Guidelines for the Blood Transfusion Services

Chapter 6: Evaluation and manufacture of blood components

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Chapter 6:

Evaluation and manufacture of blood components

6.1: Scope of the guidelines

These guidelines provide a framework on which Blood Establishments should assemble standard operating procedures (SOPs) for the manufacture of blood components.

These guidelines apply to single-donor and small-pool components (up to and including 12 donors) prepared from units of whole blood or by apheresis. Should a proposal be made to change the specifications for a pooled blood component by increasing the pool size this should follow the usual procedures as set out in Chapter 8, including risk assessment and validation.

Blood Establishments should ensure that the hospital blood banks that they supply are informed of these component production guidelines, and should consult with them on proposed changes to existing component processing and on the adoption of new components.

Technologies for pathogen inactivation of blood components are now being used in Europe. Within the UK, the medicinal product solvent detergent treated pooled plasma is in use. Treatment of plasma and of platelets with amotosalen ultraviolet (UV) treatment or riboflavin UV treatment is CE marked and may be used in the UK in the future. Specifications for these and similar products will be considered as and when they are adopted. At present no CEmarked technology exists for pathogen inactivation of red cells, although some companies are working on suitable approaches.

Occasionally processes may require deviation from a supplier’s Instructions for Use (IFU), in which case the deviation must comply with the Medical Device Regulation (EU 2017/745) article 5 sub-section 5, and the associated component must be fully validated. Additional guidance can be found in Chapter 8 (section 8.1).

6.2: Setting and maintaining specifications

The wide variability of the source material from which blood components are prepared makes it difficult to set stringent limits. Nevertheless, realistic minimum specifications should be set and complied with.

Concessionary release limits are also set for certain components that are subject to non-destructive quality monitoring, such that components that are excessively out of specification are only used therapeutically under specific circumstances and subject to formal clinical approval (Table 6.1).

All blood components tested and found outside concessionary release limits should have the testing repeated to confirm the original result and the production process should be reviewed as necessary.

Some abnormal results could have implications for the health of the donor and should be reviewed by a Designated Clinical Support Officer. Further samples or referral to an appropriate clinical service may be required for the donors of:

- Red Cells in Additive Solution, Leucocyte Depleted, where the Hct is >0.70
- Platelet components collected by apheresis, where the platelet count is below any lower concessionary release limit
- For Fresh Frozen Plasma, Leucocyte Depleted where the FVIII is <0.3IU/mL

Table 6.1 Concessionary release limits

Blood component	Parameter	LOWER Limit (less than)	UPPER Limit (more than)
Red Cells in Additive Solution, Leucocyte Depleted	Haemoglobin (g/unit)	30	None
	Volume (mL)	210	375
	Haematocrit (L/L)	0.40	0.70
Red Cells, Washed, Leucocyte Depleted	Haemoglobin (g/unit)	30	None
	Volume (mL)	210	375
	Haematocrit (L/L)	0.40	0.70
	Residual Protein (g/unit)	None	0.50
Red Cells for Intrauterine Transfusion, Leucocyte Depleted	Haemoglobin (g/unit)	40	None
	Volume (mL)	150	350
	Haematocrit (L/L)	0.70	0.85
Red Cells for Exchange Transfusion (not Whole Blood), Leucocyte Depleted	Haemoglobin (g/unit)	40	None
	Volume (mL)	220	420
	Haematocrit (L/L)	0.50	0.60
Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted	Haemoglobin (g/unit)	30/no. of splits manufactured	None
	Haematocrit (L/L)	0.40	0.70
Platelets, Pooled • Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted • Platelets, Pooled, Buffy Coat Derived, in Additive Solution and Plasma, Leucocyte Depleted	Platelet Yield ($\times 10^9$/unit)	160	Defined by pack type [1]
	Volume (mL)	150	380
Platelets, Apheresis, Leucocyte Depleted	Platelet Yield ($\times 10^9$/unit)	160	Defined by pack type [1]
	Volume (mL)	150	380

Platelets in Additive Solution, Leucocyte Depleted	Platelet Yield ($\times 10^9$/unit)	160	Defined by pack type [1]
Platelets for Intrauterine Transfusion, Leucocyte Depleted	Volume (mL)	50	120
	WBC ($\times 10^6$/unit)	None	2.5
Platelets, Neonatal Use, Leucocyte Depleted	Platelet Yield ($\times 10^9$/unit)	40	Defined by pack type [1]
	Volume (mL)	30	95
Platelets in Plasma and Additive Solution for Neonatal Use, Leucocyte Depleted	Platelet Yield ($\times 10^9$/unit)	40	Defined by pack type [1]
Fresh Frozen Plasma, Leucocyte Depleted	Volume (mL)	200	340
	Factor VIII (IU/mL)	0.3	None
	Residual Platelet Count ($\times 10^9$ /L), pre-freeze in starting component	None	100
Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted	Residual Platelet Count ($\times 10^9$ /L), pre-freeze in starting component	None	100
Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted	Factor VIII (IU/mL)	0.3	None
	Residual Platelet Count ($\times 10^9$ /L), pre-freeze in starting component	None	100
[1] Upper concessionary release limit where stated by manufacturer of platelet pack.			

Component and process quality monitoring results should be subjected to statistical analysis so that trends can be identified. Guidance on appropriate approaches to statistical process monitoring is given in the Council of Europe guide,[1] and in Beckman et al. (2009).[2] A flowchart adapted from Beckman et al., to aid in selection of appropriate methods, is reproduced as Figure 6.1.

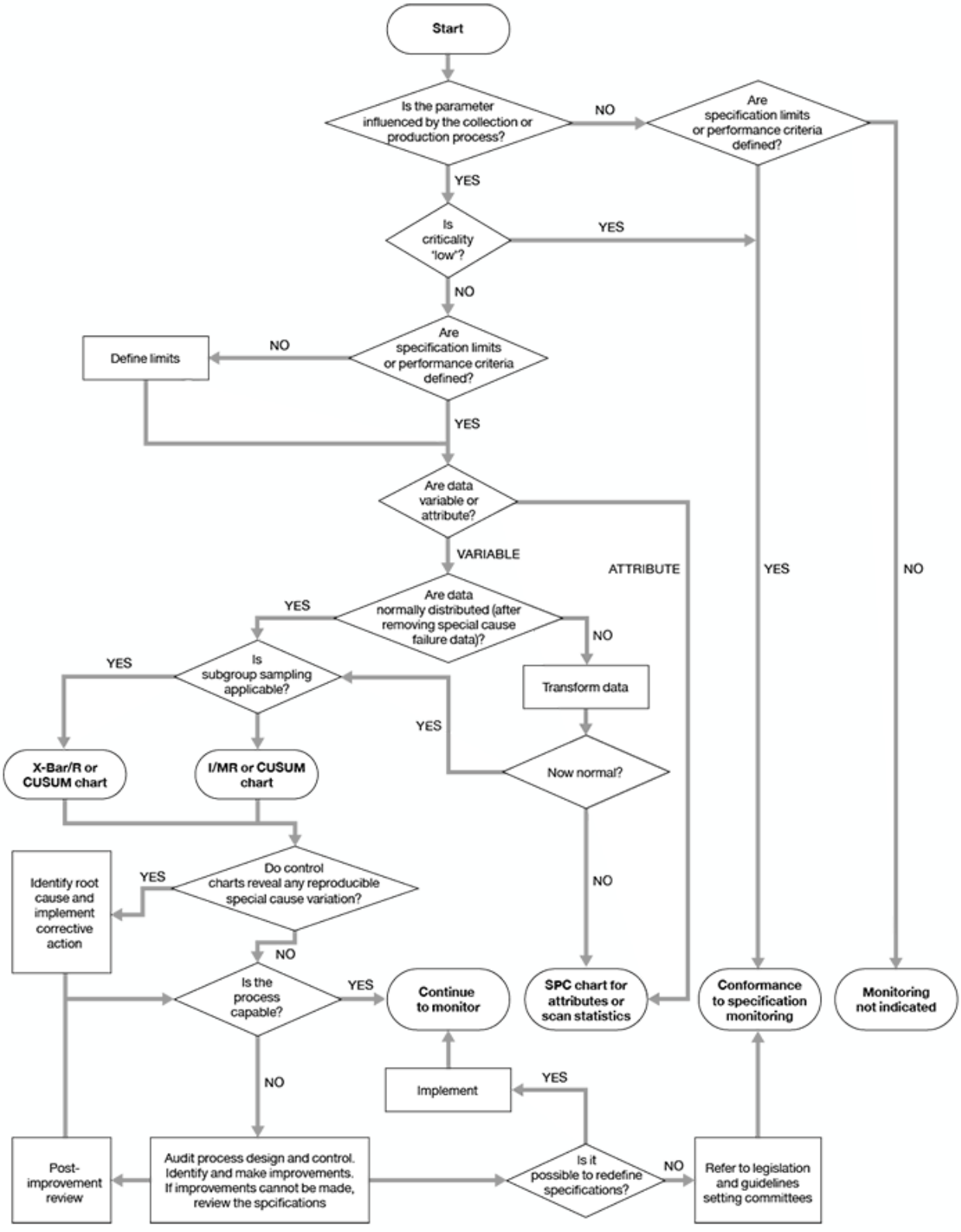

Figure 6.1 Algorithm for the selection of quality monitoring methods

If the results of analyses show a consistent trend towards the minimum requirements specified in Chapter 7, the cause should be investigated. The criteria to be investigated must be detailed in the relevant SOP together with the corrective action to be taken. The steps to be considered should include the following:

- An investigation of the collection, testing, production and distribution procedures as appropriate.
- Checking that procedures are up to date and are not being deviated from.
- Checking the operation of equipment and storage conditions (this may include reviewing validation documentation and/or revalidation).

The person responsible for quality assurance and/or production may initiate investigations beyond the scope of written procedures.

6.3: Component and process monitoring tests

These guidelines also indicate the minimum level of other process monitoring tests necessary to ensure components are prepared to specification.

Any assay used for blood component quality monitoring should be validated and documented before introduction and before any changes to methodology or manufacture are brought into use. Blood Establishments should ensure that they participate in the National External Quality Assessment Scheme (NEQAS) or other available external quality assurance schemes for the assays used to assess component quality.

Each component should be visually inspected at each stage of processing and immediately prior to issue. The component must be withdrawn if there is evidence of leakage, damage to or fault in the container, excessive air, suspicion of microbial contamination or any other contraindications such as platelet clumping, unusual turbidity, haemolysis or other abnormal colour change.

6.3.1: Sampling procedures

Sampling procedures should be designed and validated, prior to acceptance as standard practice, to ensure the sample truly reflects the contents of the component pack.

Validation of sampling procedures should be repeated before application to new components, relevant changes to blood pack design or different quality parameters, or before the introduction of new sampling equipment. Also there should be a procedure for continuous assessment of staff competence/sampling techniques.

Where test samples are removed from a component to be issued for transfusion, the sampling procedure should be designed and validated to ensure that the sterility and essential properties of the component are not adversely affected.

Samples for leucocyte counting must be taken and tested within 48 hours of donation, unless the sampling and testing times used have been validated to yield equivalent results.

6.3.2: Frequency of tests

The regularity with which components are made and the extent of their compliance with specification influences the frequency with which component and process monitoring tests are required.

If there is a trend towards the minimum requirements specified in Chapter 7, the frequency of quality monitoring tests should be increased according to defined procedures and/or in consequence of corrective actions until the relevant component attributes have been brought under control.

The testing protocol should take into account all major production variables and ensure samples are representative of these.

6.3.3: Component weight:volume

To provide information that is useful for clinicians, the component specifications given in Chapter 7 generally require the component label to indicate a volume. This may be either the calculated volume or nominal volume, and the nominal volume may be based on a national or locally established volume specification.

Since volume generally is calculated by dividing the component weight by its specific gravity, the following conventions should apply in order to ensure some element of standardisation:

- Whole blood volume is most appropriately calculated by deducting the weight of the pack assembly and dividing the resulting weight by the nominal specific gravity of 1.06.
- To provide quality monitoring data that demonstrate the capability of the blood collection process, deduct the weight of the anticoagulant before converting to volume.
- To provide quality monitoring data that reflect the provision of whole blood as a component, the volume given on the component label should include whole blood and anticoagulant.
- For red cell components, volume is calculated by weighing the pack, deducting the weight of the pack assembly only, and dividing the resultant weight by the nominal specific gravity 1.06. The weight of anticoagulant and, if relevant, additive solution are not deducted when calculating the volume of red cell components.
- For platelets suspended in plasma and plasma components, volume is calculated by weighing the pack, deducting the weight of the pack assembly and dividing the resulting weight by the nominal specific gravity of 1.03.
- For platelets suspended in platelet additive solution and plasma, volume is calculated by weighing the pack, deducting the weight of the pack assembly and dividing the resulting weight by the nominal specific gravity of 1.02.
- For platelets suspended in platelet additive solution, volume is calculated by weighing the pack, deducting the weight of the pack assembly and dividing the resulting weight by the nominal specific gravity of 1.01.

6.4: Component processing

6.4.1: Premises

Component production areas should satisfy the requirements defined in the current *Rules and Guidance for Pharmaceutical Manufacturers and Distributors*.[3] In addition:

- the ambient temperature of blood component processing areas should be maintained within a range that would not be expected to adversely affect component viability/shelf life

- where appropriate, steps should be taken to ensure that air quality in the blood component processing environment does not increase the bioburden to which blood components are exposed.

6.4.2: The starting material

The starting material for component preparation is whole blood or the products of apheresis collected from donors who satisfy current donor selection criteria. Components must be collected into blood packs /apheresis harness assemblies that are CE marked.

Before use, packs/apheresis harness assemblies that have not previously been validated, or contain component parts that have not previously been validated, should be subject to validation or process qualification as appropriate according to the protocols set out in Chapter 8.

Starting material for component preparation should be transported as described in section 6.11.2.

As a route to reducing the incidence of transfusion-related acute lung injury (TRALI), large plasma volume products (clinical fresh frozen plasma; platelet concentrates stored in plasma) should be made using plasma from male donors (or non-parous or antibody screened parous female donors) wherever feasible.

Unless subjected to a validated pathogen inactivation process, components for use in intrauterine transfusion, neonates and infants under one year must be prepared from previously tested donors who have given at least one donation in the last two years. This donation must have been either negative for all mandatory markers, or if repeat reactive, confirmed to be non-specific reactive and the donor reinstated in accordance with section 9.4 (on reinstatement of blood donors).

All components prepared in the UK have been leucodepleted since 1999.

6.4.3: Prevention of microbial contamination

Infections associated with the microbial contamination of blood and blood components still occur. While there is no evidence to suggest that routine, retrospective sterility testing of blood components diminishes or eliminates such instances of infection, the following measures will minimise the risks:

- Creating and maintaining the highest level of awareness among all personnel of the constant care and attention to detail needed to minimise microbial contamination, e.g. validation of the effectiveness of venepuncture site preparation and re-validation of process change.

- Using validated procedures designed to minimise microbial contamination of the environment and prevent microbial contamination of components.

- Diverting the first part of the donation into a sample pouch, to avoid entry into the primary donation. This may be used for mandatory screening tests.

- Monitoring the microbial load in equipment and in the environment of component preparation areas. Assessing the contamination rate in outdated components may provide additional, indirect evidence of processing cleanliness.

It is important that data derived from such monitoring exercises are accumulated and regularly examined with a view to taking appropriate action.

Screening of platelet components for bacterial contamination has been evaluated and implemented by some Blood Establishments to help reduce the risks associated with bacterial contamination. However, it does not eliminate this problem, at least with current testing technologies.

6.4.4: Closed system

The term ‘closed system’ refers to a system in which the blood pack assembly is manufactured under clean conditions, sealed to the external environment and sterilised by an approved method.

6.4.4.1: Venting

With the exception of the venepuncture procedure and strict requirements for open processing (see section 6.4.5), the blood pack system and its contents must not be vented to the external environment at any stage during blood collection or processing.

6.4.4.2: Sealing

Blood pack and apheresis harness fluid pathways must at all times be protected from the external environment by:

- hermetic seal(s) incorporated during manufacture or Blood Establishment use
- other validated devices for effecting a permanent seal
- break seal closure(s)*
- port(s) incorporating a tamper-proof closure and pierceable membrane*
- microbial filter(s).*

**These devices must comply with the requirements of the current versions of relevant standards for medical devices, including ISO 3826 Part 1 (blood bags), Part 2 (graphic symbols), Part 3 (blood bags with integrated features), and Part 4 (apheresis blood bags). The devices must be validated by the manufacturer and must be provided with clear instructions for use.*

Before severing any sub-component of the pack assembly, the pack contents must first be protected from the external environment by a minimum of one permanent seal made using a validated hermetic sealer cleaned and maintained according to SOP.

Temporary sealing clamps/clips must be used only to control the flow of fluid within a closed system. They must not be used as the sole means of protection from the external environment.

When a device for making a sterile connection is used the system can be regarded as closed provided that the process of joining and sealing has been validated and shown not to lead to an increased risk of microbial contamination of the component. The procedure for use should ensure that the operator carefully checks the suitability of every weld and also pays particular attention to effective cleaning of the working parts of the equipment.

Cleaning should be by validated procedure with regular checks to ensure conformance to procedures.

Pressure or tensile testing the strength of welds should be performed during the validation or qualification of equipment.[4,5]

Where a sterile connecting device has been used to add satellite packs, the components must not be issued with the weld in place.

6.4.4.3: Pre-donation sampling

Pre-donation sampling must only be carried out using blood pack assemblies that incorporate a device to prevent the return of blood and/or air from the sample pouch towards the donor and donation. The procedure must be validated by the Blood Establishment and documented in blood collection SOP.

After filling, the sample pouch must be permanently sealed from the donation before collecting blood samples.

In the event of inadvertent contamination of the donation by blood or air from the sample pouch, the donation must be discarded.

6.4.5: Open system

The term ‘open system’ refers to a system in which the integrity of the closed system must be breached but where every effort is made to prevent microbial contamination by operating in a clean environment, using sterilised materials and aseptic handling techniques. In such circumstances, positive pressure should be exerted on the original container and maintained until the container is sealed. Open system processing should be undertaken in a designated clean environment as defined in the current *Rules and Guidance for Pharmaceutical Manufacturers and Distributors*.[3]

The sterility of components prepared in an open system should be monitored using validated methods.

Blood components prepared by an open system should be used as soon as possible. If storage is unavoidable, components with a recommended storage temperature of 22 ±2°C should be used within 6 hours. Components with a recommended storage temperature of 4 ±2°C should be used within 24 hours.

Components are rendered unsuitable for clinical use when breached and the requirements defined for an open system have not been observed, unless issued under medical concession.

Any new development in component preparation by an open procedure must be validated to ensure the maintenance of sterility before the procedure can be used to produce components for therapeutic use.

Procedures for collecting samples for sterility testing must not adversely affect the sterility of components intended for subsequent transfusion.

6.5: Component shelf life

Component storage specifications are given in Chapter 7.

Where components are pooled or undergo procedures that influence the shelf life, the maximum shelf life of the component must not exceed the expiry date of the oldest constituent component or the expiry date of the new component produced by the procedure, whichever is the shorter.

For all other components the date of collection will be assigned Day 0 of the shelf life. Day 1 of storage will commence at one minute past midnight on the day after collection.

6.6: Labelling

6.6.1: Component labelling

Barcoded labels and on-demand printing must be used whenever possible.

The design, content and use of labels for blood components should conform to specifications set out in Chapter 23.

Procedures should be established to ensure labels are satisfactory for their intended use.

Pre-printed labels to be attached to blood donations, documentation and components should be stored under secure conditions.

6.6.2: Donation/donor identification

The use of a unique barcoded/eye-readable donation number links the donation to its donor. Donation numbers must be attached to all integral packs, sample tubes and corresponding documents at the time of donation.

When component production requires the use of subsidiary packs which are not an integral part of the pack assembly (e.g. filtration, pooling, freezing), a secure system must be in place to ensure that the correct eye-readable and barcoded donation number is placed on each additional pack used.

When components are pooled there should be a system that ensures that the pool carries a unique barcoded and eye-readable identification number(s). This barcode must be able to be read by component manufacturers and blood banks.

When a component is divided a secure system must be in place to ensure that all sub-batches can be traced.

6.7: Component storage

6.7.1: Specifications for component storage areas

Storage areas for blood components must operate within a specified temperature range and should provide adequate space and suitable lighting, and be arranged and equipped to allow dry, clean and orderly storage.

Good manufacturing practice requires that components of different status are appropriately identified and effectively separated.

Recognised status categories are noted below.

6.7.1.1: Quarantine

Procedures should ensure that untested components are not quarantined with components which have produced, or are likely to produce, repeatably reactive results in mandatory microbiological screening tests.

Secure and exclusive quarantine storage should be available for known biohazard material awaiting disposal (see section 6.8.2).

6.7.1.2: Non-conforming

Components which do not comply with the specification for mandatory tests or are otherwise unsuitable for transfusion should be categorised as non-conforming. Normally, such components would be discarded. However, if they are to be issued for therapeutic, reagent or research use, a concessionary release procedure must be used (see section 6.10).

6.7.1.3: Returned

Components that have been returned from areas outside the direct control of the blood supplier should not normally be returned to stock.

Components that have been returned to the blood supplier with substantive evidence that they have been stored appropriately and within specification, should be held securely pending possible reinstatement to stock by a designated person.

6.7.1.4: Stock

Only those components which have been deemed satisfactory for issue by a designated person should be held in stock (see section 6.9).

Appropriate security and status labelling of component storage areas are essential.

A current inventory should be maintained of components in each storage category/area.

Areas/equipment in which components are to be stored should be validated before their introduction into routine use and checked for calibration to a documented schedule thereafter.

A permanent, continuous record of storage temperatures should be made, reviewed and stored. There should be a log of alarm events that describes the corrective actions taken.

6.7.2: Procedures for component storage

Written procedures must be established for the storage of blood components. These should include the following:

- a procedure to ensure components are not released to stock unless authorised by a designated person (see section 6.7.1.4)
- definitions of the designated storage areas including the storage specification, the status of components to be stored in each area and the persons who are authorised to access each specific area
- procedures for validating and monitoring the conditions of storage
- procedures for ensuring the good order and cleanliness of storage areas
- procedures to ensure the storage of blood components does not jeopardise their identity, integrity or quality
- a procedure which ensures appropriate stock rotation.

6.8: Non-conforming components and biohazards

6.8.1: Discard of non-conforming components (including outdated components)

Procedures for the discard of non-conforming components should ensure that an appropriate record of discard is maintained. This includes:

- the donation number
- the component identity
- the reason for discard
- the date of discard
- the identity of the person effecting the discard.

If the discard process involves recording as a discard on computer software and physically discarding, then adequate records are required for both steps.

6.8.2: Biohazards

Components from donations that are repeatably reactive in mandatory microbiological screening tests or from donors whose records indicate their components should be destroyed because they are on a high-risk deferral registry or because of previous mandatory test results are classified as biohazards.

Secure and effective procedures are required to ensure that all components and samples from biohazard donations are retrieved for safe disposal in accordance with Blood Service policies and with the *Department of Health's Safe Management of Healthcare Waste*.[6] Procedures should include:

- a system which ensures all components prepared from any donation can be traced
- maintaining a record of the person who retrieves each biohazard component, including laboratory sample

When biohazard material (e.g. plasma) is retained for laboratory use, it must be appropriately labelled to prevent it ever being used for therapeutic purposes and must be stored in a secure freezer or other storage unit that is clearly labelled to prohibit the storage of material for therapeutic use. An inventory of freezer (or other storage unit) contents of such samples, record of 'sample' retention, reason for retention and fate should be maintained.

6.9: Component release

All components must be appropriately labelled in accordance with these guideline specifications including those general guidelines outlined in section 6.5 and Chapters 23 and 26.

Standard procedures must ensure that blood and blood components cannot be released to stock until all the required laboratory tests, mandatory and additional, have been completed, documented and approved within a validated system of work and it has been ascertained that conditions of production and storage have been satisfactory. Compliance with these requirements may be achieved by the use of a computer program, or suite of programs, which requires the input of valid and acceptable test results for all the mandatory and discretionary laboratory tests before permitting, or withholding, the release of each individual unit.

Where a computer-based system is not used or is temporarily unavailable, documented approval for the release of each individual unit should be by a designated person.

All biohazard donations and components otherwise unsuitable for issue should be reconciled and accounted for, preferably prior to releasing accompanying 'usable' blood components to stock.

6.10: Release of components which do not conform to specified requirements

Blood and/or blood components may be issued for research, for reagent and, in exceptional cases, for therapeutic use when they do not conform to specified requirements. Each Blood Establishment must have written instructions detailing the circumstances under which such concessionary issues can be made and the procedures to be followed.

For major non-conformances in components intended for therapeutic use (e.g. an HLA-matched platelet that is significantly below specified cell counts, extension of shelf life for an autologous donation or, in extreme circumstances, a donor sample not tested for mandatory microbiological marker etc.) the instructions should, as a minimum, include the following:

- that such component issues are authorised by a Blood Establishment consultant to the relevant registered medical practitioner
- that the reason for the issue is fully documented
- that a verbal and written warning indicating an increased level of risk is given by a Blood Establishment consultant to the receiving registered medical practitioner who should sign a statement indicating that he/she is willing to accept these risks
- that the name of the recipient is entered on the issue documentation
- that the component is clearly identified with a label indicating that it does not conform to specification, the details of the non-conformance, the name of the recipient and that it must not be used for any other patient.

Issues of non-conforming components should be subjected to a formal review process.

Minor non-conformances in components intended for therapeutic use (e.g. non-critical blood pack faults, minor label issues) should be referred for assessment by the quality manager.

6.11: Transportation of blood components

6.11.1: General considerations

Donated blood and blood components should be transported by a secure system using transit containers, packing materials and procedures which have been validated for the purpose to ensure the component surface temperature can be maintained within the correct ranges during transportation (Chapter 7).

Monitoring of routine transport temperatures should be performed periodically.

Revalidation should be performed if changes are made to the transport containers, packing materials or procedures.

As far as is practicable, transit containers should be equilibrated to a component’s storage temperature prior to filling.

Transport containers should be appropriately labelled and should be secure and protect components and samples from damage during transit.

Documentation should accompany components in transit to permit their identification.

Transport containers should not be exposed to temperatures beyond the range and time for which they have been validated.

Where melting ice is used to achieve an appropriate storage temperature, it should not come into direct contact with the components.

Dead air space in packaging containers should be minimised.

Written procedures for the transportation of components should be established and should ensure compliance with the guidance given above. In addition, written procedures should include the following:

- definition of approved systems of packaging, transportation and transport conditions required for each component
- a requirement for monitoring the performance of approved systems of packaging and transportation.

6.11.2: Transportation from collection site to processing centre

Blood and samples from donor sessions must be transported to the receiving blood supplier under appropriate conditions of temperature, security and hygiene.

Donations from which it is intended to prepare platelets should be transported in conditions that ensure the surface temperature of the blood packs does not drop below 18°C.

Blood and samples being transported from donor sessions must be accompanied by documentation, which ensures that all donations in the consignment can be accounted for. (Note: ‘Documentation’ includes information in writing or in electronic format.)

6.11.3: Transport of components from Blood Establishments to hospital blood banks/users

Blood components should be transported under conditions which are as close as possible to their specific storage requirements and comply with the requirements of Chapter 7. Transport time should be kept to a minimum.

It should be noted that, occasionally, red cell components are issued before they have been cooled to their storage temperature (4 ±2°C). In such circumstances, it may be neither possible nor necessary to maintain the transport temperature within the range 2-10°C and local judgement should be exercised.

Components dispatched from a blood supplier should be accompanied by a dispatch note detailing as a minimum:

- the donation number of each component
- if relevant, the component’s ABO and D blood group
- date and time packed
- the signature(s) and designation of the person(s) responsible for the issue
- space for the signature(s) and designation of the person(s) receiving the consignment.

A copy of the signed and annotated dispatch note (either paper or an electronic equivalent acceptable to the quality director) should be returned to the blood supplier for storage.

6.12: Component recall and traceability

There must be a documented system available in each Blood Establishment whereby adverse effects caused by the administration of any component, or the identification of a component quality problem, can enable the recall, if appropriate, of all unused components derived from that donation or all donations which are a constituent of a component pool. Similarly, there must be a documented system in each Blood Centre for the recall of any component or constituent of a component pool where reasonable grounds exist for believing it could cause adverse effects.

Any recall of a component should lead to a thorough investigation with a view to preventing a recurrence.

A system must be in place that ensures that any transfused (or discarded) blood component can be linked to the original donation and donor from which it was derived.[7]

6.13: References

1. Council of Europe (2023). *Guide for the Preparation, Use and Quality Assurance of Blood Components, 21st edition*. Council of Europe Publishing.
2. Beckman N, Nightingale MJ, Pamphilon D (2009). Practical guidelines for applying statistical process control to blood component production. *Transfusion Medicine*, 19, 329–339.
3. Medicines and Healthcare products Regulatory Agency (2022). *Rules and Guidance for Pharmaceutical Manufacturers and Distributors* (Orange Guide) 2022. London: Pharmaceutical Press.
4. Nightingale MJ, Lees B, Biset R, Mertens W (2006). Use of a (proposed) standard protocol to validate Terumo TSCD-II connections between dissimilar blood bag tubing. *Vox Sanguinis*, 91, 241–269.
5. Nightingale MJ, De Korte D, Chabenel A, Hughes W, Rowe GP, Nicholson G (2011). Eurobloodpack: a common European design for blood bag systems with integral leucodepletion filters. *Vox Sanguinis* , 101, 250–254.
6. Department of Health: Health Technical Memorandum 07-01: *Safe Management of Healthcare Waste* . Published by TSO (The Stationery Office) 2013. https://www.england.nhs.uk/publication /management-and-disposal-of-healthcare-waste-htm-07-01
7. UK Blood Safety and Quality Regulations (BSQR). Available at www.legislation.gov.uk/uksi/2005/50. BSQR amendments available at www.legislation.gov.uk/uksi/2005/2898 and www.legislation.gov.uk /uksi/2006/2013