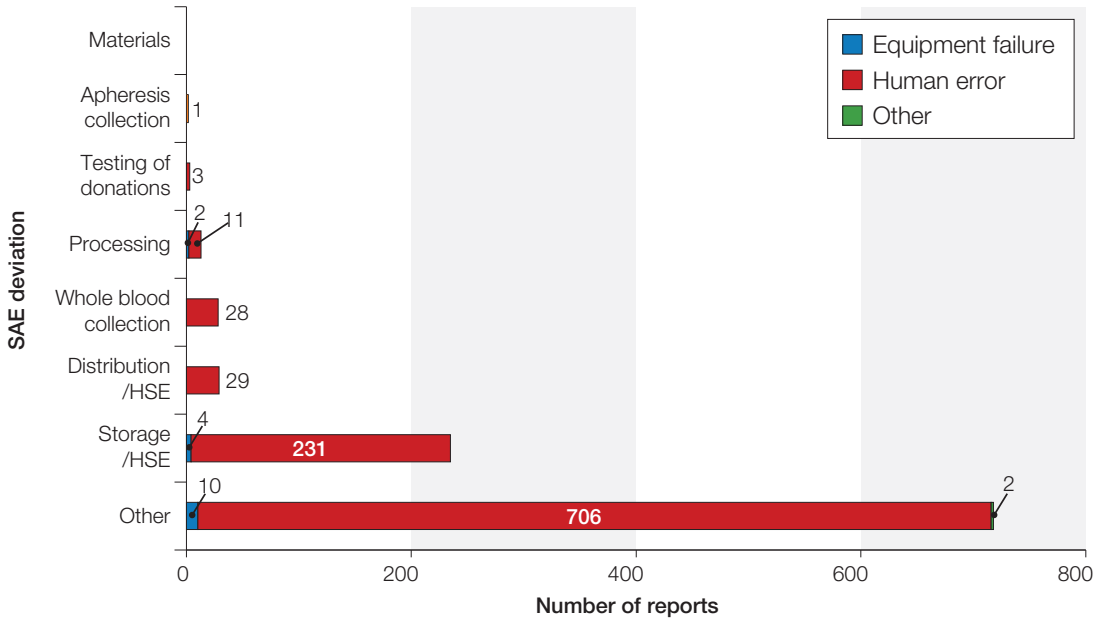
In 2015 approximately 2.7 million components were issued in the UK, with 765 SAE confirmation reports submitted to Europe. That represents 283 SAE per million components issued or 0.03%. In 2016 this has increased to 1027 SAE reports for approximately 2.5 million components issued, representing 411 SAE 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
Total	**235**	

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 7th most common storage SAE from the 3rd 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.

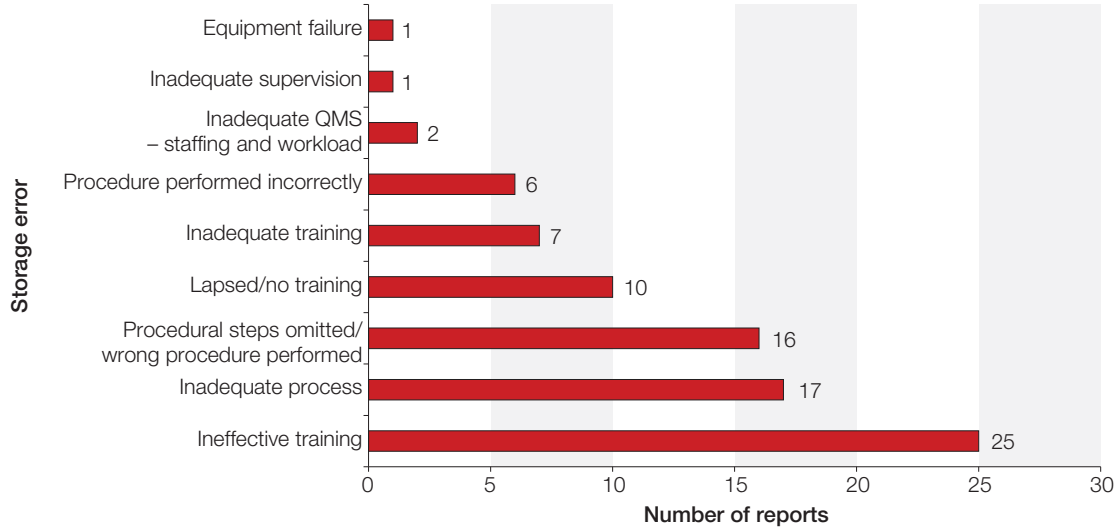


Figure 25.3: Incorrect storage of component by specification 2016

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 3rd 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.

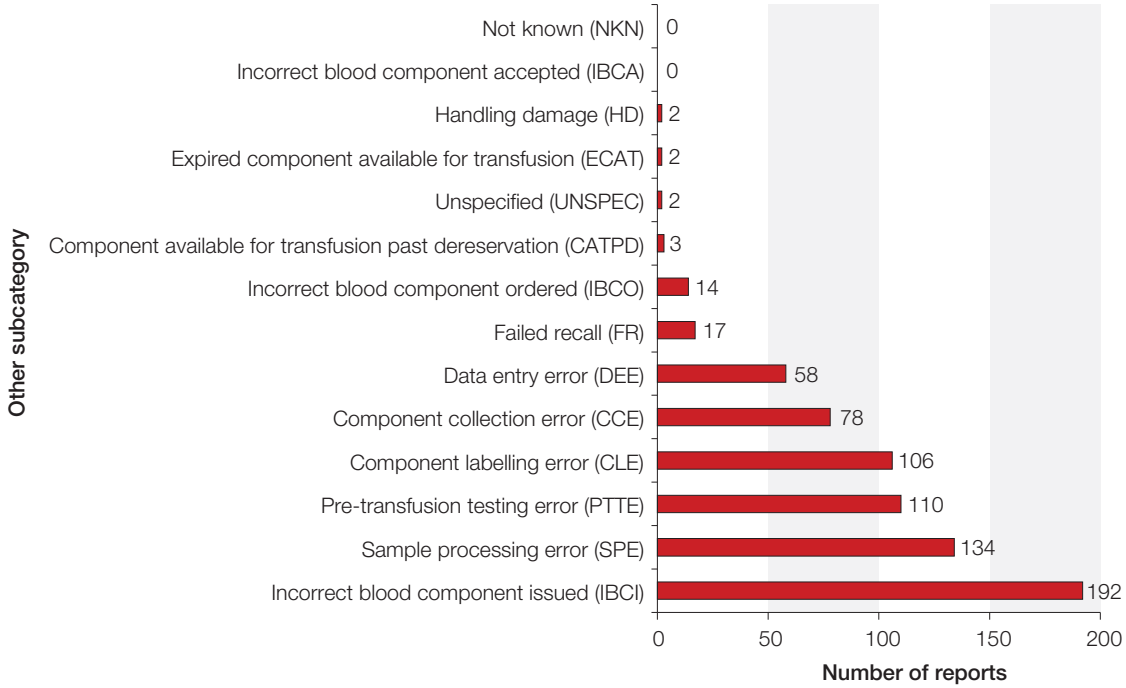
Other n=718

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=
Total	**718**	

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 sub-category. 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.

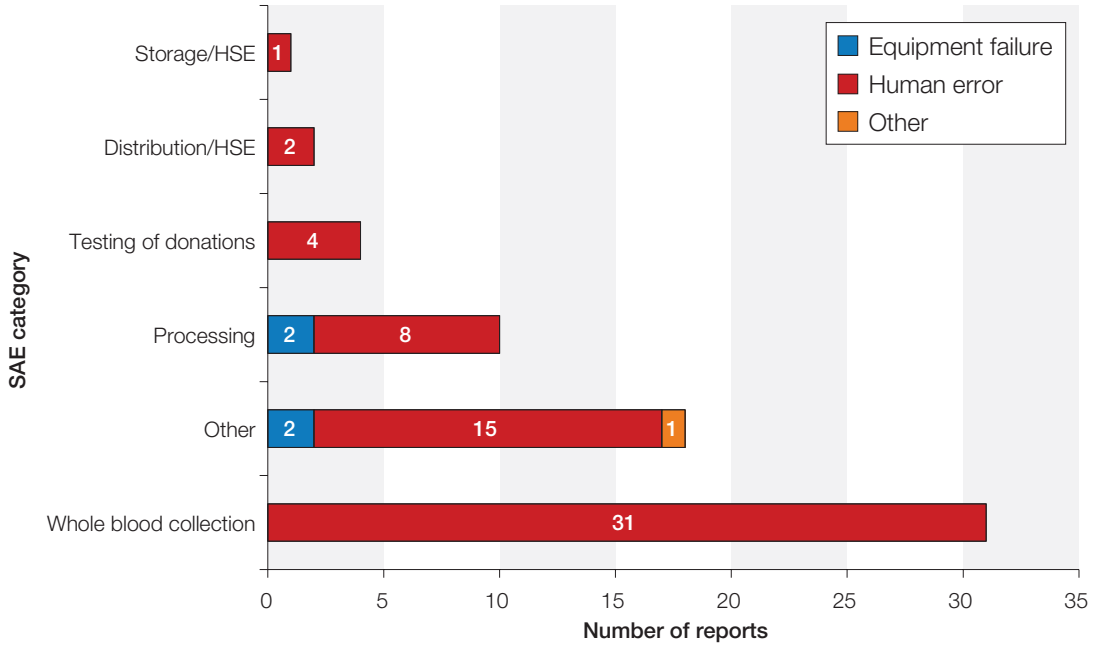


Figure 25.6: BE SAE category by specification n=66

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
SAR reports by imputability score	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 clarify 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

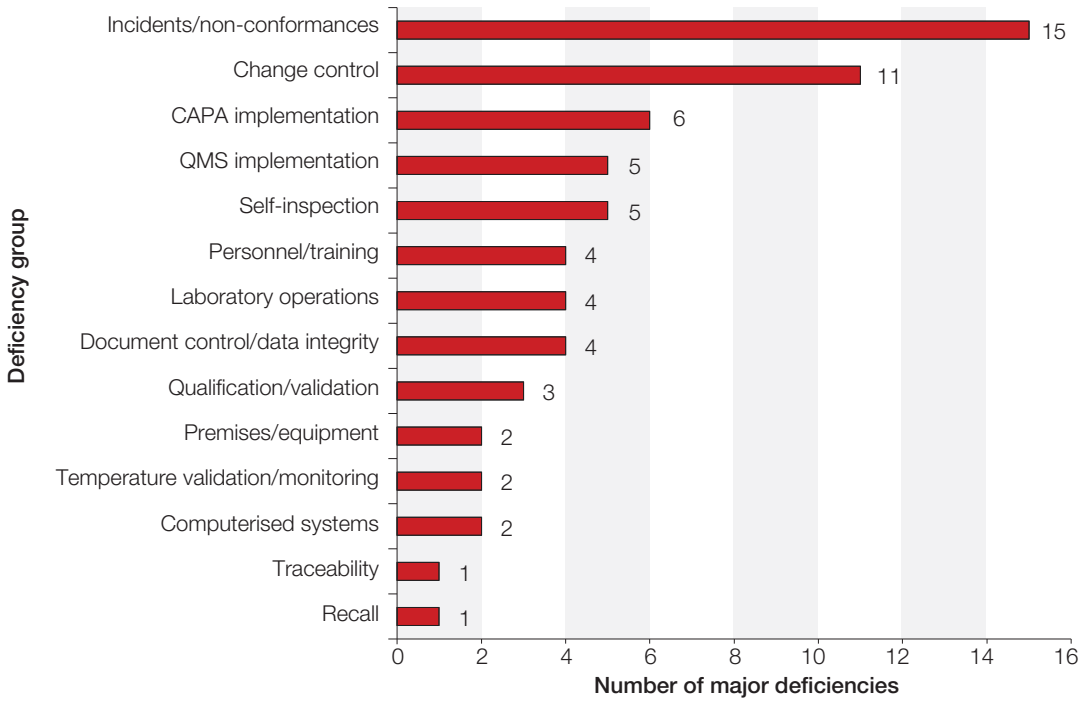
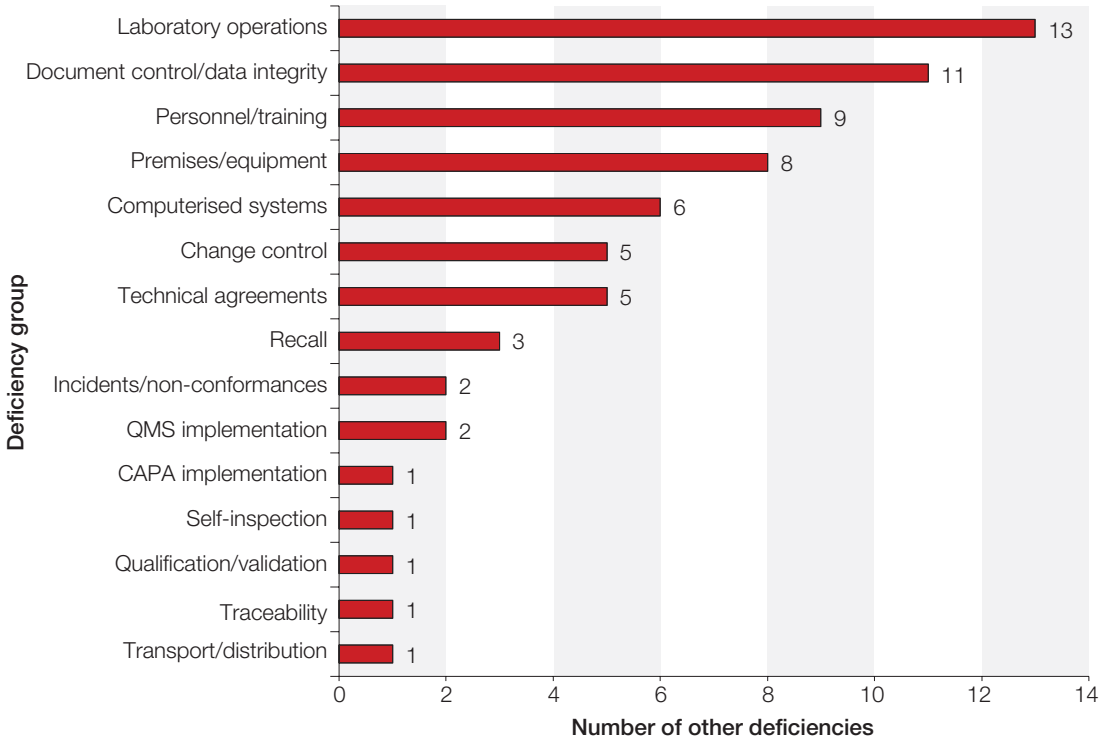


Figure 25.8: Other deficiency groups



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 trial
- 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