Medicines and Healthcare products Regulatory Agency (MHRA) Report

29

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Key MHRA messages

There has been an increase in the number of serious adverse event (SAE) reports made during 2024. The types of reports and the human factors involved remain largely similar to previous years and therefore the key messages remain unchanged. Special attention must be given to improving the quality and depth of investigations to uncover the human factors involved. These must be addressed with suitable corrective measures that seek to improve quality systems rather than addressing only the members of staff involved.

Summary

The recent change in Serious Adverse Blood Reactions and Events (SABRE)/SHOT reporting platform has presented the MHRA's two person Haemovigilance Team with an enormous challenge. The significant increase in workload as a result of implementing these changes means it has been difficult to produce our normal annual report. The report presented here will be the usual raw data, but with limited commentary.

SABRE report data

Table 29.1 and Figure 29.1 show the total numbers of reports and the numbers of reports submitted as SAE and serious adverse reaction (SAR) for the previous 10 years.

Table 29.1: Submitted confirmation reports 2015–2024

	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024
SAE	764	1027	1076	1198	1197	1093	1143	1118	1325	1371
SAR	262	464	508	408	497	590	526	710	731	677
Total	**1026**	**1491**	**1584**	**1606**	**1694**	**1683**	**1669**	**1828**	**2056**	**2048**

Figure 29.1: Submitted confirmation reports 2015-2024

SAE=serious adverse event; SAR=serious adverse reaction

Serious adverse events n=1371 (+46)

Definition: (Department of Health, 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.

Table 29.2: Total number of SAE reports by event category

Event category	Number of reports
Materials	0
Apheresis collection	2
Whole blood collection	4
Testing of donations	7
Processing	8
Distribution	15
Donor selection	87
Storage	292
Other	956
Grand total	**1371**

Table 29.2 shows the total number of SAE reports received by event category. Proportions of reports received remain similar to previous years.

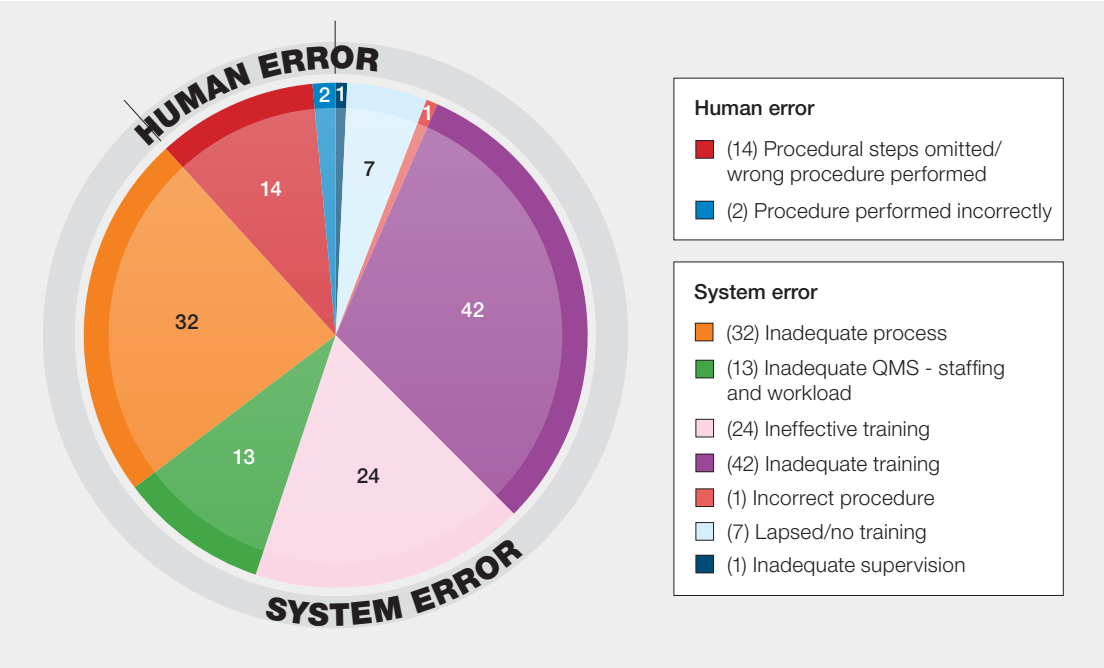
Storage data n=292 (-34)

Storage remains the second largest individual error category (after 'other') and comprises of all Blood Safety and Quality Regulations (BSQR) reportable storage SAE in both the laboratory and clinical areas. The MHRA Haemovigilance Team lead has broken this category down further to try and identify specific storage error sub-types, Table 29.3. For a description of the sub-categories used, see Appendix 1.

Table 29.3: SAE storage error sub-classifications

Storage sub-classification	2024 (+/- 2023)	2023 position
Incorrect storage of component	136 (-20)	1
Component expiry	42 (-16)	2
Sample expiry	39 (+3)	4
Return to stock error	22 (-15)	3
Failure to action alarm	21 (+12)	6=
Security	15 (+2)	5
Storage temperature deviation	9 (NC)	6=
Miscellaneous	7 (NC)	8
30- or 60-minute rule	1 (NC)	9
Total	**292 (-34)**	**X**

Figure 29.2: Root causes of incorrect storage of components sub-category (n=136)



QMS=quality management system

As the single largest sub-category of storage, Figure 29.2, shows the breakdown of incorrect storage by root cause.

89% of all incorrect storage of component errors are related to one or more deficiencies in the quality system, with only 11% related to human error where staff have knowingly followed the wrong procedure or skipped steps in a process.

24% demonstrate either inadequate design of processes to maintain the quality and safety of blood and blood components or involved multiple system failures.

54% are in some way related to training:

- 18% show the training to be ineffective
- 31% show the training to be inadequate
- 5% show staff have either not received training or their previous training has lapsed

Common themes from the narratives of incorrect storage of component reports show:

- Processes and procedures are not clear on how blood should be stored safely and correctly
- Errors are made when staff do not handle blood regularly and have forgotten their training
- Training of staff in blood and blood component storage is not given a high enough priority during staff induction training
- Training material does not always cover all aspects of storage e.g., how to distinguish between components and their different storage requirements
- Errors often occur because shifts are not staffed with adequate numbers of trained staff
- Agency/bank staff training is not adequate
- Agency/bank staff are expected to handle components without having been trained in the local procedures

All storage errors are covered by the requirements of the BSQR. Most of these storage errors occur in clinical areas. It is still a widely held belief that storage errors in clinical areas are clinical errors and that

investigation and reporting of these errors is not covered by the BSQR. This is, and has always been, incorrect. All storage errors that affect the quality and safety of blood and blood components must be fully investigated as per the requirements of the BSQR and the Good Practice Guide (GPG) (Department of Health, 2005; EDQM, 2023).

Recommendation

- Hospital Trusts/Health Boards must improve all areas relating to the quality and safety of blood and blood component storage and the investigation of such storage errors

Action: Hospital transfusion teams

Other n=956 (+82)

Table 29.4: 'Other'

Other sub-category	2024 (+/- 2023)	2023 position
Incorrect blood component issued (IBCI)	196 (+2)	1
Pre-transfusion testing error (PTTE)	170 (+22)	2
Sample processing error (SPE)	167 (+21)	3
Component collection error (CCE)	151 (+24)	4
Data entry error (DEE)	115 (+26)	6
Component labelling error (CLE)	95 (-20)	5
Incorrect blood component ordered (IBCO)	16 (+9)	9
Component available for transfusion past de-reservation (CATPD)	14 (+4)	8
Failed recall (FR)	13 (-11)	7
Unspecified (UNSPEC)	7 (+6)	13
Expired component available for transfusion (ECAT)	5 (-1)	10
Handling damage (HD)	4 (+1)	12
Incorrect blood component accepted (IBCA)	3 (-1)	11
Total	**956 (+82)**	**X**

Table 29.4 shows the number of reports in the 'other' category of SAE. There has been an increase in events that fall into this category. This increase is likely to have been partly due to the increase in errors reported as a result of the South London cyber-attack. The increase in workload resulting from having to resort to manual processes increased the numbers of reports from the sites affected.

Please see Appendix 2 for a description of the subcategories.

Human and system error categories and human factors

The BSQR requires that 'preventable causes' of SAE are investigated and reported (Department of Health, 2005). The GPG also states 'Where human error is suspected or identified as the cause of the deviation, this should be formally justified and care should be exercised so as to ensure that process, procedural or system-based errors or problems are not overlooked, if present.' (EDQM, 2023).

What this means is that for all SAE reported on SABRE, the root cause investigation must first identify any system-based causes, or 'human factors'. Human factors are all the factors which influence an individual's behaviour. These can be factors associated with an organisation itself, the task or the process being undertaken, including the environment and equipment used as well as factors associated with an individual's personality and actions. Therefore, human factors, or ergonomics, are exactly the system-based factors reporters are required to investigate according to the requirements of the BSQR and the GPG.

The MHRA assign a category on review of an SAE report to reflect the most prominent causative factor.

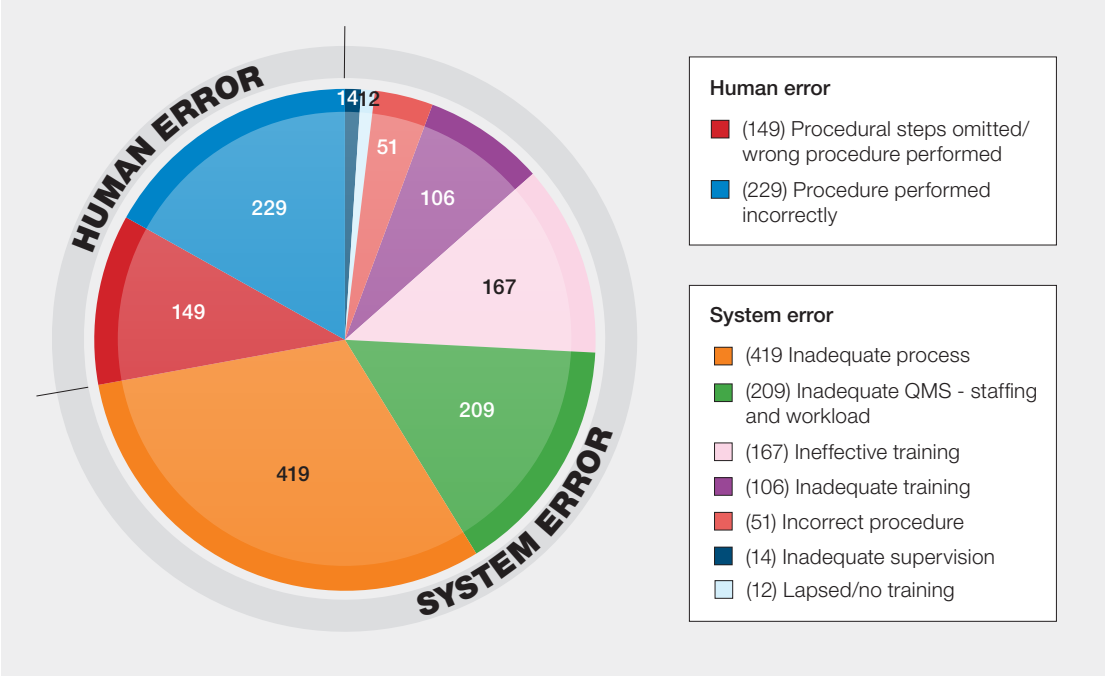
Assessment of these reports can distinguish between events caused by system errors and human errors (slips/lapses/omissions). For a description of the categories used, see Appendix 3.

Table 29.5 shows the breakdown of reports in the human/system error sub-categories.

Table 29.5: Human/system error sub-categories, 2024

Human error sub-category	Total 2024 (+/- 2023)	2023 position
System error/inadequate process	419 (+23)	1
Human error/procedure performed incorrectly	229 (-23)	2
System error/inadequate quality management system (QMS) – staffing and workload	209 (+64)	4
System error/ineffective training	167 (-28)	3
Human error/procedural steps omitted/wrong procedure performed	149 (+5)	5
System error/inadequate training	106 (+10)	6
System error/incorrect procedure	51 (-1)	7
System error/inadequate supervision	14 (+3)	9
System error/lapsed/no training	12 (-3)	8
Total	**1356 (+50)**	**X**

Figure 29.3: Human/system error sub-categories (n=1356)



QMS=quality management system

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

- The root cause (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. 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 MHRA with enough information may not be sub-categorised appropriately

Table 29.5 shows an increase in reports attributable to human factors. The largest increase is in the 'staffing and workload' sub-category. While the South London cyber-attack would have accounted for

some of this increase, it did not account for all of it.

Common themes from the narrative of these investigation reports show:

- 31% of these reports either demonstrate a weak process or system design or involve multiple system deficiencies
- Inadequate process errors may involve the poor identification and mitigation of distractions
- 15% of these reports are directly related to staffing, workload, or skill-mix issues and is now the second largest 'system error' sub-category. However, it must be noted that some of the 31% inadequate process reports, may also include some aspects of staffing and workload issues
- Many reports note errors are made when staff are 'busy'. It may not always be possible to directly link these to staffing and workload since improved prioritisation of workloads may have prevented the error from occurring
- Many reports do not reflect the seriousness of the event as they only reflect actual harm and not potential harm
- Many confirmation reports initially assign a RC as human error without fully identifying process or system deficiencies
- Many corrective and preventive actions (CAPA) are initially proposed to be reminding staff to 'be more vigilant' and to 'follow procedures'. This is not acceptable as it demonstrates a failure to identify genuine causes and adequate CAPA
- RC are often identified as a failure to perform an adequate second check. Failure to perform second checks are not RC as the error has already occurred by the time the second check would be performed
- Many reports continue not to be reported 'as soon as known'. This especially applies to the confirmation report
- Many confirmation reports are delayed due lack of engagement from clinical areas or by reviews of investigation reports

Recommendations

- All reporters must continue to thoroughly investigate all SAE, even those with no actual harm to patients. It is through thorough investigations that improvements can be identified to reduce risks to the quality and safety of blood and blood components and reduce the risk of harm to patients
- When investigating an incident, reporters must have taken care to ensure that process, procedural or system-based errors or problems have not been overlooked. For example, if distractions have been identified then these distractions must be addressed in the CAPA to avoid reoccurrence
- CAPA must correct the error made and not just rely of making error checking more robust
- Engagement from staff in clinical areas must be improved. It is the responsibility of the Trust to ensure all SAE are investigated and reported in a timely manner as per the requirements of the BSQR
- Reporters are reminded to report 'as soon as known'. You are required only to submit a confirmation report with RC and 'proposed' CAPA. Changes to CAPA following review can be added to SABRE reports as footnotes

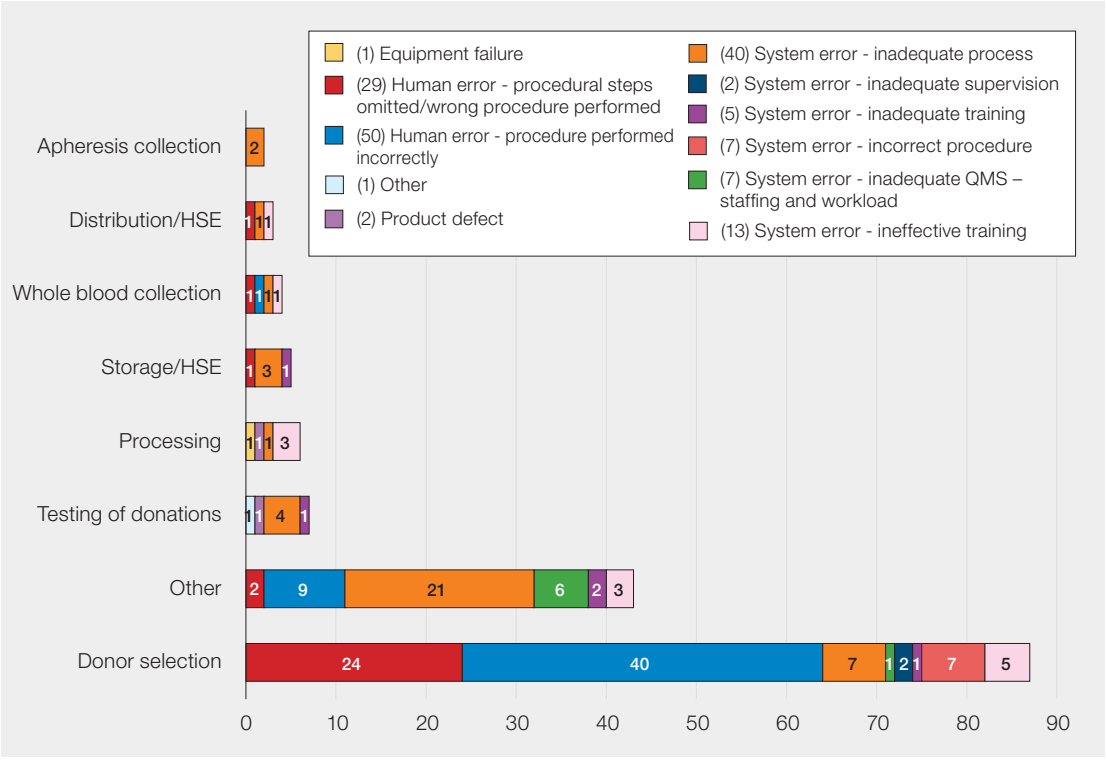
Action: Hospital transfusion teams

Blood establishment reporting n=157 (+12)

Although reports from blood establishments (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 29.4 displays the reported BE SAE in 2024.

Figure 29.4: Blood establishment SAE event category by specification (n=157)

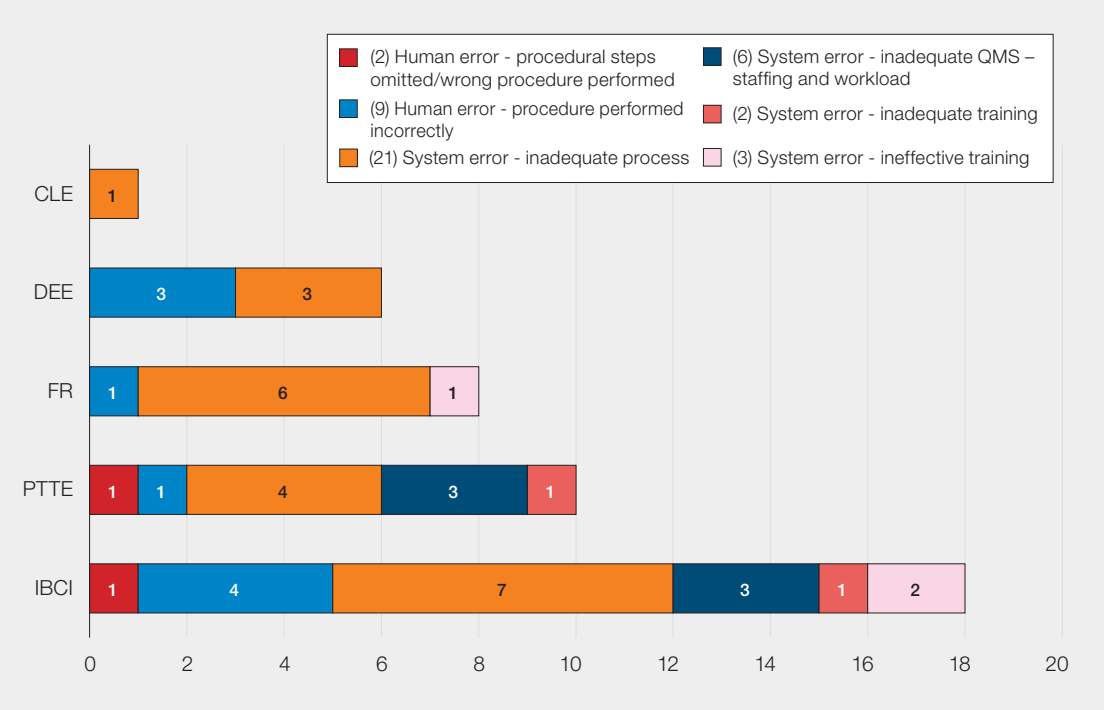


QMS=quality management system

The majority of the reports fall into the donor selection category and typically involve errors where a donor is accepted despite requiring deferral for travel, medical or life-style reasons. Although the diagram indicates that most of these reports are due to 'human' error, i.e., slips, lapses and omissions, this is usually because the error is not spotted until after the donor's next donation. This makes it difficult to assess if the error is a 'system' error. However, all BE when reporting donor selection errors perform recalls and assess the current donation for the deferral reason. Also, processes, procedures and training are regularly reviewed so the risk to the patient is classed as low.

Figure 29.5 shows a breakdown of the 43 reports which fall into the 'other' category.

Figure 29.5: BE reports in 'other' category (n=43)



See Appendix 2 for key to category abbreviations

QMS=quality management system

Much work has been done by SHOT in collaboration with MHRA and Blood Establishments to improve reporting of SAE relating to work in diagnostic and blood issue laboratories. This accounts for an increase in the total number of reports and is likely to increase in coming years.

Serious adverse reactions (SAR)

Definition: (Department of Health, 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

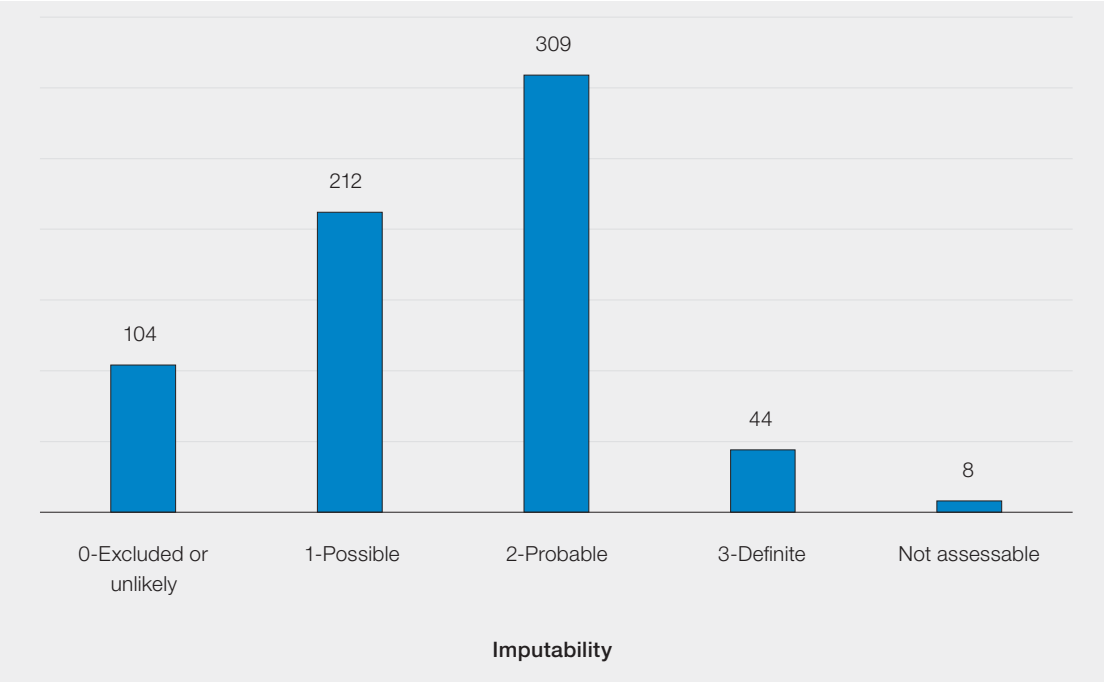
Blood products

Adverse reactions involving blood products (i.e. licensed medicines such as anti-D Ig, Octaplas® (solvent detergent-treated fresh frozen plasma), or coagulation factor concentrates should be reported to the MHRA via the Yellow Card scheme (https://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 that qualify for reporting to MHRA under the BSQR, see Figure 29.6.

Figure 29.6: SAR reports, by imputability, reported to SABRE in 2024 (n=677)



MHRA inspection report

An overview of the compliance management escalation processes used by the good manufacturing practice inspectorate, including information on the Inspection Action Group and Compliance Management Team 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 has remained fairly consistent from the previous year and included:

Management of change

The control of change continues to be a deficiency that is commonly raised at blood inspections. The deficiencies raised include:

- The absence of a user requirement specification
- The lack of a validation master plan to guide management through the validation and qualification of the change
- Inadequate or absence of a risk assessment and actions to mitigate risks
- The lack of evidence of sign off of stages of the change control prior to implementation
- The lack of validation evidence to show that the system was fit for task before implementation
- Failure to carry out a post implementation effectiveness check

Management of non-conformances

The management of non-conformances is regularly raised as a deficiency due to the following:

- Inadequate investigation for an appropriate root cause therefore the inadequate implementation of an effective CAPA to avoid reoccurrence

- Failure to consider the potential for harm as well as actual harm especially Trusts using the Datix system
- The lack of an adequate justification for human error being identified as a root cause
- The lack of justification for the late closure of deviations and performing impact risk assessments
- Tracking and trending systems employed not identifying recurring problems due to an emphasis on consequence rather than root cause

The availability of trained and competent staff

Issues with adequate capacity within the laboratory is an ongoing problem and is often raised as highlighted by:

- The absence of an effective capacity management plan or similar document to ensure adequate management of blood transfusion operations and the quality management system
- The inadequate management of risk register entries such as reducing the risk score without an appropriate justification
- Risk scores being reduced before the suggested mitigation was in place and deemed effective
- Staff working significantly above their contracted hours to ensure staff rotas are adequately staffed
- Trusts failing to meet several quality metric targets

Blood collection and training

Blood collection and training was not being adequately managed in that:

- Blood collection training and competency audits showing that Trusts were not meeting their key performance indicators for staff blood collection training
- Inadequate systems in place to control infrequent users of the system and blocking staff who had left the Trust

Steps to control access to blood component storage areas

Steps to control unauthorised access was not being adequately managed in that:

- Main access doors being unsecured and propped open
- Issue refrigerators being located in areas that was used by hospital staff and patients as a thoroughfare
- The doors to the blood component refrigerators and freezers not being closed and locked
- Where keypad access was being used to access blood component storage areas had no record of ever being changed

Computerised patient databases and data integrity measures

There have been several examples where patient and result data bases have never been checked for the integrity of the stored data evidenced by:

- There was no record that sites had reviewed the retention of backed-up data on the laboratory information management system (LIMS)
- The laboratory had no evidence that they had performed any audit checks to detect the potential presence of duplicate patient records on their LIMS database
- The laboratory had no evidence that the backed-up testing records on the automated blood transfusion analysers had ever been checked

Recall

- The timelines set for recall procedures had not been formalised

For further information on MHRA and the Regulation of Blood please refer to the MHRA website:

Blood regulation and safety - GOV.UK

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.

https://forums.mhra.gov.uk/forumdisplay.php?60-Blood-Forum

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- or 60-minute rule	Red cells are returned to a refrigerator after 30 or 60 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 not following the 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