Medicines and Healthcare products Regulatory Agency (MHRA) Report on Blood Safety and Quality Regulation (BSQR) in 2019

26

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Key MHRA messages

- In accordance with the requirements of the good practice guide (GPG) (Council of Europe, 2018) reporting establishments must improve their formal arrangements for investigating deviations and non-conformances. Identifying human error as the root cause should be justified only after having ruled out other improvements to the quality management system (QMS)
- The Blood Safety and Quality Regulations (BSQR) cover both laboratory and clinical activity relating to the quality and safety of blood and blood components
- All staff involved in transfusion must work together to prevent errors at source and use resources appropriately. Detecting errors made in the clinical areas requires allocation of significant laboratory resource

Abbreviations used in this chapter

BCR	Blood compliance reports
BE	Blood establishments
BSQR	Blood Safety and Quality Regulations
BMS	Biomedical scientist
CAPA	Corrective and preventive action
CATPD	Component available for transfusion past de-reservation
CCE	Component collection error
CLE	Component labelling error
CMT	Compliance Management Team
CMV	Cytomegalovirus
DEE	Data entry error
ECAT	Expired component available for transfusion
EI	Electronic issue
EU	European Union
FR	Failed recall
GPG	Good practice guide
HBB	Hospital blood banks
HD	Handling damage
HSCT	Haemopoietic stem cell transplant
IAG	Inspection Action Group
IAT	Indirect antiglobulin test
IBCA	Incorrect blood component accepted
IBCI	Incorrect blood component issued
IBCO	Incorrect blood component ordered
IVDR	In Vitro Diagnostic Regulations
LIMS	Laboratory information management system
NBTC	National Blood Transfusion Committee
PTTE	Pre-transfusion testing error
QMS	Quality management system
RC	Root causes
RCA	Root cause analysis
SABRE	Serious adverse blood reactions and events
SAE	Serious adverse event
SAR	Serious adverse reaction
SOP	Standard operating procedures
SPE	Sample processing error
UNSPEC	Unspecified
URS	User requirement specification

Summary

An increase in the number of serious adverse reaction (SAR) reports has increased the total number of reports confirmed to the MHRA on the serious adverse blood reactions and events (SABRE) system in 2019. Assessment of the serious adverse event (SAE) reports has demonstrated a reduction in SAE that have resulted from hospital blood transfusion laboratories, but an increase from blood establishments (BE) and hospital areas outside of the laboratory. Assessment of the root causes (RC) has demonstrated an increase in the number of reports where improvements to the QMS have been identified and a reduction in the numbers where staff have been made solely accountable for slips and lapses. All data correct as of 22nd January 2020.

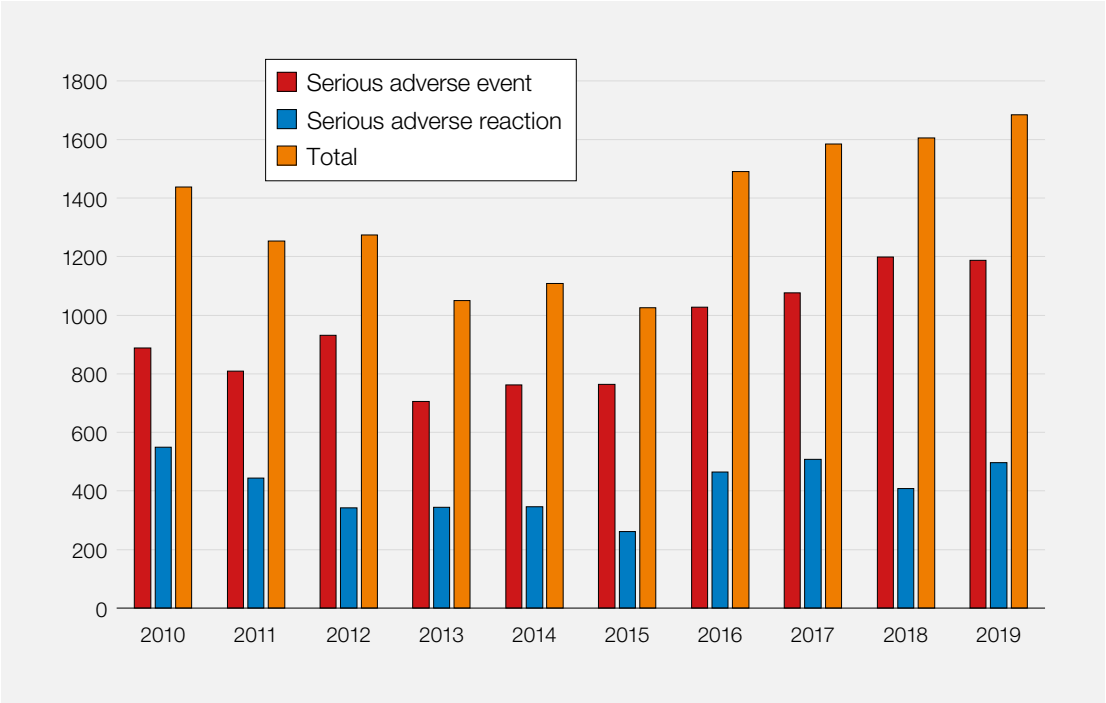
SABRE report data

Table 26.1 and Figure 26.1 display the total number of confirmation reports that were submitted and satisfy the European Commission reporting criteria for SAR and SAE since 2010. Since even old data are live, and subject to amendment, the table has been updated to reflect changes made to historic reports.

Table 26.1: Submitted confirmation reports 2010–2019

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019
SAE	889	810	931	705	762	764	1027	1076	1198	1187
SAR	549	444	343	345	346	262	464	508	408	497
Total	**1438**	**1254**	**1274**	**1050**	**1108**	**1026**	**1491**	**1584**	**1606**	**1684**

Figure 26.1: Submitted confirmation reports 2010-2019



There has been a minor increase in the total number of reports received by the MHRA that qualify for onward reporting to the European Union (EU) (5%) in 2019. However, the number of SAE reports received has remained static with the increase coming from a rise in the number of SAR reports submitted. The MHRA receive SAR confirmation reports from SHOT following expert review.

Serious adverse events n=1187 (-11)

Definition: (BSQR 2005) 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.

The MHRA works closely with reporters when assessing SAE reports. If the initial investigation and report appears not to have identified or addressed the RC and contributory factors or identified appropriate and robust corrective and preventive action (CAPA), the SABRE team will discuss areas for improvement with the reporter. In many cases, working together with reporters has identified RC that had not been considered. Once the true RC have been identified, more robust CAPA can be proposed which will improve the QMS.

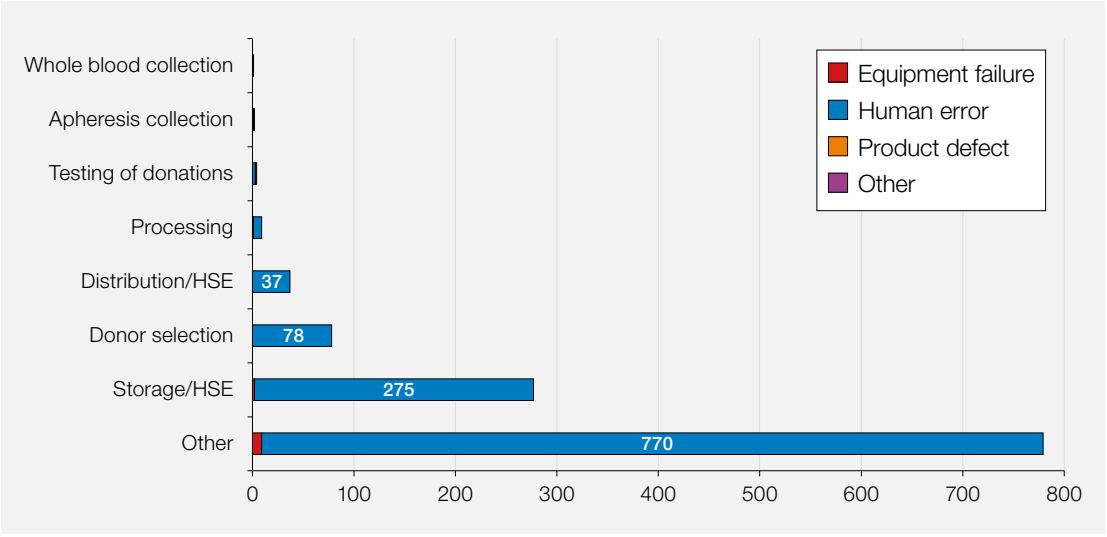


Figure 26.2: 2019 SAE confirmation reports by deviation and specification

HSE=handling and storage errors

Numbers too small to be annotated on the figure: Whole blood collection: human error=1; Apheresis collection: human error=1, other=1; Testing of donations: human error=3, product defect=1; Processing: equipment failure=1, human error=8; Storage/HSE: equipment failure=2; Other: equipment failure=9

The number of SAE reports and type of reports have remained similar. There is an increase in the number of storage SAE and a reduction in the number that fall into the 'other' categories.

Storage data n=277 (+25)

Storage remains the second largest individual error category and comprises of all BSQR reportable storage SAE in both the laboratory and clinical areas. The MHRA has broken this category down further to try and identify specific storage error subtypes, Table 26.2. For a description of the sub-categories used, see Appendix 26.1.

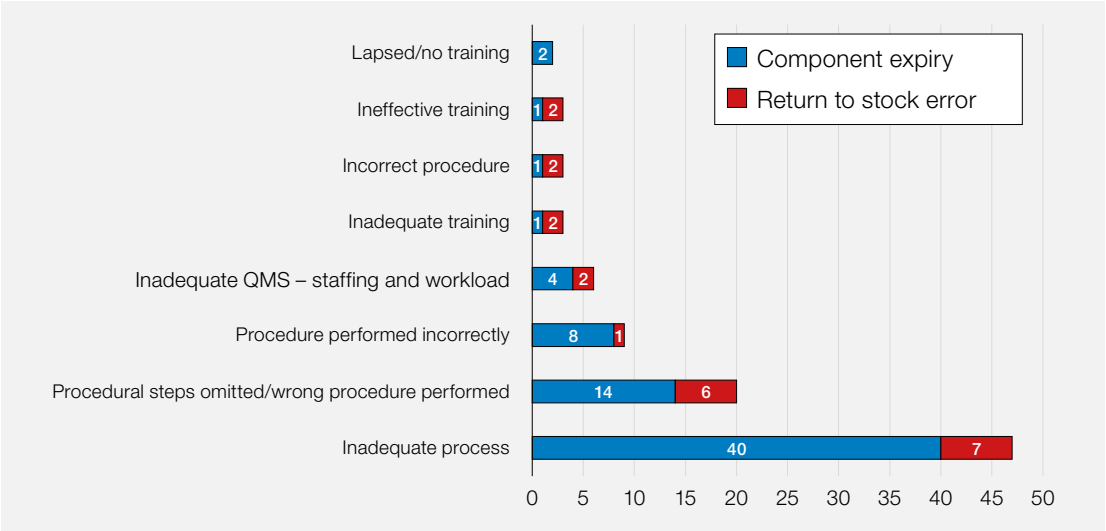
Storage sub-classification	2019 (+/- 2018)	2018 position
Incorrect storage of component	102 (+4)	1
Component expiry	71 (+14)	2
Sample expiry	39 (-2)	3
Return to stock error	22 (+14)	6
Storage temperature deviation	15 (-3)	4
Failure to action alarm	12 (+1)	5
Miscellaneous	8 (+2)	8
Security	5 (NC)	9
30minute rule	3 (-5)	6
Total	**277 (+25)**	

Table 26.2: SAE storage error sub-classifications

NC=no change

The number of reports has increased by approximately 10%. Most of these increases are in the component expiry and return to stock sub-categories. Although typically laboratory-based activities, there may be some element of error outside the laboratory, e.g. clinical areas not completing storage records correctly or not returning expired or expiring components according to agreed procedures.

Figure 26.3: Human error sub-categories of the two most increased storage errors



QMS=quality management system

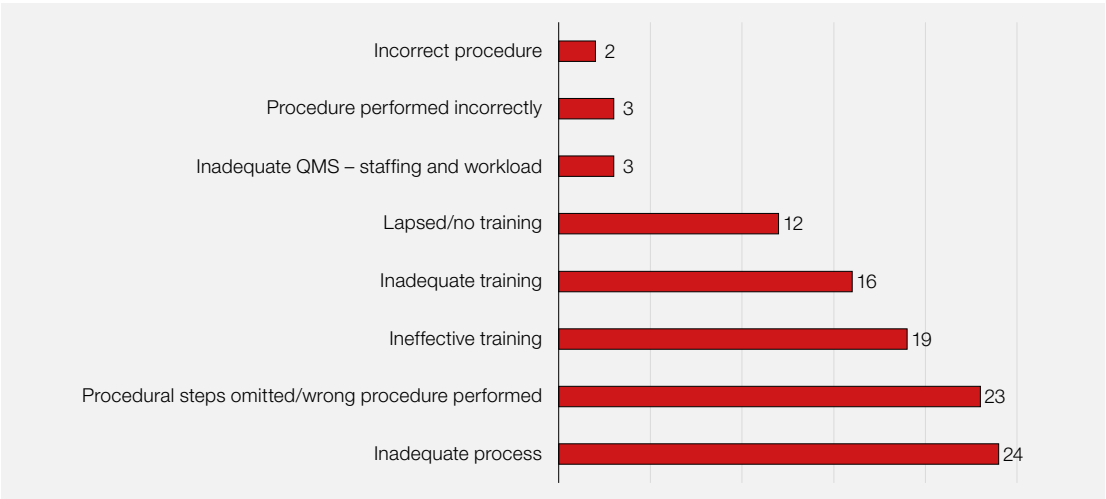
Analysis of the human error sub-category for these errors shows that over half of all the reports demonstrate inadequate process. The MHRA defined 'human error' category can be found in Appendix 26.3.

Recommendations

- Improve the design of processes used to identify and quarantine expired components, preventing them being used
- Improve the design of the processes used to capture storage data and verifying components are suitable to return to the supply chain

Action: Hospital transfusion teams

Figure 26.4: Incorrect storage of component by specification



QMS=quality management system

Although the storage of components occurs in both the laboratory and clinical areas, most of the errors in this category occurred outside the laboratory setting. Typical examples of error are;

- Components stored in unmonitored drug refrigerators
- Components stored in decommissioned blood refrigerators
- Components stored at the incorrect temperature
- Errors often involve untrained staff including bank and locum staff

Investigation of these errors has demonstrated various causes and factors.

Recommendations

- Improve the design of processes involved in storage and quarantine of components. This includes arrangements for when storage equipment is temporarily decommissioned
- All staff involved in handling and storage of components must be appropriately trained to do so
- Ensure staff are identified for training, that training material is thorough and that staff competencies are assessed and updated frequently
- Ensure new, locum and bank staff are informed of storage arrangements before they can handle blood

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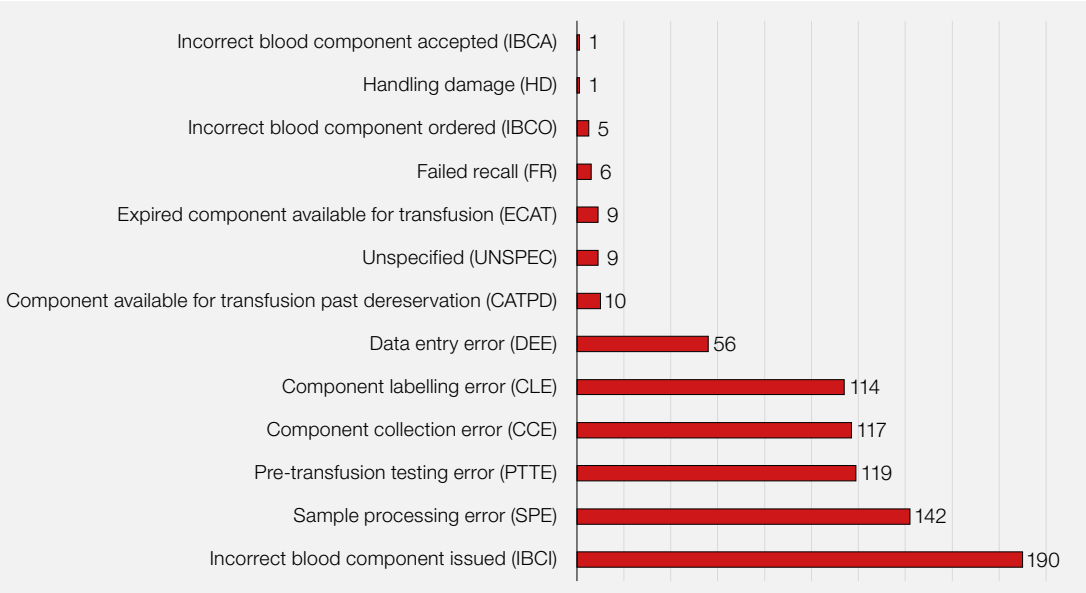
Other n=779 (-58)

Since 'other' is the largest category of SAE reports, the MHRA haemovigilance team has created sub-categories to further analyse this type of error, Table 26.3. For a description of sub-categories, see Appendix 26.2.

Table 26.3: 'Other'

Other sub-category	2019 (+/- 2018)	2018 position
Incorrect blood component issued (IBCI)	190 (-22)	1
Sample processing error (SPE)	142 (-43)	2
Pre-transfusion testing error (PTTE)	119 (+26)	5
Component collection error (CCE)	117 (+3)	4
Component labelling error (CLE)	114 (-17)	3
Data entry error (DEE)	56 (-17)	6
Component available for transfusion past de-reservation (CATPD)	10 (+4)	7
Expired component available for transfusion (ECAT)	9 (+4)	10
Unspecified (UNSPEC)	9 (+4)	9
Failed recall (FR)	6 (NC)	7
Incorrect blood component ordered (IBCO)	5 (+1)	11
Handling damage (HD)	1 (-1)	12
Incorrect blood component accepted (IBCA)	1 (NC)	13
Total	**779 (-58)**	

Figure 26.5: 'Other'



There has been a 7.5% reduction in the number of reports in the 'other' category. Except for component collection errors, the errors in the 'other' category are typically laboratory-based. The data show improvements to;

- Selection of components for issue meeting specific requirements
- Rejection of incorrect samples and forms
- Entry of data, particularly when registering new patient details
- Labelling of components

However, there has been an increase in pre-transfusion testing errors. Analysis later in this chapter will show that the most commonly occurring PTTE errors are due to inadequate process design and ineffective training, possibly relating to the education of new staff.

Although work still needs to be done to reduce SAE further in transfusion laboratories, it should be noted, with cautious optimism, the reduction is SAE associated with the regulated activities of transfusion laboratories.

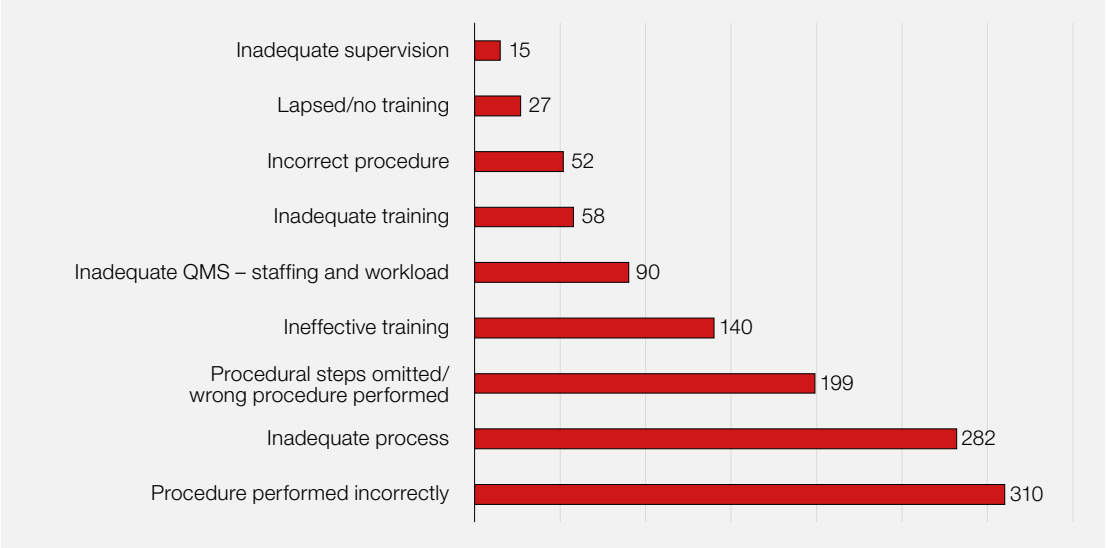
Human error category and human factors

To understand reports in the human error category, the MHRA have continued to use sub-categories which can be applied to the report narratives to help understand the human factors involved. For a description of the categories used, see Appendix 26.3. Table 26.4 shows the breakdown of reports in the human error subcategories.

Table 26.4: Human error sub-category, 2019

Human error sub-category	Total 2019 (+/- 2018)	2018 position
Procedure performed incorrectly	310 (-50)	1
Inadequate process	282 (+69)	3
Procedural steps omitted/wrong procedure performed	199 (-51)	2
Ineffective training	140 (+14)	4
Inadequate QMS – staffing and workload	90 (-8)	5
Inadequate training	58 (+1)	6
Incorrect procedure	51 (+16)	7
Lapsed/no training	27 (+5)	8
Inadequate supervision	15 (+1)	9
Total	**1173 (-3)**	

Figure 26.6: Human error sub-category



NOTE: These numbers should be used as guidance only. The quality of this data is limited by several factors.

QMS=quality management system

- The RC of incidents are usually the result of many contributory factors. The sub-category chosen reflects the most likely reason for the main SAE category. However, this year, if multiple factors are involved relating to the QMS, then 'inadequate process' has been chosen as the sub-category rather than choosing a category that best fits the main SAE reported
- The sub-category 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 sub-categorised appropriately

In last year's chapter it was pointed out that many reports lacked detail and indicated that staff were solely responsible for errors. It was stated that poor quality investigations and RC analyses could have given the wrong impression about the factors behind why errors were occurring. Much work has been done in helping transfusion professionals improve the quality of their investigations during training and education days and at the 2019 SHOT Symposium. The presentation can be found here http://forums.mhra.gov.uk/showthread.php?4150-Incident-reporting-presentation.

The data show that there has been a reduction in those SABRE reports which have been interpreted as slips and errors by individual members of staff. Increases in categories that relate errors to processes, procedures and training demonstrate that improvements to QMS have taken place. It is hoped that reduction in the number of SAE in this category is a direct result from improvements to QMS identified through better investigations and the identification of the true RC and robust CAPA.

Recommendations

- Continue to improve the quality of investigations and incident reporting
- In accordance with the good practice guide (GPG), if human error is determined to be the root cause, this must be justified having ruled out improvements to other areas of the quality management system (QMS)
- Before concluding that an error is due to an individual, consider if the workload, staffing, skill-mix and working environment and conditions led to the behaviour that caused the error

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Top 5 SAE

Slips and lapses account for 44% of the SAE reported. Assessment of the other 56% of QMS errors provides the top 5 areas where errors occur, and improvement is required.

SAE deviation sub-category	Specification sub-category
Incorrect blood component issued (IBCI)	Inadequate process
Component collection error (CCE)	Ineffective training
Pre-transfusion testing error (PTTE)	Inadequate process
Incorrect blood component issued (IBCI)	Ineffective training
Pre-transfusion testing error (PTTE)	Ineffective training

Table 26.5: Top 5 SAE with human error sub-category

The following examples have been used to illustrate what might be considered effective CAPA to address the RC. 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 designed to focus on improvements to systems, practice and transfusion laboratories.

1) Incorrect blood component issued (IBCI) – inadequate process (n=59)

Case 26.1: Patient requiring irradiated blood post auto haemopoietic stem cell transplant (HSCT) transfused with non-irradiated blood

The laboratory information management system (LIMS) contained two records for the patient, only one of which had an alert flag for irradiated blood components recorded against it. Sample received and booked in against the patient record with no alert flag. Verbal request later received for red cells and non-irradiated red cells selected and transfused.

Duplication of records was not identified in the laboratory and irradiated blood requirements not identified from the clinical details of previous samples.

There was no indication that irradiated blood was required on the group and screen request form or the transfusion prescription chart. Staff performing the bedside checks were not aware that the patient required irradiated components.

Recommendations

- The laboratory must have processes in place to create records that avoid duplication and to merge records according to defined and documented processes
- Where a laboratory has access to data regarding the specific requirements of a patient, these records may be held in various formats in both hard and electronic copy. Traceability between the formats must be maintained

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2) Component collection error (CCE) – ineffective training (n=33)

Case 26.2: Adult emergency blood that was not cytomegalovirus (CMV)-negative taken instead of paediatric emergency blood

A nurse who was new to the hospital was asked to collect the 'infant flying squad blood'. Despite having been trained, the nurse thought that 'infant flying squad blood' was for helicopter use and removed an adult unit.

Recommendations

- Whether involving new or agency staff, ensure they are thoroughly trained in any collection procedures
- Ensure that the training covers all terms and types of component in use, as new staff will be unfamiliar with local procedures and used to procedures elsewhere

Action: Hospital transfusion teams

3) Pre-transfusion testing error (PTTE) – inadequate process (n=27)

Case 26.3: LIMS allowed electronic issue (EI) when the analyser transferred a blank result

The antibody result on the blood grouping analyser could not be deciphered as positive or negative. A blank entry in the LIMS was transferred and allowed the EI of blood without a valid antibody result.

It was unclear if the LIMS set up was incorrect from its installation or following an upgrade. It was clear that initial validation and subsequent re-validations were not adequate.

Recommendations

- Introduction of new equipment, software and processes, including upgrades and amendments must be adequately managed through change control processes
- Validation and qualification of LIMS and processes must be robust to ensure that the equipment performs as intended

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4) Incorrect blood component issued (IBCI) – ineffective training (n=22)

Case 26.4: Incorrect patient blood group issued during LIMS downtime

A patient grouped as group O D-negative, but a unit of group O D-positive was selected for indirect antiglobulin test (IAT) crossmatch in error during LIMS downtime. Investigation showed that there was unfamiliarity with the downtime process and confusion over the correct procedures and checks.

Recommendations

- Consideration should be given to more frequent refresher training in processes that are less often performed, or processes performed by staff who spend less time in transfusion
- Consideration should be given to practicing emergency and downtime processes
- Procedures must be clear and unambiguous
- Staff must consult standard operating procedures (SOP) if unsure or unfamiliar with a process instead of assuming or improvising

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5) Pre-transfusion testing error (PTTE) – ineffective training (n=19)

Case 26.5: Incomplete antibody identification leading to transfusion of incorrectly selected red cells

Two red cells were requested for a patient with known antibodies requiring a full crossmatch. Two different panels were completed out-of-hours, and two units crossmatched and issued. The next day another biomedical scientist (BMS) checked the results and noticed a reaction in another cell that had not been noticed previously. Another panel was completed, and a new antibody identified.

Although trained and competency assessed six months previously, the initial BMS had not followed the correct procedure and had omitted to annotate the antigram with a conclusion. CAPA required their re-training with the laboratory manager.

The investigation also demonstrated several other factors which may have contributed to the actions of the BMS. Long term vacancies disrupted their training where the manager had been required to cover shifts. The testing in this incident should have been conducted during the day and not out-of-hours. CAPA also identified in the report included filling staff vacancies with locums until full-time staff employed.

Recommendations

- Ensure training is planned adequately to ensure staff fully understand processes and procedures before they are assessed as competent to work alone
- If long term vacancies are impacting the laboratory's ability to function, this must be flagged to senior management and resolved as soon as practicable
- All training must include a robust competency assessment to ensure competency of individuals both during routine and out-of-hours

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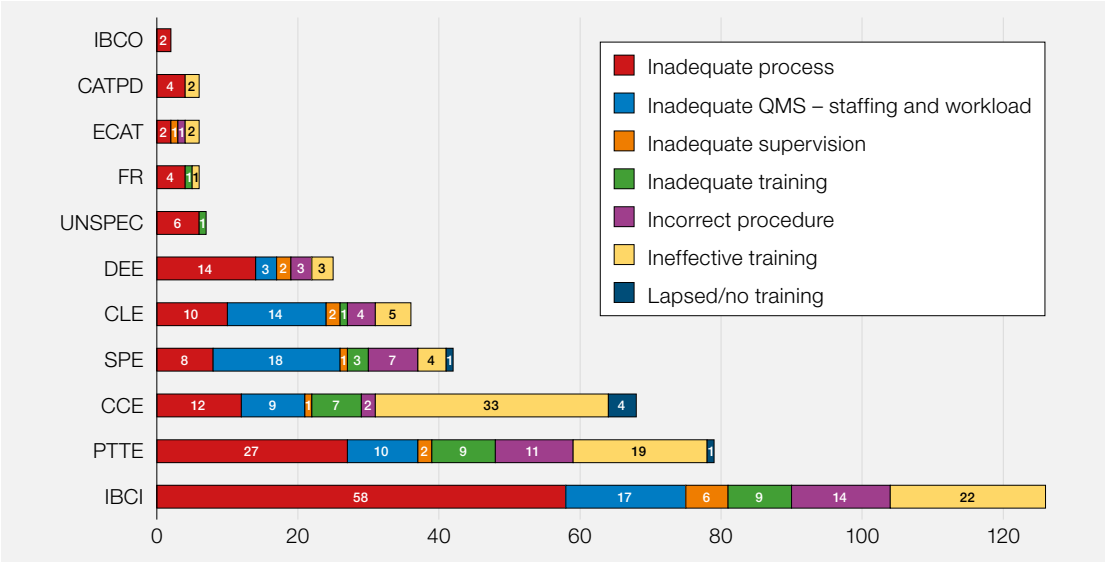
Figure 26.7: Other Sub-category and root cause for all SAE other than procedural steps omitted/wrong procedure performed and procedure performed incorrectly

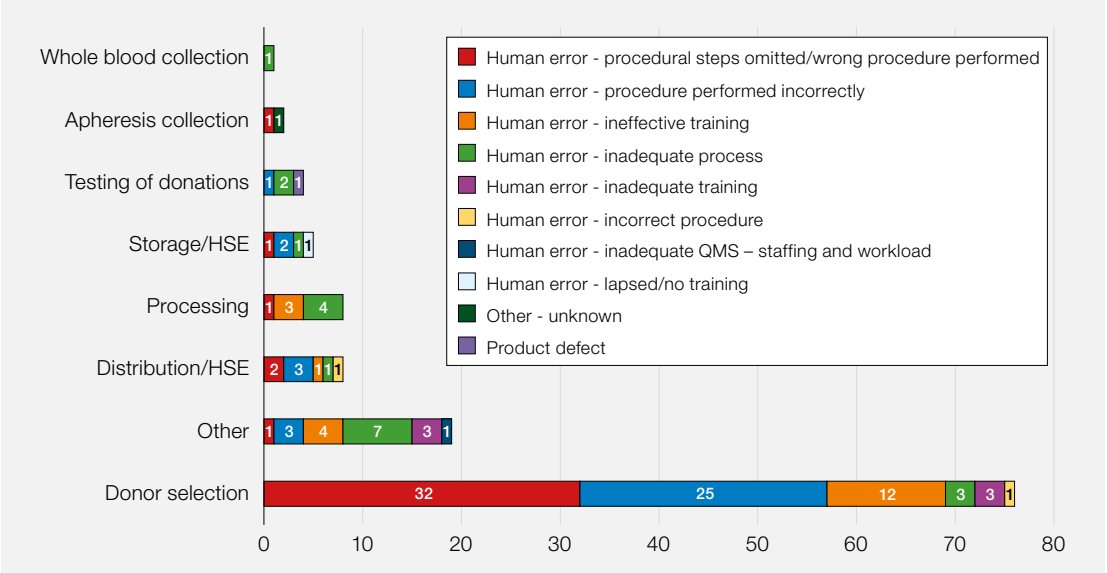


See Figure 26.5 for key to category abbreviations

Blood establishment reporting n=123 (+24)

Although reports from BE are included in the main analysis, the specific nature of the SAE reports from BE are lost in the greater numbers of reported hospital transfusion laboratory SAE. Figure 26.8 displays the reported BE SAE in 2019.

Figure 26.8: Blood establishment SAE event category by specification



HSE=handling and storage errors; QMS=quality management system

There has been an increase in the number of reports from BE, the majority being in the donor selection category. It is interesting to note that most of these reports originate from one country. These errors are usually picked up by the QMS before blood is issued which may account for the low numbers of these types of error reported by the other three UK BE. Assessment of these reports do not demonstrate significant weaknesses of the process but rather a healthy and open reporting culture. Reporting these errors has allowed that BE to demonstrate improvements to its training in donor selection.

Assessment of the 'other' category, Figure 26.9, shows that BE are also reporting errors associated with the selection of components and pre-transfusion testing, but assessment of the CAPA demonstrates improvements have been identified in process design and training.

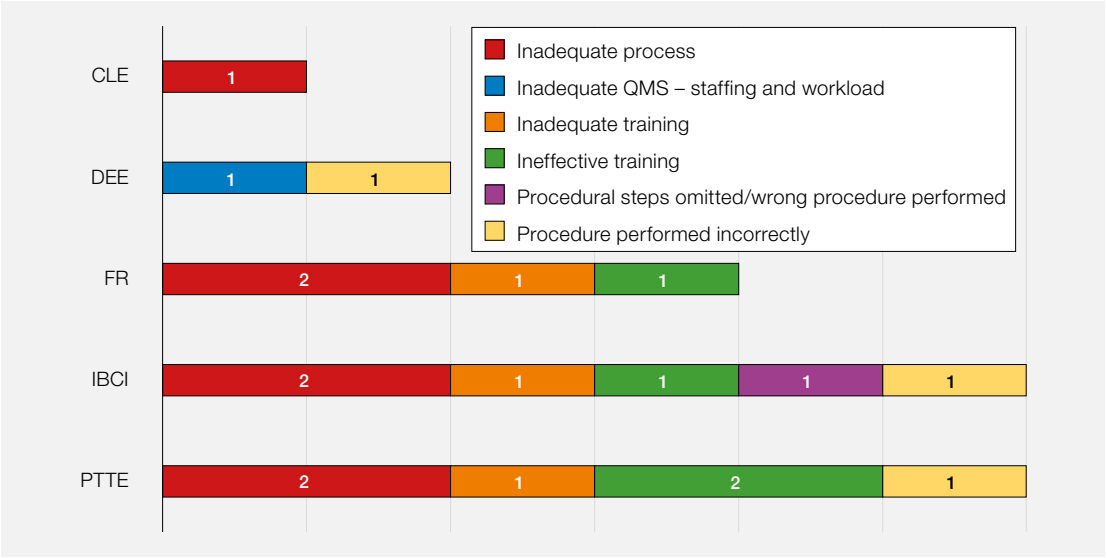


Figure 26.9: BE reports in 'other' category

See Figure 26.5 for key to category abbreviations

Comment from Julie Staves, Chair of the National Blood Transfusion Committee (NBTC) Laboratory Managers' Working Group

It is pleasing to see that once again the transfusion laboratory community continue to ensure appropriate adverse incidents are reported through the correct processes to MHRA and SHOT. This is of particular note given that laboratory staffing is an ongoing area of concern.

The reduction in SAE resulting from the laboratory is a positive result. It is also of note that there has been an increase in the identification of improvements to the QMS which resulted from investigations which is indicative of better knowledge of investigation processes which was highlighted as a concern in the previous Annual SHOT Report.

The ongoing problems seen in the errors occurring in returning units to stock and in components being available to the clinical area after they have expired is worrying, and reviewing the processes involved should be a priority.

Serious adverse reactions (SAR)

Definition: (BSQR 2005) 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).

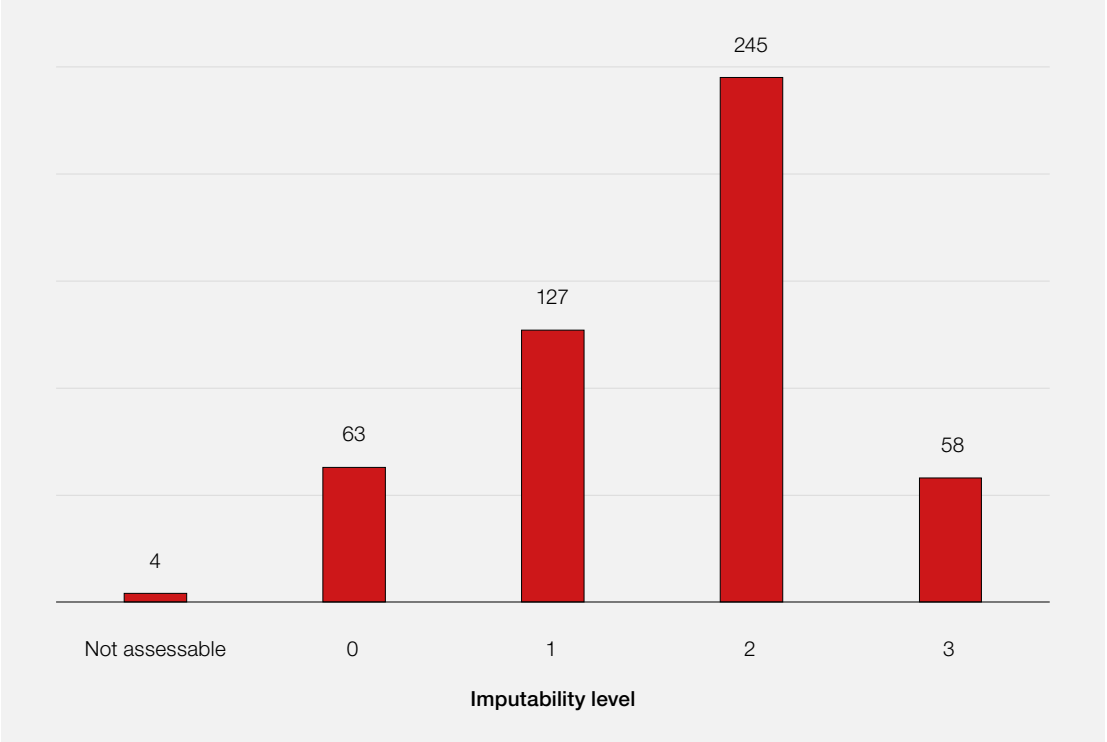
Summary of SAR report data

To avoid any confusion, the MHRA will only supply, in this Annual SHOT Report, total SAR figures reported to Europe, see Table 26.6

Table 26.6: SAR reports, by imputability, 2019 (n=497)

	Imputability score				
	0	1	2	3	N/A
SAR reports by imputability score	63	127	245	58	4

Figure 26.10: SAR reports, by imputability, reported to SABRE in 2019



Haemovigilance team managers update 2019/20

Author: Mike Dawe

The responsibilities of the post are designed to support the transfusion community in all aspects of the regulatory process that the competent authority is responsible for at all levels, of the transfusion management chain whilst ensuring the MHRA remain impartial.

2018-2019 activity

Activity	Number
HBB, BE, RTC/laboratory managers/TP meetings	20
Manufacturers	6
Education days	7 (4 further days arranged for early 2020)
Total	**33 (37)**

RTC=regional transfusion committee; TP=transfusion practitioner

Findings and recommendations

The following observations have been noted:

Lack of available capacity and knowledge to balance operational need with MHRA compliance

Sections 1.2.2, 1.2.5 and 2.2 of the GPG underpins the fact that personnel are a central cog in the management of every QMS, and as such the management has the ultimate responsibility for providing resource that is fit for task to ensure business continuity by developing an adequate capacity plan.

A capacity plan must be in place to demonstrate that staffing levels are sufficient to cover the workload, that not only includes out-of-hours shifts, but also the effective implementation, development and management of an effective QMS. Where a shortfall is identified, senior management should take action to ensure sufficient resource is made available. To achieve this, sites must map their processes so the component parts can be identified, and the relevant internal and external pressures and relationships can be established.

Manufacturers not meeting a site's needs

The Haemovigilance Team Manager has engaged with manufacturers to help them understand their role in sites meeting their regulatory requirements highlighting that a collaborative approach, between the manufacturer and the site, is key to maintaining and developing an effective QMS.

The following issues have been identified but are not limited to:

1. LIMS systems upgrades and patches being installed without an appropriate explanation and assessment of their impact – failing to adequately assess the full impact has shown a detrimental effect on a sites compliance. Examples of this include but not limited to:
   - An increased burden on available resource and business continuity by sites being forced into deviating from normal procedures via the introduction of additional and extra steps
   - Users being unaware of the duplication of patient records allowing for special requirement flags not being met and altering the EI algorithm allowing for the inappropriate EI of units to patients
2. Analysers not meeting the users expectations and as a result secondary processes and systems being introduced within the operation process flow – introducing secondary systems, although not necessarily inappropriate, can raise other issues. For example breaking the electronic chain for patients to qualify for EI, causing a deviation from routine procedures putting pressure on available resource as these deviations must be documented, carefully investigated for causative factors of any defect and, where necessary, followed up by the implementation of CAPA to prevent recurrence

If an error/deviation is the fault of the analyser/LIMS then the laboratory will be expected to show a detailed examination, root cause analysis (RCA), risk assessment and CAPA has been made and implemented. To achieve this, it may require close collaboration with the manufacturer to resolve any issues that are found as software and/or technical changes may need to be made. In most circumstances these changes can only be made by the manufacturer but must stay in line with the sites business processes.

Sites are reminded that LIMS/software manufacturers must provide clear and unambiguous release notes for every version of any upgrade so the site can assess its impact in line with good practice principles. These release notes must be made readily available so the appropriate assessment of their impact can be made, and the associated risks mitigated. This includes all version upgrades i.e. if a site has version 1 and upgrades to version 3 then the manufacturer must provide the release notes to both 2 and 3 before version 3 is installed so an appropriate change control and validation process can be achieved.

Sites are reminded that to avoid these issues, they should:

1. Process map their systems, so they know the component parts and their relationships within the whole QMS
2. Create a detailed user requirement specification (URS) that captures everything within the business process and reflects a site's operational outputs i.e. levels of false or unexpected results

3. Agree contracts that cover

- Expected and unexpected downtime periods
- Expectation on a manufacturer regarding level of detail within release notes for upgrades and software changes
- Regular review of the contract to assess if allowances have been made for QMS changes as a result of any lifecycle change of a sites business and operational processes

This list is not exhaustive but further relevant information can be found in the GPG sections 4.7. Control of equipment and materials and 8 Outsourced activity management.

- A lack and loss of experienced staff in good practice principles

As a response for more widespread support to the transfusion community the haemovigilance team offers education days for the transfusion community to provide advice and help within the regulatory framework. Please contact mike.dawe@mhra.gov.uk or chris.robbie@mhra.gov.uk for further details.

- Delays to SABRE investigations

There is an increasing concern where SABRE confirmation reports have been delayed because of the Trust taking over the investigation process, some reports have been delayed by over 6 months. In cases like these reporters are reminded to provide an update via a footnote, in the SABRE report, that includes:

- What the immediate mitigation/action that has been put in place to ensure, at least in the short term, a repeat error does not occur
- That an interim report be submitted within 30 days to inform the MHRA of progress
- An explanation as to why the investigation final report has been extended and delayed based on good practice principles
- An appropriate assessment of the risk and the mitigation that has been put into place due to the extension of the investigation

Sites are reminded that the following section of the BSQR is relevant in this situation and as such sites must comply.

(3) A person responsible for management of a reporting establishment shall ensure that the reporting establishment notifies the Secretary of State as soon as is known, using the notification formats set out in Section A of Part 8 of the Schedule, of all relevant information about serious adverse events which may put in danger donors or recipients other than those directly involved in the event concerned.

(4) A person responsible for management of a reporting establishment shall ensure that the reporting establishment—

(a) as soon as is reasonably practicable after each serious adverse event, evaluates that serious adverse event to identify preventable causes within the process;

(b) upon completion of the investigation, completes the serious adverse event notification, using the format set out in Section B of Part 8 of the Schedule;

Section A and B of part 8 of the schedule relating to the Notification and Confirmation reports on SABRE respectively.

BSQR and medical device regulations

BSQR 2005 as amended does not specifically cover medical devices, however there may be overlap if a medical device impacts BSQR compliance. To achieve an appropriate and compliant solution sites must have a proper understanding of how medical device regulation and BSQR's work together within the regulatory framework.

It is also important to remember that sites must report the failure of any medical device to the MHRA via the Yellow Card Scheme through the following link https://yellowcard.mhra.gov.uk/.

In addition, sites and manufacturers must be aware that the new In Vitro Diagnostic Regulations (IVDR) are being introduced in 2022 and this means that some software will now be regulated under these new regulations and therefore include some elements of LIMS and analyser software.

It's not the full LIMS system that will be included but rather those algorithms (modules) used to determine a result used for direct patient treatment decision points such as AKI, Warfarin dosing and EI to name just a few. These algorithms will therefore need a CE Mark.

The link to the new regulations is: https://www.gov.uk/guidance/medical-devices-eu-regulations-for-mdr-and-ivdr.

To help you identify if certain algorithms/modules fall under the IVDR then the following link to a flowchart (https://www.gov.uk/government/publications/medical-devices-software-applications-apps) can be used, and if that doesn't give an answer, then MHRA might be able to advise if they can review specific details of the algorithm/module function in the context of its use.

If the manufacturer/provider of the LIMS has CE marked the algorithms then sites will have to validate it in accordance with good practice principles (GPG), but if sites have the algorithm changed to suit their own needs then they may need to CE mark it themselves, if it falls under the IVDR, unless they can make a case for an in house exemption. The specific details for these exemptions is still under review but the consultation information can be found at https://www.gov.uk/government/consultations/health-institution-exemption-for-ivdrmdr.

Summary

The feedback of the haemovigilance team's assistance continues to be well received and continues to help sites with their regulatory responsibilities, manufacturers with their understanding of how their products can impact within the regulatory framework where they are placed.

Sites and manufacturers have found that post visits/communicates direct from the haemovigilance team manager has achieved the following outcomes:

- Advice centred on moving a transfusion laboratory led to the Trust reversing this decision and postponing the movement until a more suitable area is found
- Obtaining the appropriate and clear and unambiguous release notes for software upgrades when they were not immediately forthcoming
- Stopping an inappropriate LIMS system being introduced when the regulations were applied to the sites proposed plan
- Advice on UKAS and MHRA inconsistencies leading to MHRA setting up a review with UKAS once BREXIT is completed
- Resolving issues between manufactures and sites regarding data integrity and false positive results to achieve both the manufacturer and the site resolving an ongoing issue with a positive outcome
- Engagement with manufacturers to assist with the products that they are introducing does not impact on a sites QMS

This list is not exhaustive.

It is also advised that sites create a communication flow where everybody can share success and failure between different sites, regarding the development and maintenance of an effective QMS. The MHRA forum is an ideal tool and as such please use the forum as much as you can via the following link: http://forums.mhra.gov.uk/forumdisplay.php?60-Blood-Forum.

MHRA Inspection activity on hospital blood banks 2018-2019

Author: Shirley Stagg

A total of 303 blood compliance reports (BCR) were submitted for review for the reporting period 01 April 2018 to 31 March 2019. Twenty-seven hospital blood banks (HBB), including two 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.

All deficiencies identified at these inspections were referenced against the GPG for blood establishments and hospital blood banks.

Inspection outcomes

Inspections for the reporting period 01 April 2018 to 31 March 2019 are performed in the following year, i.e. from 01 April 2019 to 31 March 2020. At the time of writing, a total of 23 inspections had been performed at 23 sites, and four planned inspections were affected by actions taken in response to COVID19. The numbers of deficiencies from the completed inspections are as follows:

Table 26.7: MHRA inspection deficiencies

Critical	Major	Other
0	28	70

Two HBB were referred to IAG following inspection and three were referred to CMT.

An overview of the compliance management escalation processes used by the 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/.

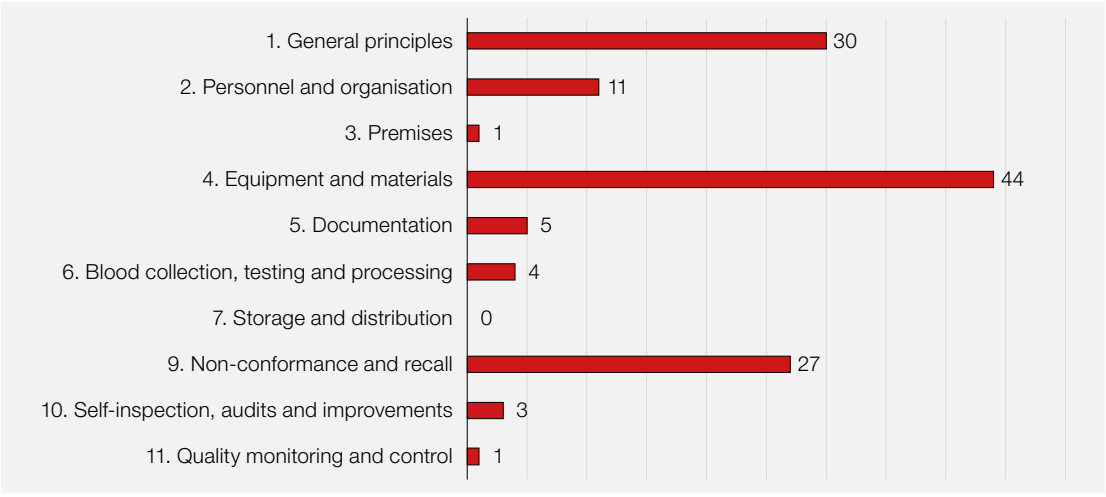
Summary of significant issues identified at inspected sites

The following data is shown in terms of references to the Good Practice Guideline for Standards and Specifications for Implementing the Quality System in Blood Establishments (GPG) for each inspection deficiency. Each deficiency cited may have multiple sub-points each with a specific GPG reference; there are therefore a higher number of GPG references than deficiencies.

Deficiencies

The most frequently cited GPG references in major and other deficiencies were associated with Section 1: General principles, Section 4: Equipment and materials, Section 5: Documentation and Section 9: Non-conformance and recall. The following paragraphs will give some detail on the types of deficiencies that were raised during inspections.

Figure 26.11: Good practice section referenced in major deficiencies 2019



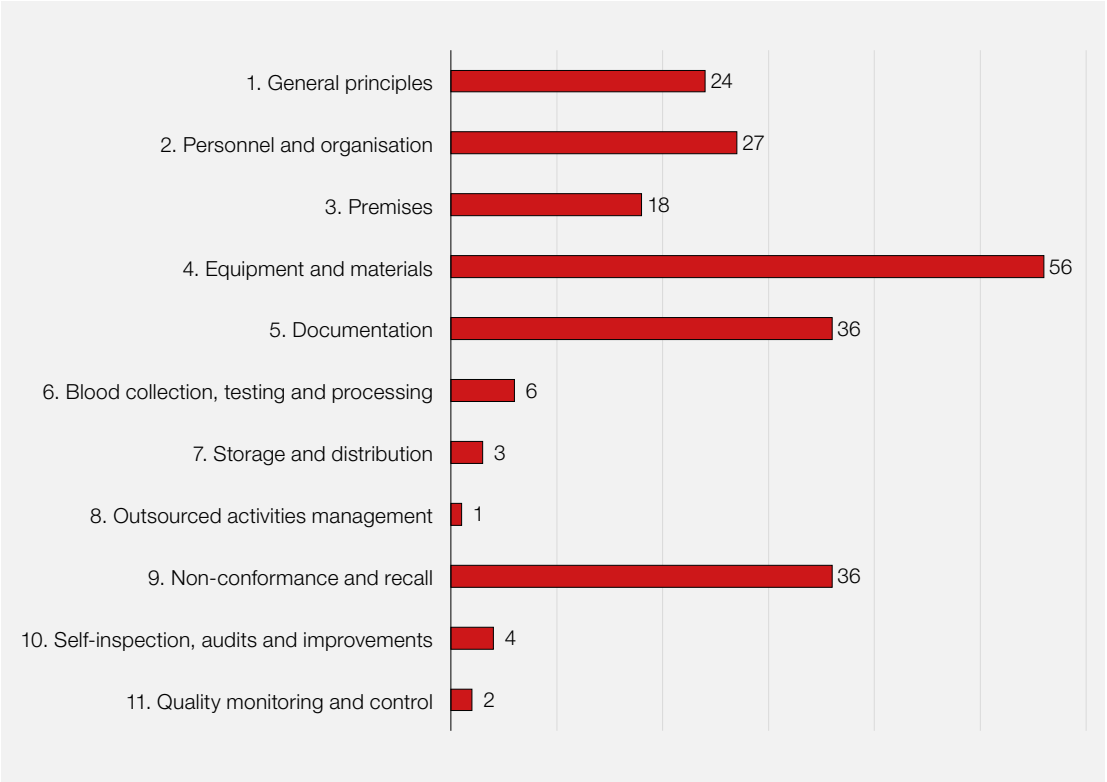


Figure 26.12: Good practice section referenced in other deficiencies 2019

Equipment and material

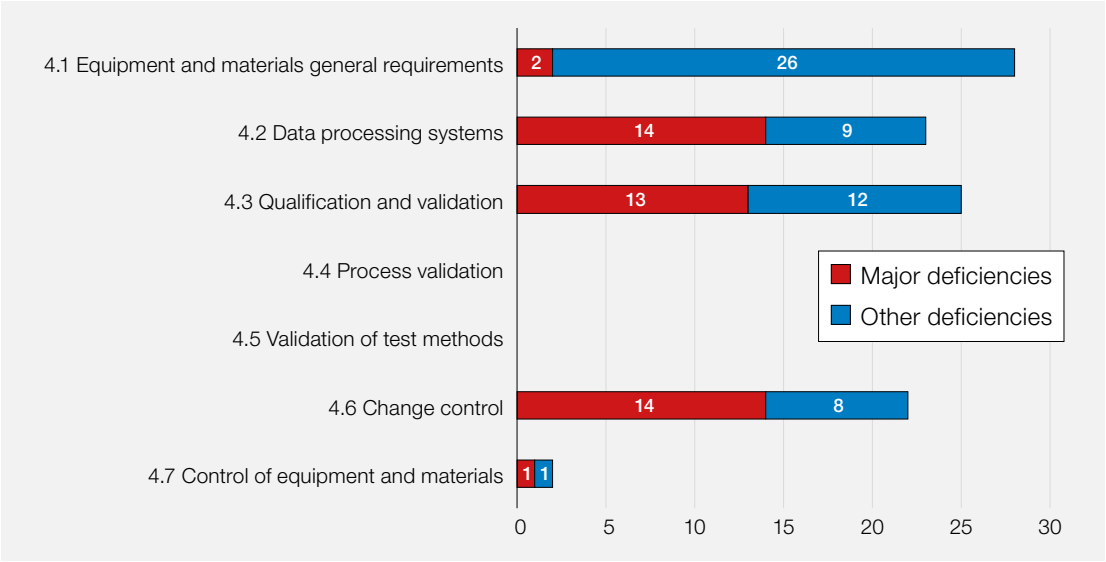
The main issues found in relation to equipment and materials were associated with qualification and validation of equipment. The following were areas of concern:

- Validation master plans did not contain the key elements of the site qualification and validation programme
- Qualification and validation documents were not appropriately reviewed and authorised
- Qualification and validation did not cover the full scope of laboratory activities
- No deviations were raised for non-compliant test results during validation activities
- There was no validation summary, or similar document, to record formal release before the next stage or completion of validation

There were issues with the calibration of equipment used for measurement. Calibration reports were not reviewed and signed to show acceptance of the document and there was no assessment of the impact of any failed calibrations. Computerised system access was not appropriately controlled, with evidence of unlocked and unattended systems and unnecessary use of administrator access for routine use of equipment.

There were examples of change controls not being raised or being raised late in the change process. Change controls should be raised at the initial concept of a proposed change. The potential impact of changes was not robustly assessed to avoid unintended consequences or plan validation. There were several instances where laboratories did not consider effectiveness checks after implementing changes.

Figure 26.13: Good practice section 4: equipment and materials



Non-conformance and recall

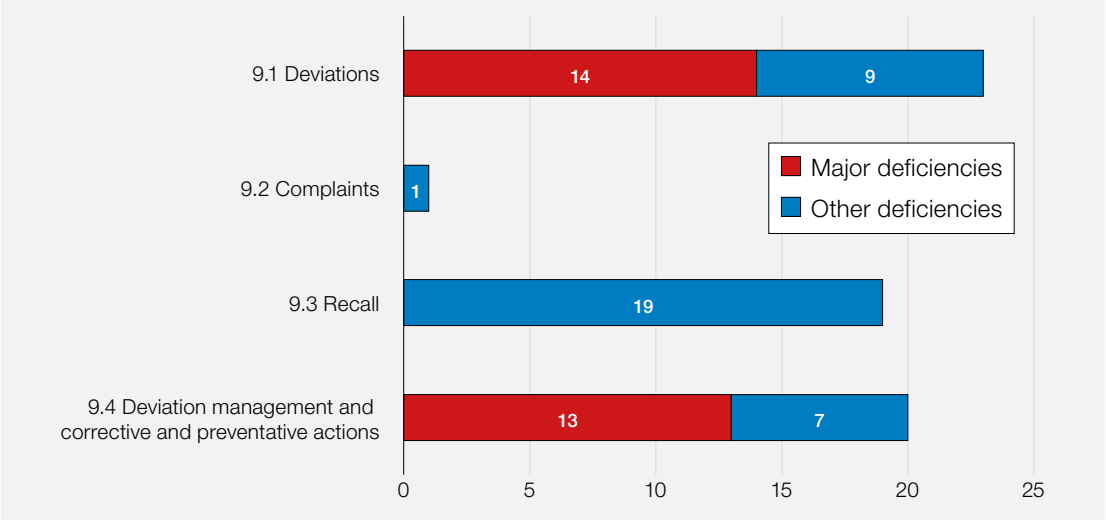
The main issues in relation to non-conformance/deviation management were associated with the level of detail contained within incident reports, the level of root cause analysis work applied and the effectiveness of CAPA.

There were several examples where the classification of non-conformances was inappropriate and this commonly related to the fact that the potential for causing patient harm was not considered. Root causes were attributed to human error without a comprehensive investigation to check for process, procedural and system-based errors. Procedures must be checked to ensure that they contain an appropriate level of detail to maintain compliance. Root cause analysis procedures within laboratories often mandated the use of tools such as 'five-whys' or 'cause and effect diagrams', however, there was little evidence of the use of such tools.

CAPA should ensure that non-conformity or quality problems are corrected, and that recurrence of the problem is prevented. There were examples seen during inspection of CAPA not addressing the identified root cause(s). Where multiple factors were involved in a non-conformance then each one must be considered in the CAPA. Evidence of actions only being partially carried out and CAPA not tracked or reviewed were seen during the review of deviation management during inspections.

The main issue identified around recall was the lack of regular evaluation of recall arrangements. Blood banks often did not consider the full scope of situations that may lead to an internal recall such as a reagent failure.

Figure 26.14: Good practice section 9: non-conformance and recall



Documentation

The generation and control of documentation was the most cited subsection of the documentation section of the GPG. Common issues included:

- Procedures that lacked detail
- Records not being completed as required. These included analyser internal quality control failure forms and return to service forms for equipment
- Requested changes to documents not being carried out in a timely fashion
- A failure to ensure that staff acknowledged new or revised SOP promptly
- Overdue document reviews
- Overwriting

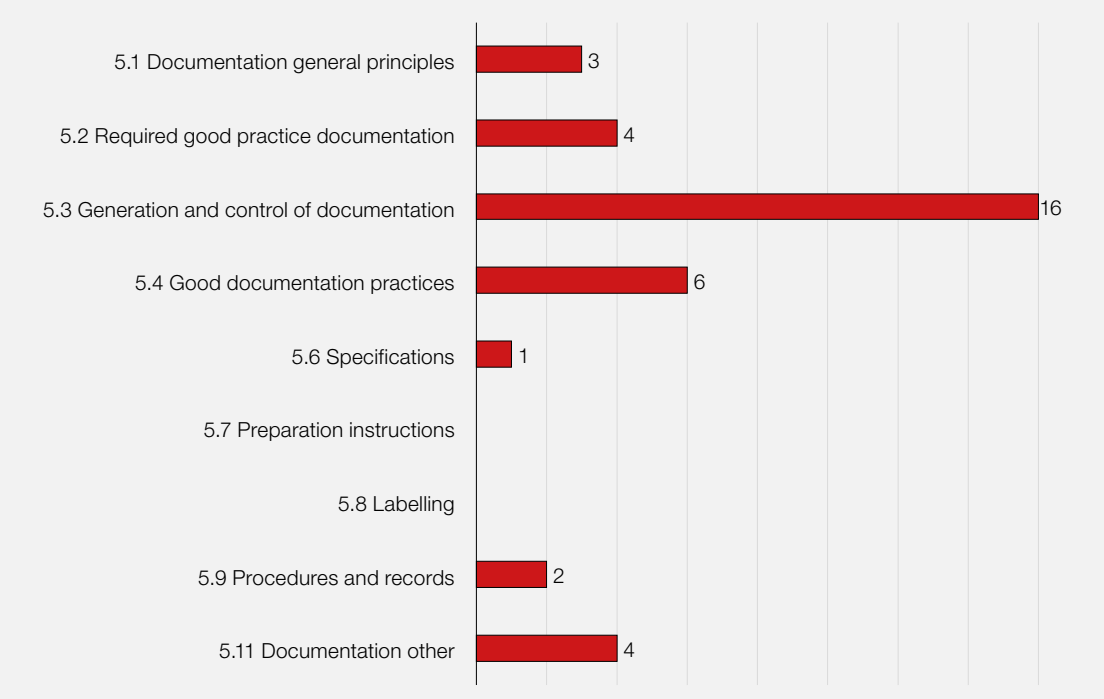


Figure 26.15: Good practice section 5: documentation

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.

Appendices

Appendix 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 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 special requirements have not been matched

Appendix 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 following the wrong procedure
Inadequate process	Inadequate design of a process. Also includes multiple causative factors
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

Council of Europe (2018) Good Practice Guidelines for Blood Establishment Required to Comply with Directive 2005/62/EC, 15/02/2018 https://www.edqm.eu/en/good-practice-guidelines-blood-establishments [accessed 09 June 2020].

BSQR (2005) The Blood Safety and Quality Regulations ISBN 0110990412; http://www.legislation.gov.uk/uksi/2005/50/contents/made [accessed 09 June 2020].