Change Notification for the UK Blood Transfusion Services

Date of Issue: 13 March 2024 **Implementation:** to be determined by each Service

No. 03 – 2024

Red Book updates, Batch 3

Please note this document supersedes CN 03-2024 (v1) previously circulated on 31/01/24.

A typographical error has been corrected in **Table 6.1**.
The corrected final text is highlighted on **page 20**.

This notification includes the following chapters:

	BM-DSG Bone Marrow & Peripheral Blood Stem Cell	CB-DSG Cord Blood	GDRI Geographical Disease Risk Index	TD-DSG Tissue – Deceased Donors	TL-DSG Tissue – Live Donors	WB-DSG Whole Blood & Components	Red Book Guidelines for the BTS in the UK
Chapter 2 (pp. 2-18) Quality in blood and tissue establishments & hospital blood banks	○	○	○	○	○	○	●
Chapter 6 (pp. 19-30) Evaluation and manufacture of blood components	○	○	○	○	○	○	●
Chapter 7 (pp. 31-105) Specifications for blood components	○	○	○	○	○	○	●
Annexe 3 (pp. 106-123) Provisional components	○	○	○	○	○	○	●
Annexe 4 (p. 124) Redundant components	○	○	○	○	○	○	●
Annexe 5 (pp. 125-129) Blood components for contingency use	○	○	○	○	○	○	●

Dr Stephen Thomas
Professional Director of JPAC

Changes are indicated using the following key

original text	«inserted text»	~~deleted text~~

Chapter 2 Quality in blood and tissue establishments and hospital blood banks

2.1: Introduction

~~2.1.1: The quality environment~~

~~Until fairly recently, there was no formal regulation to cover blood tissues or cells. Indeed, they were all formally excluded when the Good Manufacturing Practice (GMP) Directive[1] was updated in 2003.~~

~~This omission was deliberate, in the knowledge that separate legislation was planned for blood (the 'Blood Directives') and tissues and cells (the 'Tissues and Cells Directives'). All of this legislation is described in more detail below. This legislation has changed the regulatory landscape for the Blood Services (now known as Blood Establishments), hospital blood banks (which are now subject to regulatory scrutiny for the first time) and for tissue and cell banks (which are now under formal regulation for the first time and known as Tissue Establishments).~~

~~In this chapter, the impact of these new regulatory requirements is discussed and the management of a quality management system which meets these new regulations is described based on the requirements for the Blood Safety and Quality Directives. The requirements for Tissues and Cells Directives are similar.~~

The key requirements for Blood Establishments and for hospital blood banks are defined in the Blood Safety and Quality Regulations (Statutory Instrument 2005 No. 50) «as amended,[1]» ~~,[2]~~ and are enforced by the Medicines and Healthcare products Regulatory Agency (MHRA). Those for tissues and cells are defined in the Human Tissue (Quality and Safety for Human Application) Regulations, 2007 (Statutory Instrument 2007 No. 1523),«2»~~3~~ and are enforced by the Human Tissue Authority (HTA).

These regulations require that Blood and Tissue Establishments are licensed and subject to regular inspection for compliance. Hospital blood banks are not formally licensed but must submit annual compliance reports to the MHRA. Based on these compliance reports, the MHRA select a number of hospital blood banks for inspection every year and can also decide to do 'for cause' inspections when there is evidence of non-compliance.

The MHRA and HTA have powers to remove licences from Blood and Tissue Establishments, respectively, and the MHRA can issue cease and desist orders to prevent blood banks from continuing in operation. These powers derive from the relevant UK legislation, which is designed to ensure that appropriate standards of performance are achieved and maintained. This inspection process is designed to generate a climate of continual quality improvement, and this chapter will look at the key issues which have to be addressed in achieving an effective quality management system.

2.2: Key ~~*European*~~ initiatives

2.2.1: European Union Blood Safety and Quality Directives

- Commission Directive 2002/98/EC of the European Parliament and of the Council of 27 January 2003 setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC.«3»~~4~~
- Commission Directive 2004/33/EC of the European Parliament and the Council of 22 March 2004 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components.«4»~~5~~
- Commission Directive 2005/61/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events.«5»~~6~~
- Commission Directive 2005/62/EC of 30 September 2005 implementing Directive 2002/98/EC of the European Parliament and of the Council as regards Community standards and specifications relating to a quality system for Blood Establishments.«6»~~7~~

The first two Directives came into force in UK law on 8 February 2005 as the Blood Safety and Quality Regulations 2005 (BSQR),«1»~~2~~ with their requirements becoming effective in November 2005. They set standards of quality and safety for the collection and testing of human blood and blood components, whatever their intended purpose, and their processing, storage and distribution when intended for transfusion. The regulations also cover the collection and testing of blood and blood components for autologous use. In effect, therefore, they cover the whole process from donor to patient – from 'vein to vein'.

The latter two Directives came into force in August 2006 and relate specifically to traceability requirements and notification of adverse reactions and events, and introduce EC standards and specifications relating to a quality system for Blood Establishments. They also added provisions relating to record keeping and traceability of blood and blood components to a new category of facility, defined as a hospital, another facility or service owned or managed by a health service body, a care home, an independent clinic, a manufacturer or a biomedical research institute.

The Directives define certain activities which can only be undertaken by Blood Establishments, namely:

- the collection and testing of blood or blood components, whatever their intended purpose
- the processing, storage and distribution of blood and blood components when they are intended to be used for transfusion.

Hospital blood banks are not permitted to undertake these activities unless licensed as Blood Establishments, but are able to store, distribute and perform compatibility tests on blood and blood components for use within hospital facilities.

«2.2.2: Medical devices legislation

Blood and Tissue Establishments and Hospital Blood Banks are key users of medical devices such as blood bags and *in vitro* diagnostic medical devices such as test kits for blood grouping. Some establishments also manufacture CE or UKCA marked *in vitro* diagnostic medical devices (guidelines for reagent manufacture are included in Chapter 11). The Good Practice Guidelines for Blood Establishments and the HTA Guide Quality and Safety Assurance for Human Tissue and Cells for Patient Treatment mandate the use of CE or UKCA marked medical devices wherever possible. Knowledge of medical devices legislation is therefore important for Blood and Tissue Establishments and Hospital Blood Banks.

The Medicines and Healthcare products Regulatory Agency (MHRA) is the designated authority that administers and enforces the law on medical devices in the UK. It has a range of investigatory and enforcement powers to ensure the safety and quality of medical devices placed on the UK market. Different regulatory requirements apply to Great Britain (England, Wales and Scotland) and Northern Ireland and these are set out below.

2.2.2.1: Regulation of medical devices in Great Britain

Medical devices are regulated under the Medical Devices Regulations 2002 (SI 2002 No 618, as amended) (UK MDR 2002) which is based on requirements derived from the following EU Directives:

- Directive 90/385/EEC on active implantable medical devices (EU AIMDD)
- Directive 93/42/EEC on medical devices (EU MDD)
- Directive 98/79/EC on *in vitro* diagnostic medical devices (EU IVDD)

The UKCA (UK Conformity Assessed) marking is a UK product marking used for certain goods, including medical devices, being placed on the Great Britain market. UKCA marking is not recognised in the Northern Ireland or the EU. UKCA marking requirements are based on the requirements of the relevant Annexes to the EU Directives listed above, which have been modified by Schedule 2A to the UK MDR 2002.

Under the UK MDR 2002, a CE marked device with a valid declaration of conformity or EC certificate is viewed as meeting the UKCA marking requirements whilst CE marking continues to be recognised in Great Britain - until 30 June 2023. This applies to devices that have been CE marked under and fully conform with the following applicable EU legislation:

- Directive 90/385/EEC on active implantable medical devices (EU AIMDD) (for devices that have been CE marked prior to 26 May 2021)
- Directive 93/42/EEC on medical devices (EU MDD) (for devices that have been CE marked prior to 26 May 2021)
- Directive 98/79/EC on *in vitro* diagnostic medical devices (EU IVDD) (for devices that have been CE marked prior to 26 May 2022)
- Regulation (EU) 2017/745 on medical devices (EU MDR)
- Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (EU IVDR)

From 1 July 2023, devices that are placed on the Great Britain market will need to conform with UKCA marking requirements.

2.2.2.2: Regulation of medical devices in Northern Ireland

Under the terms of the Northern Ireland Protocol, the rules for placing medical devices on the Northern Ireland market differ from those applicable to Great Britain. CE marking is needed for medical devices placed on the Northern Ireland market and the following EU Regulations apply:

- Regulation (EU) 2017/745 on medical devices (EU MDR)
- Regulation (EU) 2017/746 on *in vitro* diagnostic medical devices (EU IVDR)

In addition, the UKNI indication is required if a UK Notified Body undertakes mandatory third-party conformity assessment.

2.2.2.3: In-house manufacture of medical devices by Health Institutions

Health Institutions are exempt from the provisions of the UK MDR 2002 for products manufactured and used within the same Health Institution and either on the premises of their manufacture or on premises in the immediate vicinity without having been transferred to another legal entity. Additional requirements apply to Health Institutions in Northern Ireland and the requirements for Health Institution Exemption (HIE) set out in Article 5 of the EU MDR and IVDR must be complied with.

2.2.2.4: Off-label use and exceptional use of non-complying medical devices

Medical devices should be used as described by the manufacturer in the instructions for use. If a device is used in any other way, it is considered 'off-label' use. Without the manufacturer's approval this will be at your own risk and you or your employer could become liable for civil claims for damages from injured patients or their families if something goes wrong with the device. Modification of a device where this is not described in the manufacturer's instructions for use is also considered to be off-label use. Use of a non-CE or UKCA marked product for a medical purpose also carries risk and should be avoided; this includes use of products labelled as 'Research Use Only'. Although rare, there may be occasions where there is no option but to use a device off-label; the MHRA may authorise the use of a non-complying device on humanitarian grounds if they are satisfied that such use would be in the best interests of the patient and the protection of health. Further information on off-label use and exceptional use of non-complying medical devices is available on the MHRA web site.

2.2.2.5: Future regulation of medical devices in the UK

The MHRA are planning significant changes to how medical devices will be regulated in the UK. This will be implemented through amendments to the UK MDR 2002, and it is anticipated that these will enter in to force on 01 July 2023. Furthermore, changes to how the Northern Ireland Protocol will apply may have an impact on how medical devices are regulated. Readers are advised to check the MHRA website for up-to-date guidance on regulation of medical devices in Great Britain and Northern Ireland.»

~~*2.2.2: In Vitro Diagnostic Medical Devices Directive – 98/79/EC*~~[8]

~~*Following implementation of this Directive into UK law, users of in vitro devices must ensure that any stock produced and introduced into the supply chain is CE marked, and that only CE-marked stock can be purchased and used. There are a number of other obligations placed upon users; for example, they can be held criminally liable if they knowingly encourage the supply of non-CE marked in vitro devices. The main implication for the Blood Services surrounds the provision of reagents to third parties for their use, where CE marking is required, even if there is no payment for the reagent supplied. This is a complicated piece of legislation. Blood and Tissue Establishments and hospital blood banks are significant users and producers of in vitro devices, and they should ensure they are compliant with the legislation and should take appropriate advice to ensure they work within the legislation.*~~

~~*2.2.3: Medical Devices Directive (MDD) – 93/42/EEC*~~[9]

~~*This Directive has been brought into UK law. It was, however, amended by Directive 98/79/EC to recognise the definition of an in vitro diagnostic device, which was not originally defined, and to ensure there were common definitions between the two Directives, such as the precise meaning of 'putting into service'. It is anticipated that, while Blood and Tissue Establishments and hospital blood banks may not manufacture medical devices, they are key users of such devices, from blood bags to donation beds, so knowledge of the legislation may be beneficial.*~~

~~*At the time of writing (late 2012) a European Consultation is in progress to review the effectiveness of the European Devices legislation.*~~

«2.2.3» ~~2.2.4~~: Human Tissue Act 2004«11»~~10~~

The Human Tissue Act 2004 replaced the Human Tissue Act 1961, the Anatomy Act 1984 and the Human Organ Transplants Act 1989 as they relate to England and Wales, and the corresponding Orders in Northern Ireland.

The Human Tissue Act 2004 covers England, Wales and Northern Ireland. It established the Human Tissue Authority (HTA) to regulate activities concerning the removal, storage, use and disposal of human tissue. Consent is the fundamental principle of the legislation and underpins the lawful removal, storage and use of body parts, organs and tissue. Different consent requirements apply when dealing with tissue from the deceased and the living. The Human Tissue Act 2004 lists the purposes for which consent is required (these are called Scheduled Purposes).

There is separate legislation in Scotland – the Human Tissue (Scotland) Act 2006.

While provisions of the Human Tissue (Scotland) Act 2006 are based on authorisation rather than consent, these are essentially both expressions of the same principle.

«2.2.4» ~~2.2.5~~: The European Union Tissues and Cells Directives

- Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells.«12»~~11~~
- Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells.«13»~~12~~
- Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events, and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells.«14»~~13~~
- «Commission Directive 2012/39/EU of 26 November 2012 amending Directive 2006/17/EC as regards certain technical requirements for the testing of human tissues and cells.[15]»

These Directives establish a harmonised approach to the regulation of tissues and cells across Europe. They set a benchmark for the standards that must be met when carrying out any activity involving tissues and cells for human application (patient treatment). The Directives also require that systems are put in place to ensure that all tissues and cells used in human application are traceable from donor to recipient.

The HTA, as one of the Competent Authorities in the UK under the EU Tissues and Cells Directives, has responsibility for regulating tissues and cells (other than gametes and embryos) for human application.

«2.2.5» ~~2.2.6~~: Human Tissue (Quality and Safety for Human Application) Regulations 2007«2»~~3~~

The Directives were fully implemented into UK law on 5 July 2007, via the Human Tissue (Quality and Safety for Human Application) Regulations 2007. The HTA's remit includes the regulation of:

- procurement
- testing
- processing
- storage
- distribution
- import/export

of tissues and cells for human application.

Establishments where these activities are carried out will normally need a licence. To obtain this, establishments carrying out the above activities are required to meet the standards which are detailed in the Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment[14] as implemented by HTA Directions «001/2021» ~~003/2010~~.

The HTA also publishes Codes of Practice, which provide guidance and lay down expected standards for each of the sectors it regulates (see **www.hta.gov.uk**).

2.3: Other standards

There are a number of other standards that help define how a quality management system should be designed to meet the needs of a particular aspect of a Service's work. Table 2.1 provides information on some key «standards for inspection, licensing, accreditation and certification.» ~~inspection/licensing/accreditation/certification standards.~~

They are all applicable within England. Some apply directly to the whole of the UK (e.g. the International Standards), others to England and Wales (e.g. the NHS Litigation Authority Risk management assessment programme). Where there is not a direct cross-reference the reader should investigate further to determine how the standards might apply.

All the primary sources cited here are places where sound advice on management systems to address the various requirements of a modern Blood Service can be found. These will support the design and establishment of a system that can be confidently subjected to an external inspection process. The list is not intended to be exhaustive and by the nature of change is only current at the time of publication. It is for this reason version numbering has not been applied to the available standards; they will be constantly updated.

Table 2.1 List of some key inspection/licensing/accreditation/certification standards

Key standards	Applicable to	Responsible body	Website
~~BS 15000 IT Service Management Standard~~	~~Service management~~	~~BSI British Standards HQ, 389 Chiswick High Road, London W4 4AL, UK~~ ~~+44 208 996 9000~~ ~~BSI Online, Technical Indexes Limited, Willoughby Road, Bracknell RG12 8DW, UK~~ ~~+44 1344 404429~~	~~www.bsigroup.com~~
Caldicott Report 1997, implementation 1998	Confidentiality of patient data	Department of Health, ~~Richmond House, 79 Whitehall, London SW1A 2NL, UK~~ ~~+44 207 210 4850~~	www.dh.gov.uk
Care Quality Commission «Fundamental Standards 2014»	~~To regulate and inspect~~ Health and social care services in England	Care Quality Commission ~~National Correspondence, Citygate, Gallowgate, Newcastle upon Tyne NE1 4PA, UK~~ ~~+44 3000 616161~~	www.cqc.org.uk
«Health and Care Standards 2015» ~~Healthcare Inspectorate Wales~~	~~Healthcare Inspectorate Wales is the independent inspectorate and regulator of all~~ Healthcare in Wales	Healthcare Inspectorate Wales~~,~~ ~~Bevan House, Caerphilly Business Park, Van Road, Caerphilly CF83 3ED, UK~~ ~~+44 29 2092 8850~~	«www.hiw.org.uk»
«Health and Social Care Standard 2017» ~~NHS Quality Improvement Scotland~~	~~Improving the quality of~~ Care and treatment delivered by NHS Scotland	NHS Quality Improvement Scotland~~, Edinburgh Office, Elliott House, 8–10 Hillside Crescent, Edinburgh EH7 5EA, UK~~ ~~+44 131 623 4300~~	«www.nes.scot.nhs.uk»
«Quality standards for health and social care 2006» ~~The Regulation and Quality Improvement Authority~~ ~~Northern Ireland Department of Health, Social Services and Public Safety~~	~~Responsible for monitoring and inspecting~~ The availability and quality of health and social care services in Northern Ireland~~, and encouraging improvements in the quality of those services~~ ~~Controls assurance standards~~	The Regulation and Quality Improvement Authority, ~~9th Floor, Riverside Tower, 5 Lanyon Place, Belfast BT1 3BT, UK~~ ~~+44 28 9051 7500~~ ~~Central ALB Governance Unit,~~ Department of Health, «Northern Ireland» ~~Social Services and Public Safety, Castle Buildings, Stormont Estate, Belfast BT4 3SQ, UK~~ ~~+44 28 9052 2792~~	«www.rqia.org.uk»

European Foundation for Quality Management (EFQM) Self-Assessment	Measurement of the effectiveness and, over time, the improvement in a Blood Service's management system. Helping understand where they are on the path to excellence	British Quality Foundation~~, 32–34 Great Peter Street, London SW1P 2QX, UK~~ ~~+44 207 654 5000~~	**www.bqf.org.uk** **www.efqm.org**
European Blood Inspection System (EuBIS)	~~European project addressing~~ The safety of blood transfusion «in Europe»	Institut für Transfusionsmedizin und Immunhämatologie~~, DRK-Blutspendedienst, Klinikum der Johann Wolfgang Goethe Universität, Sandhofstrasse 1, D-60528 Frankfurt am Main, Germany~~	**www.eubis-europe.eu**
«Standards for Histocompatibility & Immunogenetics Testing» ~~European Federation for Immunogenetics (EFI)~~	Histocompatibility and Immunology (H&I) – reference and tissue typing	European Federation for Immunogenetics (EFI)~~, EFI Central Office, c/o Department of Immunohematology and Blood Transfusion, Leiden University Medical Centre, Building 1 E3-Q, PO Box 9600, 2300 RC Leiden, The Netherlands~~	**www.efiweb.eu**
«The Data Protection Act UK General Data Protection	Protection regarding processing of personal data of UK residents	Information Commissioner's Office	**www.ico.org.uk**
General Data Protection Regulation	Protection regarding processing of personal date of EU residents	EU Commission	**www.eugdpr.org**»
Good Automated Manufacturing Practice (GAMP) Guide for Validation of Automated Systems in Pharmaceutical Manufacture	Validation of computer system«s»	International Society for Pharmaceutical Engineering, ~~European Office, 7 Ave des Gaulois, B-1040, Brussels, Belgium~~ ~~+32 2 743 44 22~~	**www.ispe.org**
Good Manufacturing Practice (GMP) guidelines	Pharmaceutical environments	The European Commission publishes this online as EudraLex Volume 4	**health.ec.europa.eu/medicinal-products/eudralex/eudralex-volume-4_en**
HTA Directions «011/2021» ~~003/2010~~ – the standards required under the Human Tissue (Quality and Safety of Tissues and Cells for Human Application) Regulations 2007 HTA Codes of Practice	«Quality and Safety Assurance for Human Tissue and Cells for Patient Treatment» ~~Tissue banking activity~~	Human Tissue Authority~~, 151 Buckingham Palace Road, Victoria, London SW1W 9SZ, UK~~	**www.hta.gov.uk**
International standards for unrelated haematopoietic stem cell donor registries WMDA Accreditation Programme	Stem cell and donor registries	World Marrow Donor Association~~, WMDA Office, Europdonor Foundation, Plesmanlaan 1b, 2333 BZ Leiden, The Netherlands~~ ~~Fax: +31 71 5210457~~	**www.worldmarrow.org**
«ISO 15189 Medical Laboratories – requirements for quality and competence	Medical laboratories	UKAS	**www.ukas.com**»
ISO 17799 Information Security Management	Information security	BSI British Standards ~~HQ, 389 Chiswick High Road, London W4 4AL, UK~~ ~~+44 208 996 9000~~ ~~BSI Online, Technical Indexes Limited, Willoughby Road, Bracknell RG12 8DW, UK~~ ~~+44 1344 404429~~	**www.bsigroup.com**

ISO 9000 2000 and ISO 9001 2008 Quality management system requirements	Quality management systems	BSI British Standards ~~HQ, 389 Chiswick High Road, London W4 4AL, UK~~ ~~+44 208 996 9000~~ ~~BSI Online, Technical Indexes Limited, Willoughby Road, Bracknell RG12 8DW, UK~~ ~~+44 1344 404429~~	**www.bsigroup.com**
«ISO 20000 IT Service Management Standard	Service management	BSI British Standards	**www.bsigroup.com**
ISO 13485 Medical devices – Quality management systems – Requirements for regulatory purposes	Management of medical devices	BSI British Standards	**www.bsigroup.com**»
Joint Accreditation ICT Europe and EBMT (JACIE) assessment standard	Stem Cell Immunology – Human Progenitor Cells (SCI – HPC) collection, processing and storage	The Joint Accreditation Committee «ISCT & EBMT (JACIE)» ~~EBMT-EuroISHAGE (JACIE) Alvaro Urbano-Ispizua, JACIE Office, Hospital Clinic, Villarroel 170, 08036 Barcelona, Spain~~ ~~Tel: +34 93 454 9543~~ ~~Fax: +34 93 453 1263~~	«**www.ebmt.org**» ~~www.jacie.org/standards/interim-standards~~
NHSLA risk management assessment programme for NHS Trusts	Management of claims and litigation	National Health Service Litigation Authority~~, Napier House, 24 High Holborn, London WC1V 6AZ, UK~~ ~~+44 207 430 8700~~	**www.nhsla.com**
PRINCE2	Project control	Cabinet Office~~, Service Desk, Rosebery Court, St Andrew's Business Park, Norwich NR7 0HS, UK~~ ~~+44 845 000 4999~~	**www.best-management-practice.com**
~~Standards for the Medical Laboratory~~	~~Medical laboratories~~	~~Clinical Pathology Accreditation (UK) Limited, 21–47 High Street, Feltham TW13 4UN, UK~~ ~~Tel: +44 20 8917 8400~~ ~~Fax: +44 20 8917 8500~~	~~**www.cpa-uk.co.uk**~~

2.4: Systems

2.4.1: Quality management system

Within a Blood/Tissue Establishment an effective quality management system (QMS) is a well-designed, structured and organised method of quality assuring the provision of consistent, safe and efficacious products. It also covers all diagnostic activities, reagent production, clinical trials and R&D. It provides both a means to confirm to regulatory bodies, management and customers that the establishment's service is in compliance with relevant standards, and also a basis whereby improvement in quality may be demonstrated.

The European Blood and Safety Quality Directives require that a quality system is to be applied for any blood and blood components circulating in the EC and that member states therefore should ensure that for all blood and blood components including those coming from third countries there is a quality system in place for Blood Establishments equivalent to the quality system provided under these Directives.

The EU Tissues and Cells Directives have equivalent requirements for the provision of a quality management system. These are defined as follows: 'an efficient QMS comprises a series of inter-related elements and a quality system for Blood/Tissue Establishments should embrace the principles of quality management, quality assurance, and continuous quality improvement, and should include personnel, premises and equipment, documentation, collection, testing and processing, storage and distribution, contract management, non-conformance and self-inspection, quality control, blood component recall, and external and internal auditing'.

2.4.2: Good manufacturing practice

The application of GMP is the cornerstone of an effective QMS and provides the structure upon which the elements of the quality system can be built. The objective of GMP is formally stated as being 'to assure the quality of the medicinal product for the safety, well-being and protection of the patient'.«17»~~15~~ The BSQR requires that Blood Establishments and hospital blood banks meet the requirements of good practice. This is taken by the MHRA to mean that Blood Establishments and hospital blood banks should comply with all relevant sections of the EC Guidelines to GMP.«18»~~16~~ This applies to hospital blood banks, even though they are not manufacturing anything, but are part of the distribution chain which is defined as part of the overall manufacturing process.

The EC Guidelines to GMP are described more fully in section 2.6 using the quality system format provided by Directive 2005/62/EC.«6»~~7~~ Elements are presented under separate headings, and in practical terms all of these must be considered for each and every procedure or process to conform to the principles of good manufacturing practice.

2.5: Application of a quality management system

2.5.1: Blood Establishments

Blood Establishments are required under Directive 2005/62/EC[7] to implement EC standards and specifications relating to a quality system for Blood Establishments, taking fully into account the principles of GMP. «Commission Directive (EU) 2016/1214 of 25 July 2016 amended Directive 2005/62/EC as regards quality system standards and specifications for blood establishments.[19] This replaced article 2 with the requirement that systems should be developed taking into account the Good Practice Guidelines jointly developed by the Commission and the European Directorate for the Quality of Medicines and Healthcare of the Council of Europe and published by the Council of Europe.[20]» ~~*Article 2 of the Directive identifies the need for Good Practice Guidelines. These are in the process of preparation and the first iteration appears in the Council of Europe's Guide to the Preparation, Use and Quality Assurance of Blood Components, Annex 1.17 Over the next few editions of the guide the contents of the annex will be expanded and elaborated to fully incorporate all relevant aspects of GMP. When complete, it will become the Good Practice Guidelines referred to in Article 2 of Directive 2005/62/EC.*~~[7]

~~*In the absence of a complete guide,*~~ The approach we have taken in this chapter is to outline ~~*in this section*~~ the requirements of a quality management system in the context of the collection, processing, testing, storage and distribution of blood and blood components and tissues.

In addition, Blood Establishments should ensure they are compliant with the specific standards identified within the Blood Safety and Quality Regulations 2005«1»~~2~~ and other relevant standards and guidelines. These elements of the quality management system can be adapted to support other activities that a Blood Establishment may undertake, such as diagnostic testing and reagent production.

Blood Establishments are required to obtain a Blood Establishment Authorisation from MHRA before operating and to ensure that it is maintained through inspections scheduled every 2 years.

2.5.2: Hospital blood banks

Hospital blood banks are required to comply with the elements of the quality system outlined below relevant to their activities (see section 2.6). In addition, they must:

- Maintain donor to recipient traceability. Specifically BSQR (SI 2005 No.50) Regulation 9 (1)(e) requires hospital transfusion laboratories to 'maintain, for not less than 30 years, the data needed to ensure full traceability of blood and blood components, from the point of receipt of the blood or blood component by the hospital blood bank'.
- Undertake mandatory reporting of serious adverse events and serious adverse reactions related to transfusion to the Competent Authority. Specifically BSQR (SI 2005 No. 50) Regulation (1)(f) and Regulation 12B, Directive 2005/62 Annex, section 9.2 requires that 'there are procedures in place for quality assurance within the transfusion laboratory – Reporting Serious Adverse Events (SAE) and Serious Adverse Reactions (SAR)'.
- Complete an annual form, the Blood Compliance Report, developed by the MHRA, in which the laboratory indicates its compliance with the regulations. The form is reviewed by the Inspectorate division of the MHRA and those laboratories where there is deemed non-compliance are inspected as 'for cause' inspections. There may also be some control inspections undertaken to verify the use of the Blood Compliance Report and its completion.
- Establish their bona fides with the supplying Blood Establishment and sign a service level agreement between both parties to outline how compliance will be achieved. This must be done before a hospital blood bank can operate.

2.5.3: Tissue and cell establishments

These establishments should also operate a quality system that reflects the requirements below (section 2.6). The Tissues and Cells Directives are not as explicit on the requirements of a quality management system as the Blood Safety and Quality Directives and a quality system in the context of the Tissues and Cells Directives consists of the following elements: the organisational structure, defined responsibilities, procedures, processes, and resources for implementing quality management, and includes all activities which contribute to quality, directly or indirectly. Experience has shown that the elements below are effective in maintaining quality and safety in the procurement and supply of tissues and cells.

2.6: Quality management system

Note that where key advice is given elsewhere in the guidelines, the relevant sections have been cross-referenced. Where there is not a direct cross-reference, the reader should investigate further the relevant chapters of these guidelines and the standards in Table 2.1.

2.6.1: Personnel and organisation

The Blood Service must ensure that adequate resources are provided to implement and operate the quality management system, to continually improve its effectiveness and to satisfy customer requirements. The physical resources to undertake the work must be suitable to attain the required standards; this will include equipment, consumables, work areas, utilities etc. (see section 4.2 on staffing and training principles for donation sessions).

All personnel shall have up-to-date job descriptions that clearly set out their tasks and responsibilities. Organisations shall assign the responsibility for processing management and quality assurance to different individuals who function independently.

All personnel shall receive initial and continued training appropriate to their specific tasks. Training records shall be maintained. Training programmes shall be in place and shall include good practice.

The contents of training programmes shall be periodically assessed and the competence of personnel evaluated regularly.

There shall be written safety and hygiene instructions in place adapted to the activities to be carried out and in compliance with requirements.

2.6.2: Premises

2.6.2.1: General

Premises including mobile sites shall be adapted and maintained to suit the activities to be carried out. They shall enable the work to proceed in a logical sequence so as to minimise the risk of errors, and shall allow for effective cleaning and maintenance in order to minimise the risk of contamination (see section 6.4 on component processing).

2.6.2.2: Donation area

There shall be an area for confidential personal interviews and assessment of individuals to determine their eligibility to donate. This area shall be separated from all processing areas (see section 4.1 on premises at blood donor sessions).

2.6.2.3: Collection area

Collection shall be carried out in an area intended for safe donation, appropriately equipped for the initial treatment of donors experiencing adverse reactions or injuries from events associated with donation, and organised in such a way as to ensure the safety of both donors and personnel as well as to avoid errors in the collection procedure (see section 4.1 on premises at blood donor sessions).

2.6.2.4: Testing and processing areas

There shall be a dedicated laboratory area for testing that is separate from the processing area with access restricted to authorised personnel.

2.6.2.5: Storage areas

Storage areas shall provide for properly secure and segregated storage of different categories of blood, blood components, tissues and materials including quarantine and released materials and donations collected under special criteria (e.g. autologous donation).

Provisions shall be in place in the event of equipment or power failure in the main storage facility (see section 6.7.1 on the specifications for component storage areas).

2.6.2.6: Waste disposal area

An area shall be designated for the safe disposal of waste, disposable items used during the collection, testing and processing, and for rejected blood or blood components.

2.6.3: Equipment and materials

2.6.3.1: Equipment checks and record keeping

All equipment shall be validated, calibrated and maintained to suit its intended purpose. Operating instructions shall be available and appropriate records kept.

2.6.3.2: Selection of equipment

Equipment shall be selected to minimise any hazard to donors, personnel or blood components.

2.6.3.3: Selection of materials

Only reagents and materials from approved suppliers that meet the documented requirements and specifications shall be used. Critical materials shall be released by a person qualified to perform this task. Where relevant, materials, reagents and equipment shall meet the requirements of Directive 93/42/EEC[9] for medical devices and Directive 98/79/EC[8] for *in vitro* diagnostic medical devices or comply with equivalent standards in the case of collection in third countries (see section 4.7 on the control of purchased material and services).

2.6.3.4: Inventory records

Inventory records shall be retained for a period acceptable to and agreed with the Competent Authority.

2.6.3.5: Computerised systems

When computerised systems are used, software, hardware and back-up procedures must be checked regularly to ensure reliability, be validated before use, and be maintained in a validated state. Hardware and software shall be protected against unauthorised use or unauthorised changes. The back-up procedure shall prevent loss of or damage to data at expected and unexpected downtimes or function failures.

2.6.4: Change control

There shall be a system of change control in process. The system's aims shall be to ensure that changes are evaluated and made only if they provide tangible benefits to the organisation as judged by, for example, benefit to patients through risk reduction. It may also be driven by efficiency savings to ensure that maximum resources are devoted to patient care.

The system shall then ensure that the change is planned and implemented in a controlled way, incorporating training for staff in new procedures, and demonstration that the expected outcome has been delivered. Supporting documentation, including for example standard operating procedures (SOPs), shall ensure there is a record of the processes operated before and after the change, that the date of the change is known, and that material processes through the changed system can be identified.

There shall also be a system to ensure that the effectiveness of the newly implemented process is monitored and opportunities for further improvement are investigated and, where relevant, implemented. It shall support the organisation in trying to learn from incidents, complaints and other event information, as analysis of this will help identify potential beneficial changes.

2.6.5: Validation

Validation is a pre-defined exercise to ensure that equipment or a procedure (either current or proposed) is fit for its intended purpose and meets its pre-defined specification. The benefits of validation include assurance that critical aspects of a process are in control, increased probability of uniform product quality, reduced product waste and reduced customer complaints. New equipment, blood packs and manufacturing processes are examples where validation is essential before they are introduced into routine application.

2.6.6: Documentation

Effective documentation, whether in written or electronic format, must be accurate, authorised, controlled at issue and reviewed on a regular basis to ensure that it remains relevant. It provides clear instructions on what to do and prevents errors that may result from spoken communication. Records must be legible and made at the time actions are completed using indelible ink; corrections shall be signed and dated and made so that the original entry can be seen. This ensures consistency of manufacture and service provision, provides objective evidence that tasks have been correctly performed, permits investigation if problems arise and facilitates traceability from donor to patient and vice versa.

Records can be transferred to other media following procedures which meet applicable British or international standards.

Comprehensive documentation includes a hierarchy of documentation starting with:

- a quality manual
- policies
- specifications
- SOPs
- forms and worksheets, batch processing records, labels, equipment logbooks and investigation/validation records.

Effective document control must be practised to ensure that documents being used are current and an archive of superseded documents shall be established to provide an historical record.

2.6.7: Collection

2.6.7.1: Donor eligibility

- Procedures for safe donor identification, suitability interview and eligibility assessment shall be implemented and maintained. They shall take place before each donation and comply with legislative requirements (see section 3.2 on blood donation, and section 20.1 on tissue donation).
- The interview shall be conducted in such a way as to ensure confidentiality (see section 3.4 on informed consent for blood donation, and section 20.2 for tissue donation).
- The donor suitability records and final assessment shall be signed by a qualified health professional (see section 3.4 on informed consent for blood donation, and section 20.2 for tissue donation).

2.6.7.2: Collection of donated blood, blood components and tissues

- The collection procedure shall be designed to ensure that the identity of the donor is verified and securely recorded and that the link between the donor and the blood, blood components and blood samples is clearly established (see Chapter 5 on the collection of a blood component).
- The sterile systems used for the collection of donations and their processing shall be CE marked or comply with equivalent standards if the donations are collected in developing countries. The batch number of the key consumables shall be traceable for each blood component (see section 4.7 on the control of purchased material and services).
- Collection procedures shall minimise the risk of microbial contamination.
- Laboratory samples shall be taken at the time of donation and appropriately stored prior to testing.
- The procedure used for the labelling of records, donations and laboratory samples with donation numbers shall be designed to avoid any risk of identification error and mix-up.

- After collection, the donations shall be handled in a way that maintains their quality at a storage and transport temperature appropriate to further processing requirements.
- There shall be a system in place to ensure that each donation can be linked to the collection and processing system into which it was collected and/or processed.

2.6.8: Manufacture

2.6.8.1: Procedures and controls

Manufacturing processes must follow clearly defined procedures in order to obtain products or services of the requisite quality. The inputs to any process must be controlled: for example the use of approved suppliers to agreed specifications. Goods requiring incoming inspection must be held in quarantine until the inspection has been performed. During manufacture any in-process controls shall be carried out and recorded (see Chapter 7 on specifications for blood components). Statistical techniques may be used to provide confidence that processes remain in control.

2.6.8.2: Calibration

Calibration is a procedure that confirms, under defined conditions, the relationship between values obtained from an instrument or system and those obtained using an appropriate certified standard. Examples include any equipment from which physical measurements are obtained, for example weights, scales, temperature loggers, thermometers, light sources etc.

2.6.8.3: Quality control and quality monitoring

These provide confirmation either during or at completion of a process that manufacturing materials, processes and products meet their pre-defined specification. They may be release requirements (quality control tests), such as a non-reactive microbiological test results or demonstration of the effectiveness of a new batch of reagents (see Chapter 9 on microbiology tests for donors and donations, and section 20.5 on tissue donor testing). They may provide evidence that systems are operating as expected (quality monitoring), such as meeting a stated leucodepletion requirement by random sampling of finished product, or testing white cell content and then subjecting the result to statistical analysis perhaps by the use of control charts (see section 6.3 on component and process monitoring tests). These latter tests would not normally prevent the issue of material.

2.6.8.4: Proficiency testing

Proficiency testing monitors the capability to perform procedures within defined limits of accuracy by analysis of unknown samples. Successful outcomes are dependent on the combined outputs of operators, equipment and process. Proficiency testing exercises are applied to a wide spectrum of laboratory procedures and may be managed on a local or national basis. National External Quality Assurance Schemes (NEQAS) are widely used in the UK.

2.6.8.5: Contract manufacture

When contract manufacture/testing are undertaken the company supplying the goods or service shall have been employed following a formal contracting process. This shall include supplier audit, if the goods or service had been deemed critical, on the basis of a GMP risk assessment, by the organisation letting the contract. The goods and services provided shall be subject to regular monitoring to ensure they comply with the service specified in the original contract and may be subject to ongoing audit depending on the quality of the service/goods provided and their criticality to the organisation letting the contract.

2.6.9: Labelling

At all stages, all containers shall be labelled with relevant information of their identity. In the absence of a validated computerised system for status control, the labelling shall clearly distinguish released from non-released units of blood and blood components (see section 6.6 for labelling of blood components).

The labelling system for the collected donations, intermediate and finished blood components, tissues and samples must unmistakably identify the type of content, and comply with the labelling and traceability requirements.

For autologous blood and blood components, the label also shall comply with requirements.

2.6.10: Release of blood and tissue components

There shall be a safe and secure system to prevent release until all mandatory requirements have been fulfilled (see Chapter 9 on microbiology tests for donors and donations for blood, and section 20.11 on release criteria for tissues). Each establishment shall be able to demonstrate that each blood, blood component, tissue, reagent or diagnostic test result has been formally released by an authorised person. Records shall demonstrate that before a blood component or tissue is released, all current declaration forms, relevant medical records and test results meet all acceptance criteria.

Before release, blood and blood components, tissues and reagents shall be kept administratively and physically segregated from released items. In the absence of a validated computerised system for status control a labelling system shall identify the release status.

In the event that an item fails release due to a confirmed positive infection test result, a check shall be made to ensure that other components from the same donation and components prepared from previous donations given by the donor are identified. There shall be an immediate update of the donor record.

2.6.11: Storage and distribution

Procedures for storage and distribution shall be validated to ensure blood and blood component quality during the entire storage period and to exclude mix-ups of blood components (see section 6.7 on component storage).

Autologous blood, blood components and tissues as well as blood components and tissues collected and prepared for specific purposes shall be stored separately.

Appropriate records of inventory and distribution shall be kept.

Packaging shall maintain the integrity and storage temperature of blood or blood components during distribution and transportation (see section 6.11 on transportation of blood components).

Return of blood, blood components and tissues into inventory for subsequent reissue shall only be accepted when all quality requirements and procedures laid down by the Blood Establishment to ensure tissue and blood component integrity are fulfilled.

2.6.12: Traceability

There must be a system to ensure that material can be traced through the procurement, testing, and production and issue systems to a patient (for blood, see sections 5.2.1 on donor identification, and 5.5.3 on labels). If the material is donated then traceability must be maintained from the donor to the patient. Any products must be uniquely identified to help support traceability. For example, for reagents this can be to batch level. Where appropriate this should be to individual units, for example apheresis donations split into multiple doses. Any material obtained from outside the EU must maintain a standard of traceability to its origin equivalent to that expected within a Blood Establishment. Under the terms of the BSQR, traceability records of blood components must be maintained for a minimum of 30 years. A similar requirement is in place for tissues and cells under the terms of the Tissues and Cells Directive.«12»~~11~~

2.6.13: Continuous improvement

It is important to take a holistic view using all available information, including information derived from analysis of incidents, errors, near misses and complaints as well as from audit processes, litigation and peer organisations. This approach will help prioritise those improvements that will be most beneficial to patients, donors and staff. As root cause analysis places a significant drain on expert resources it should be targeted on activities that on the balance of risk are most critical to the organisation. This process should be linked to the Blood Establishment's planning process so that improvements that require significant resources can be given sufficient consideration and support in their implementation.

2.6.14: Non-conformance

2.6.14.1: Deviations

Blood components or tissues deviating from required standards shall be released for transfusion only in exceptional circumstances and with the recorded agreement of the prescribing physician and the Blood Establishment physician.

2.6.14.2: Complaints

All complaints and other information, including serious adverse reactions and serious adverse events, which may suggest that defective blood components or tissues have been issued, shall be documented, carefully investigated for causative factors of the defect and, where necessary, followed by recall and the implementation of corrective actions to prevent recurrence. Procedures shall be in place to ensure that the Competent Authorities are notified as appropriate of serious adverse reactions or serious adverse events in accordance with regulatory requirements.

2.6.14.3: Recall

A system (usually, but not necessarily, computer software) shall be in place to allow full traceability of products. This will ensure that efficient recall of products can be effected and that look-back studies can be undertaken. The recall operation shall be capable of being initiated promptly and at any time. It is essential that all recalled products are stored separately and securely until a decision is made on the fate of the product. Records of recall must be maintained. A review of the recall procedures for effectiveness needs to be carried out periodically (for blood, see section 6.12 on component recall and traceability).

2.6.14.4: Serious adverse events and reactions

Serious adverse events (SAEs) and serious adverse reactions (SARs) (as defined in the EU Directives) must be reported to the relevant Competent Authority through the relevant website reporting tool:

- For blood and blood components, these are reported to the MHRA as serious adverse blood reactions and events
- For tissues, these are reported to the HTA as serious adverse events and reactions.

2.6.15: Audit (self-inspection)

Quality audit is a planned process of inspection conducted in an independent and detailed way by competent, trained individuals to ensure that procedures and associated quality assurance comply with the principles of GMP. The results of such inspections shall be recorded and non-compliances reported in writing to a designated individual whose responsibility it is to ensure corrective and preventive actions are applied in an effective and timely manner.

There will also be an opportunity to learn from the problems identified through audit, to identify underlying root cause and possibly to support conclusions on areas to improve, identified through incidents and error reporting. As noted above this process should also be linked to the Blood Service's planning process so that improvements that require significant resources can be given sufficient consideration and support in their implementation.

For Blood and Tissue Establishments, audits shall extend to suppliers of goods and services. The frequency or appropriateness of audit shall be decided on the basis of risk. This can be incorporated into the procurement system.

2.7: Reporting of incidents to external bodies

2.7.1: Serious Hazards of Transfusion (www.shotuk.org)

For blood components, serious adverse reactions and events must be reported to the MHRA (see section 2.6.14.4). However, in addition, blood banks and Blood Establishments are encouraged to report to the Serious Hazards of Transfusion (SHOT) scheme. SHOT collects data on serious sequelae of transfusion of blood components. Through the participating bodies, the information obtained contributes to improving the safety of the transfusion process, informing policy within the transfusion services, improving standards of hospital transfusion practice and aiding production of clinical guidelines for the use of blood components.

Participation in the scheme is voluntary, and covers both NHS and private hospitals in the UK and Ireland. Reports are made via SABRE (see www.mhra.gov.uk/Safetyinformation/Reportingsafetyproblems/Blood/index.htm).

Near misses should also be reported to SHOT. These are incidents where an action has placed a patient at risk. This could include, for example, the placing in stock of incorrectly labelled blood components where the discrepancy in blood group, genotype or test status would have placed a patient at risk of an adverse outcome if the component had been transfused.

It is assumed that if transfusion of products in this 'near miss' category occurs resulting in adverse outcome the incident would be reported back to the supplying service, so that they can investigate, identify root cause and prevent further occurrence. In this case it is important that it is understood that in these situations capturing data about events is not about

assigning blame or liability but is about improving systems and reducing risk. Such incidents should also be reported to SHOT.

2.7.2: Devices (www.mhra.gov.uk)

The remit of the Medicines and Healthcare products Regulatory Agency (MHRA) is to enhance and safeguard the health of the public by ensuring that medicines work and are acceptably safe.

Blood Services, blood and tissue banks shall have a mechanism to report problems with medicines, medical devices or *in vitro* diagnostic devices to the MHRA. This will provide an opportunity for problems with medicines and devices to be viewed on a UK or European-wide level.

There may be additional local requirements which also must be met. For example, in Northern Ireland there has been a recent Directive that all critical adverse incidents be reported directly to the Northern Ireland Department of Health, Social Services and Public Safety.

«Adverse incidents involving medical devices in England and Wales should be reporting using the Yellow Card scheme or via the Yellow Card app. Such incidents should be reported to the Northern Ireland Adverse Incident Centre in Northern Ireland and to Health Facilities Scotland online incident reporting system in Scotland.»

2.7.3: Serious untoward incidents

Serious untoward incidents can be defined as 'something out of the ordinary, or unexpected, with the potential to cause serious harm, and/or likely to attract public and media interest that occurs on NHS premises or in the provision of an NHS or a commissioned service' (NHS London, 2007).[«21»~~18~~] Blood Services may choose to refine this definition further.

Many of these incidents will be captured and investigated using a Blood Service's quality management system processes. Investigations shall be undertaken promptly, be coordinated by a board director and shall be considered for reporting externally.

Reports may be referred to:

- Department of Health or equivalent
- National Patient Safety Agency (NPSA), although the lead report should be from the Trust or facility where the patient involvement occurred. If this is not a Blood Service then the final report should contain the blood service's contribution
- National Health Service Litigation Authority (NHSLA) if litigation may result
- NHS Information Authority (NHSIA) for IT-related events
- Police in the case of criminal activity
- Health and Safety Executive (HSE) – RIDDOR
- Department of Health Estates and Facilities for fires
- Local Counter-Fraud Specialist (LCFS) for fraud
- Department of Health Estates and Facilities for defect and failure reporting in plant or facility or associated services
- Other stakeholders identified as relevant during the investigation of the serious untoward incident.

2.8: References

«

1. Statutory Instrument 2005 No. 50. The Blood Safety and Quality Regulations 2005. Available at **www.legislation.gov.uk**
2. Statutory Instrument 2007 No. 1523. The Human Tissue (Quality and Safety for Human Application) Regulations 2007. Available at **www.legislation.gov.uk**

3. Commission Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC. OJ, L 33, 08.02.2003, p. 30.

4. Commission Directive 2004/33/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components. OJ, L 91, 30.03.2004, p. 25.

5. Commission Directive 2005/61/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events. OJ, L 256, 01.10.05, p. 32.

6. Commission Directive 2005/62/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards Community standards and specifications relating to a quality system for blood establishments. OJ, L 256, 01.10.05, p. 41.

7. Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on *in vitro* diagnostic medical devices'. OJ, L 331, 07.12.1998, p. 1.

8. Council Directive 93/42/EEC of 14 June 1993 concerning medical devices. OJ, L 169, 12.7.1993, p.1–43.

9. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices, amending Directive 201/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC. OJ, L 117, 05.05.2017, p.1-175

10. Regulation (EU) 2017/746 of the European Parliament and of the Council of 5 April 2017 on *in vitro* diagnostic medical devices and repealing Directive 98/79/EC and Commission Decision 2010/227/EU. OJ, L 117, 05.05.2017, p.175-332.

11. Human Tissue Act 2004. Available at **www.legislation.gov.uk/ukpga/2004/30/pdfs/ukpga_20040030_en.pdf**

12. Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. OJ, L 102, 07.04.2004, p. 48.

13. Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells. OJ, L 038, 09.02.2006, p. 40.

14. Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells. OJ, L 294, 25.10.2006, p. 32.

15. Commission Directive 2012/39/EU of 26 November 2012 amending Directive 2006/17/EC as regards certain technical requirements for the testing of human tissues and cells. OJ, L 327, 27.11.12, p. 24-25.

16. Human Tissue Authority, Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. Available at www.hta.gov.uk.

17. Medicines and Healthcare products Regulatory Agency (2007). Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007. London: Pharmaceutical Press.

18. EC Guidelines to Good Manufacturing Practice. Available at **http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm**

19. Commission Directive (EU) 2016/1214 of July 2016 amending Directive 2005/62/EC as regards quality system standards and specifications for blood establishments. OJ, L 199, 26.7.16, p. 14-15.

20. Council of Europe (2013). Guide to the Preparation, Use and Quality Assurance of Blood Components, 17th edition, Appendix 1.

21. NHS London (2007). Serious Untoward Incident Guidance. **www.london.nhs.uk/webfiles/tools%20and%20resources/NHSL_SUI_Guidance.pdf**

»

1. ~~Commission Directive 2003/94/EC laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use OJ, L 262/22, 14.10.2003.~~

2. ~~Statutory Instrument 2005 No. 50. The Blood Safety and Quality Regulations 2005. Available at www.legislation.gov.uk.~~

3. ~~Statutory Instrument 2007 No. 1523. The Human Tissue (Quality and Safety for Human Application) Regulations 2007. Available at www.legislation.gov.uk.~~

4. ~~Commission Directive 2002/98/EC setting standards of quality and safety for the collection, testing, processing, storage and distribution of human blood and blood components and amending Directive 2001/83/EC. OJ, L 33, 08.02.2003, p30.~~

5. ~~Commission Directive 2004/33/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards certain technical requirements for blood and blood components. OJ, L 91, 30.03.2004, p25.~~

6. ~~Commission Directive 2005/61/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards traceability requirements and notification of serious adverse reactions and events. OJ, L 256, 01.10.05, p32.~~

7. ~~Commission Directive 2005/62/EC implementing Directive 2002/98/EC of the European Parliament and of the Council as regards Community standards and specifications relating to a quality system for blood establishments. OJ, L 256, 01.10.05, p41.~~

8. ~~Directive 98/79/EC of the European Parliament and of the Council of 27 October 1998 on in vitro diagnostic medical devices'. OJ, L 331, 07.12.1998, p1.~~

9. ~~Council Directive 93/42/EEC of 14 June 1993 concerning medical devices. OJ, L 169, 12.7.1993, pp1–43.~~

10. ~~Human Tissue Act 2004. Available at www.legislation.gov.uk/ukpga/2004/30/pdfs/ukpga_20040030_en.pdf.~~

11. ~~Directive 2004/23/EC of the European Parliament and of the Council of 31 March 2004 on setting standards of quality and safety for the donation, procurement, testing, processing, preservation, storage and distribution of human tissues and cells. OJ, L 102, 07.04.2004, p48.~~

12. ~~Commission Directive 2006/17/EC of 8 February 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards certain technical requirements for the donation, procurement and testing of human tissues and cells. OJ, L 038, 09.02.2006, p40.~~

13. ~~Commission Directive 2006/86/EC of 24 October 2006 implementing Directive 2004/23/EC of the European Parliament and of the Council as regards traceability requirements, notification of serious adverse reactions and events and certain technical requirements for the coding, processing, preservation, storage and distribution of human tissues and cells. OJ, L 294, 25.10.2006, p32.~~

14. ~~Human Tissue Authority, Guide to Quality and Safety Assurance for Human Tissues and Cells for Patient Treatment. Available at www.hta.gov.uk.~~

15. ~~Medicines and Healthcare products Regulatory Agency (2007). Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007. London: Pharmaceutical Press.~~

16. ~~EC Guidelines to Good Manufacturing Practice. Available at http://ec.europa.eu/health/documents/eudralex/vol-4/index_en.htm.~~

17. ~~Council of Europe (2013). Guide to the Preparation, Use and Quality Assurance of Blood Components, 17th edition, Appendix 1.~~

18. ~~NHS London (2007). Serious Untoward Incident Guidance. www.london.nhs.uk/webfiles/tools%20and%20resources/NHSL_SUI_Guidance.pdf~~

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» ~~<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, ~~*methylene blue treated plasma and*~~ the medicinal product solvent detergent treated pooled plasma «is» ~~*are*~~ 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 CE-marked 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).»

~~*Filters suitable for the removal of abnormal prion from red cells have been CE marked and have been under clinical assessment in the UK. Recommendations on their use have recently been submitted to ministers and the outcome on this is awaited. As part of the validation and clinical assessment, specifications for these products have been drafted and are available in the Trial component (Annex 3) section of the online version of these guidelines.*[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» ~~*Discard*~~ 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» ~~*not*~~ 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» ~~Discard~~ limits

Please note text corrected from CN 03-2024 v1

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» ~~none~~	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» ~~30~~	«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» ~~30~~	«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» ~~prior to splitting~~	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 (×10^9/unit)	160	«Defined by pack type [1]»
	Volume (mL)	150	380
Platelets, Apheresis, Leucocyte Depleted	Platelet yield (×10^9/unit)	160	«Defined by pack type [1]»
	Volume (mL)	150	380
«Platelets in Additive Solution, Leucocyte Depleted»	«Platelet yield (×10^9/unit)»	«160»	«Defined by pack type [1]»
Platelets for Intrauterine Transfusion, Leucocyte Depleted	Volume (mL)	50	120
	WBC (×10^6/unit)	None	2.5
«Platelets, Neonatal Use, Leucocyte Depleted»	«Platelet yield (×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 (×10^9/unit)»	«40»	«Defined by pack type [1]»
Fresh Frozen Plasma, Leucocyte Depleted	Volume (mL)	200	«340» ~~360~~
	Factor VIII (IU/mL)	0.3	None
	«Residual Platelet Count (×10^9/L), pre-freeze in starting component»	«None»	«100»
«Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted»	«Residual Platelet Count (×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 (×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» ~~2~~] and in Beckman et al. (2009).[«2»~~3~~] A flowchart adapted from Beckman et al., to aid in selection of appropriate methods, is reproduced as Figure 6.1.

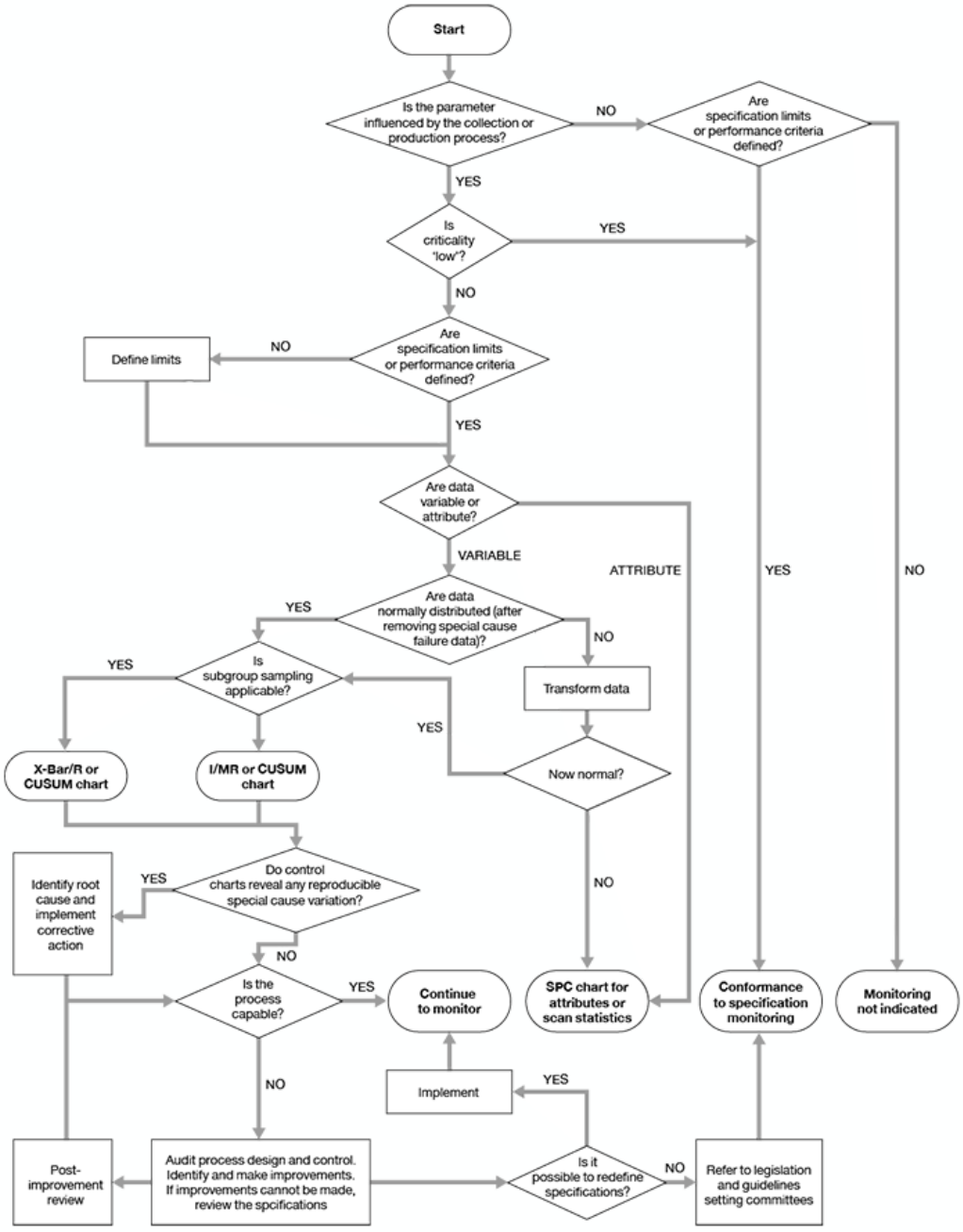


Figure 6.1 Algorithm for the selection of quality monitoring methods

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 of 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» ~~2007.~~[4] 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 1 year must be prepared from previously tested donors who have given at least one donation in the last 2 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 ~~*and periodic monitoring*~~ 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~~s~~ 1 (blood bags~~, 2010~~), «Part» 2 (graphic symbols~~, 2008~~) ~~and~~ «, Part» 3 (blood bags with integrated features~~, 2006~~) «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» ~~5,6~~]

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» ~~*2007.*~~[4]

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.» ~~*Chapters 23 and 26. It is planned that a more extensive library of relevant blood component labels will be available within the electronic component portfolio being developed for the website for the Guidelines for the Blood Transfusion Services in the United Kingdom.*~~[1]

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»~~7~~ 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 samples.

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 they are 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 ~~Rh~~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»~~8~~

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**

»

~~*1. Guidelines for the Blood Transfusion Services in the United Kingdom (The Red Book). Available at www.transfusionguidelines.org.uk.*~~

~~*2. Council of Europe (2010). Guide for the Preparation, Use and Quality Assurance of Blood Components, 16th edition. Council of Europe Publishing.*~~

~~*3. Beckman N, Nightingale MJ, Pamphilon D (2009). Practical guidelines for applying statistical process control to blood component production. Transfusion Medicine, 19, 329–339.*~~

~~*4. Medicines and Healthcare products Regulatory Agency (2007). Rules and Guidance for Pharmaceutical Manufacturers and Distributors 2007 (the 'Orange Guide'). London: Pharmaceutical Press.*~~

~~*5. 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.*~~

~~*6. 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.*~~

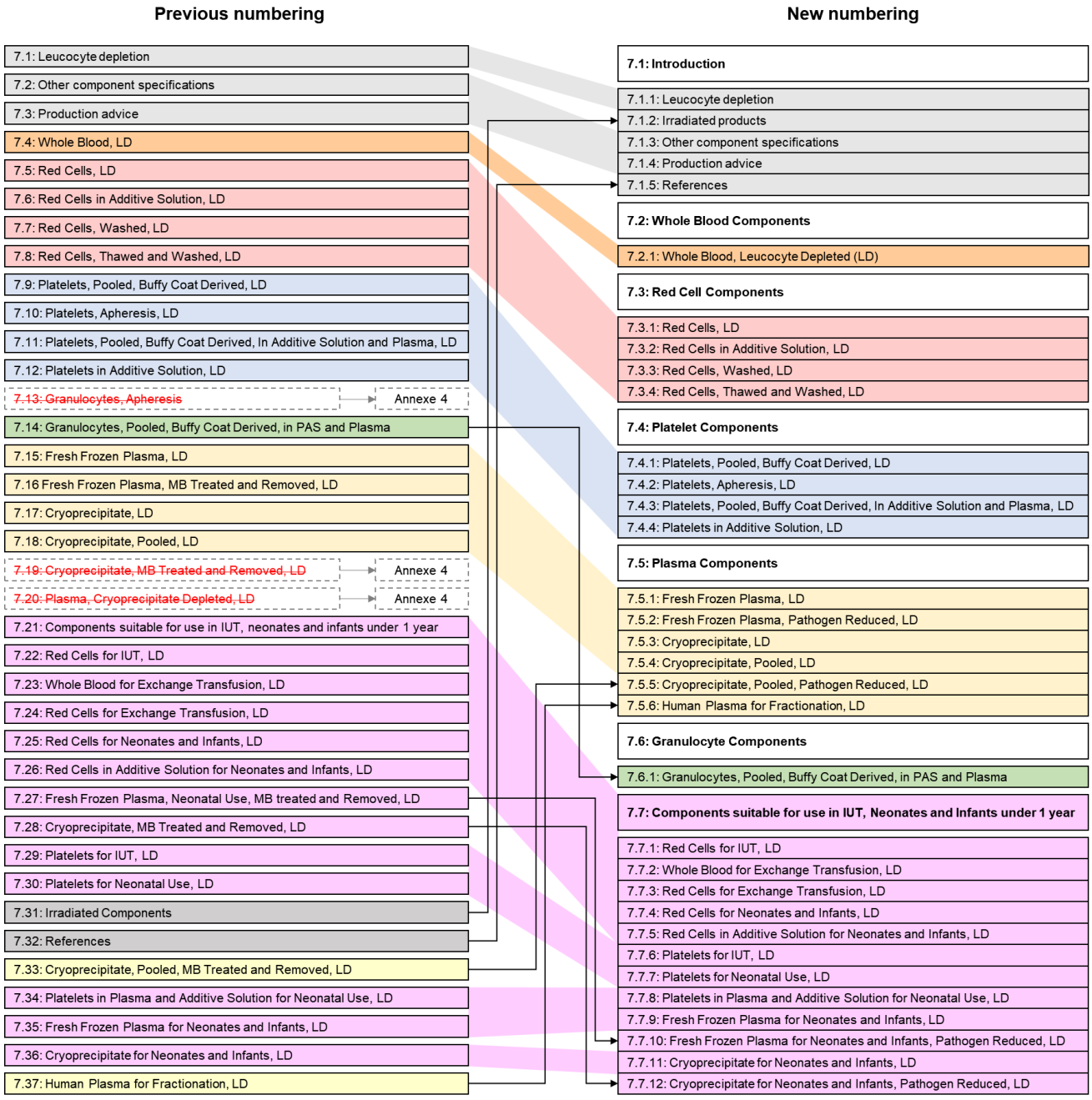
~~*7. Department of Health: Health Technical Memorandum 07-01: Safe Management of Healthcare Waste. Published by TSO (The Stationery Office) November 2006.*~~

~~*8. 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*~~

Chapter 7 Specifications for blood components

In addition to updating the text within Chapter 7, the numbering of blood component specifications has also been amended (now grouped by product type) to facilitate the future addition of new components within relevant subgroups. An overview of the amended numbering system is shown below.

Many specifications retain their original order within the new subgroups (with new numbers). Those specifications that have been repositioned within the new grouping system are indicated by arrows.



«7.1: Introduction

This chapter details process, product, quality monitoring, labelling, discard, storage and transport specifications for blood components currently manufactured in the blood transfusion services in the UK. Blood components are grouped together into the following component types.

In addition, to the blood components described in chapter 7:

- Provisional components are found in Annexe 3
- Redundant blood components are found in Annexe 4
- Blood components for contingency use are found in Annexe 5»

«7.1.1» ~~7.1~~: Leucocyte depletion

With very few stated exceptions (e.g. granulocytes), from November 1999 all allogeneic blood components produced in the UK have been subjected to a leucocyte depletion process. The term 'LD' may be used where necessary instead of 'leucocyte depleted' or 'leucocyte depletion' although component names will state 'Leucocyte Depleted' where appropriate. The UK specification for leucodepletion is that more than 90% of leucocyte-depleted components from relevant processes should have less than 1×10^6 leucocytes and more than 99% of components should contain less than 5×10^6 leucocytes, both with 95% confidence. Process performance should be assessed against the 1×10^6 limit when using statistical process control (statistical process monitoring) measurements.

Leucocyte depletion can be achieved by a number of methods, which must be validated before use. If filtration is used the recommended capacity of the filter must not be exceeded.

Currently, it is not feasible to assess all components for the effectiveness of the leucodepletion process. Therefore, the UK Blood Transfusion Services (UKBTS) should apply recognised statistical process monitoring methodologies such as those proposed by the International Society of Blood Transfusion Biomedical Excellence for Safer Transfusion (ISBT) BEST Expert Working Party, published in Transfusion«1»,~~1~~ to ensure the following:

- conformance of the process to the LD process specification
- identification of LD component specified limit failures
- stability of the process over time.

The residual leucocyte testing schedule should be defined in process monitoring and conformance checking procedures.

It is advisable to identify results to a production run or 'batch' and to ensure conformance of components to relevant specifications before release of components to stock or to ensure that a monitored filter batch is producing components that conform to specification.

A leucocyte depletion process is controlled if a control chart or equivalent is in use and does not currently display control limit or trend warnings.

A leucocyte depletion process is uncontrolled if a control chart or equivalent is not in operation for the process or if a current control chart or equivalent displays control limit or trend warnings.

Where statistical process monitoring methodology is not judged appropriate due to an inability to control the process or the production of small numbers of components, all components routinely issued to stock must have been shown to contain less than 5×10^6 leucocytes.

Issue (to stock) of components, which do not meet the leucocyte depletion specified limit of «less than» 5×10^6/unit, must follow a concessionary release procedure (see Section 6.10).

Patient-designated components should not be discarded before referral to a clinician.

Secondary components or split components produced from primary components do not require a leucocyte count provided the primary process is controlled or the individual primary component is tested and found to be acceptable.

Plasma components derived from whole blood filtration do not require residual leucocytes to be monitored provided the associated red cell process is controlled.

Leucocyte or platelet counts on components produced from frozen and thawed material should be made, where necessary, prior to the initial freezing process unless otherwise validated.

If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.

Leucocyte depletion of components should take place before the end of Day 2 (Day 0 is the day of collection).

Once a red cell component has been cooled to its storage temperature (i.e. 4 ±2°C) prior to leucodepletion, and when leucodepletion by filtration is to take place at ambient temperature, the ambient temperature of the room in which filtration takes place should not exceed 26°C (see also section 6.4).

If components are removed from their designated storage temperature to undergo a leucodepletion process, they must be returned to their storage temperature as soon as possible and in any event within 3 hours (see also section 6.4).

«7.1.2» ~~7.31~~: Irradiated components

- For the whole of this section X-irradiation may be regarded as equivalent to gamma irradiation. Times when irradiation should be undertaken and the permitted post-irradiation storage times are the same, as are the required labelling and dosing (recommended minimum dose achieved in the irradiation field is 25 Gy, with no part receiving >50 Gy) (±10% at 95% confidence interval).
- Note that the X-ray equipment should be dose-mapped prior to release from the factory and at installation, and the manufacturers recommend routine dosimetry at 6-monthly intervals (gamma-irradiation equipment requires annual dosimetry). A radiation-sensitive label specifically for use with X-irradiation is available.
- It is not necessary to irradiate the following components:
    - cryopreserved red cells after washing
    - plasma components «that have been frozen below –25°C».
- For more information, refer to the «British Society for Haematology (BSH)» ~~BCSH~~ Guidelines on the Use of Irradiated Blood Components.«2»~~3~~
- Irradiated components not used for the intended recipient can safely be used for recipients who do not require irradiated components provided the other requirements of Chapters 6 and 7 have been satisfied. However, any reduction in shelf life resulting from the irradiation process must be observed.
- Irradiated components should conform to their appropriate specification previously given in this chapter. In addition, the guidelines shown below should be observed.

«7.1.2.1» ~~7.31.1~~: Description

Irradiated components are components that have been irradiated by a validated procedure.

«7.1.2.2» ~~7.31.2~~: Technical information

- Other than for use in intrauterine transfusion, exchange transfusion, or large-volume transfusion of neonates, red cells can be irradiated at any time up to 14 days after collection.
- Platelets can be irradiated at any stage in their storage.
- Granulocytes should be irradiated as soon as possible after production.
- «Liquid plasma can be irradiated at any stage in its storage. (Liquid plasma refers to plasma that has not been frozen and has been stored throughout its shelf life at 4 ±2°C).»
- For red cells, platelets «, liquid plasma» and granulocytes the recommended minimum dose achieved in the irradiation field is 25 Gy, with no part receiving >50 Gy (±10% at 95% confidence interval).
- Laboratories performing irradiation of blood components must work to a clearly defined specification and are strongly recommended to work closely with a medical physicist. The defined irradiation procedure must be validated and there must be regular monitoring of the blood component dosimetry and the laboratory equipment. Provided the blood dosimetry uncertainty of measurement used by blood establishments is equal to or less than the uncertainty as it was measured in the original study data ~~(Pelzsynski et al, 1994)~~ (±10%)«3», there is no clinical indication to include the uncertainty of measurement within routine mapping to confirm ongoing specification compliance.
- It is recommended that irradiation of blood components is carried out using dedicated blood irradiation machines. If radiotherapy machines are used, equivalent protocols should be developed.
- Appropriate radiation-sensitive labels should be used as an aid to «differentiate» ~~differentiating~~ irradiated from non-irradiated components. However, it may not be necessary to attach a radiation-sensitive label to every component pack, provided that the irradiation procedure follows a validated, documented and well-controlled system of work that is integrated with the component labelling and release mechanism and permits retrospective audit of each stage of the irradiation process.
- There should be a permanent record of all units irradiated. This should include details of irradiation batch and donation numbers, component type, the site of irradiation, when irradiation was performed and by whom.

«7.1.2.3» ~~7.31.3~~: Labelling

- Irradiated components must be identified by the applied labelling and include ~~the date of irradiation and~~ any reduction in shelf life.
- Labels which are sensitive to irradiation and «undergo a visual» change ~~from 'NOT IRRADIATED' to 'IRRADIATED'~~ are available and are considered a useful indicator of exposure to irradiation. The dose at which the label changes to «indicate irradiated status» ~~'IRRADIATED'~~ must be marked on the label. It must be remembered that such labels simply reflect that the unit has been exposed to radiation and their use does not replace the need for regular and precise dosimetry nor carefully controlled working procedures.

«7.1.2.4» ~~7.31.4~~: Storage

For general guidelines, see section 6.7.

- Red cell components, other than washed red cells and those for intrauterine transfusion, exchange transfusion, or large-volume transfusion of neonates and infants can be irradiated at any time up to 14 days after collection and stored for up to 14 days thereafter, provided the other requirements of this section are adhered to.
- «Washed red cells can be irradiated at any time up to 14 days after collection. Irradiation should take place after washing.» Following irradiation washed red cells that are suspended in a validated additive solution should be transfused as soon as possible and no later than ~~a maximum of~~ 5 days «after irradiation» if irradiated «on the day of washing,» ~~at the point of manufacture~~ or 48 hours if irradiated «after the day of washing» ~~later in shelf life~~. ~~Red cells washed and stored in saline must be transfused within 24 hours of irradiation or production.~~

«7.1.3» ~~7.2~~: Other component specifications

Other component and process monitoring specifications are detailed later in this chapter. As far as possible, all parameters tested should be derived from a single component. Because of biological variability, it is acceptable if a minimum of 75% of the results from component and process monitoring tests (other than leucocyte depletion specifications, «or others where specified» ~~platelets for intrauterine transfusion, washed red cells, and prion-reduced red cell components~~) achieve the specifications.

«Allowing for losses due to material retained in the associated tubing, yield» ~~Yield~~ specifications (e.g. platelet yield/unit, total haemoglobin/unit) for components produced by splitting primary components should be the indicated specification for the primary component divided by the number of split components produced.

Haemolysis measurements on red cell components are performed at the end of the component shelf life. Due to intermittent availability of outdated red cell components, each primary process should be validated to give haemolysis of <0.8% of the red cell mass at the end of component shelf life in >75% of components with a minimum of 20 components tested. Revalidation of the red cell preparation processes for red cell haemolysis must be performed at least annually and after any alteration to the production method.

For mandatory microbiology screening and blood grouping tests, all components must conform to the requirements specified in Chapter 9. Concessionary procedures for release of components that do not conform to these requirements are given in section 6.10.

«7.1.4» ~~7.3~~: Production advice

The timing and method of separation depends on the components to be prepared from a given donation.

If the production, washing or splitting process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.

Where a production process amends the expiry date of the component, there are different consequences, dependent on the process.

Further processing or irradiation may reduce the expiry date of the component. Here the expiry date of the new component must not exceed that of the primary component or the expiry date limitations conferred by the process.

Components produced by pooling primary components must have an expiry date of the shortest dated component used.

When remanufacturing neonatal or paediatric red cell components into adult components, to avoid unnecessary wastage, the expiry date may be extended.

Processing of a red cell component to allow frozen storage will result in a lengthened expiry date.

The method of preparation should ensure that plasma components have the maximum level of labile coagulation factors with minimum cellular contamination.

Donations from donors with clinically significant human platelet antigen (HPA) and/or human leucocyte antigen (HLA) antibodies should not be used for the production of plasma-rich blood products (e.g. fresh frozen plasma, platelet concentrate, whole blood, cryoprecipitate). Red cells suspended in additive solution can be produced from such donations.

Platelet and plasma components should not be produced from lipaemic or icteric donations or be contaminated with red cells. Procedures should exist for assessing these findings.

An upper platelet concentration should be assigned for each platelet component type based on pack validation data or the pack manufacturer's recommendations.

pH measurements on platelet components should be made between 20°C and 24°C or the measurements corrected to 22°C.

Unless a validated pathogen inactivation process is used, blood components for use in intrauterine transfusion «and for» ~~,~~ neonates and infants (see also section «7.7» ~~7.21~~) must be derived from selected donors who fulfil the following criteria:

- Have given at least one donation in the last 2 years, which was either negative for all mandatory markers, or if repeat reactive, has been confirmed to be non-specifically reactive and the donor reinstated in accordance with section 9.4 (on reinstatement of blood donors).
- Negative results were obtained for mandatory microbiology markers with the current donation.

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.

«7.1.5» ~~7.32~~: References

«

1. Dumont L, Dzik W, Rebulla P, Brandwein H and members of the BEST Expert Working Party of the ISBT (1996). Practical guidelines for process validation and process control of white cell-reduced blood components: report of the Biomedical Excellence for Safer Transfusion (BEST) Working Party of the International Society of Blood Transfusion (ISBT). Transfusion, 36, 11–20.
2. Foukaneli T, Kerr P, Bolton-Maggs PHB, Cardigan R, Coles A, Gennery A, Jane D, Kumararatne D, Manson A, New HV, Torpey N on behalf of the British Society for Haematology Guidelines Transfusion Task Force (2020) Guidelines on the use of irradiated blood components. British Journal of Haematology, 191, 704-724.
3. Pelszynski MM, Moroff G, Luban NL, Taylor BJ, Quinones RR (1994). Effect of gamma irradiation of red blood cell units on T-cell inactivation as assessed by limiting dilution analysis: implications for preventing transfusion-associated graft-versus-host disease. Blood, 83,1683-1689.
4. Bashir S, Stanworth S, Massey E, Goddard F, Cardigan R (2008). Neutrophil function is preserved in a pooled granulocyte component prepared from whole blood donations. British Journal of Haematology, 140, 701–711.
5. Massey E, Harding K, Kahan BC, Llewelyn C, Wynn R, Moppett J, Robinson SP, Green A, Lucas G, Sadani D, Liakopoulou E, Bolton-Maggs P, Marks DI, Stanworth S (2012). The granulocytes in neutropenia 1 (GIN 1) study: a safety study of granulocytes collected from whole blood and stored in additive solution and plasma. Transfusion Medicine, 22, 277–284.
6. New HV, Berryman J, Bolton-Maggs PH, Cantwell C, Chalmers EA, Davies T, Gottstein R, Kelleher A, Kumar S, Morley SL, Stanworth SJ on behalf of British Committee for Standards in Haematology (2016). Guidelines on transfusion for fetuses, neonates and older children. British Journal of Haematology, 175, 784-828.

»

~~1. Dumont L, Dzik W, Rebulla P, Brandwein H and members of the BEST Expert Working Party of the ISBT (1996). Practical guidelines for process validation and process control of white cell-reduced blood components: report of the Biomedical Excellence for Safer Transfusion (BEST) Working Party of the International Society of Blood Transfusion (ISBT). Transfusion, 36, 11–20.~~

~~2. Bashir S, Stanworth S, Massey E, Goddard F, Cardigan R. (2008). Neutrophil function is preserved in a pooled granulocyte component prepared from whole blood donations. British Journal of Haematology, 140, 701–711.~~

~~3. British Committee for Standards in Haematology Blood Transfusion Task Force (2010). Guidelines on the Use of Irradiated Blood Components. Available at www.bcshguidelines.com/documents/Irradiation_BJH_2011.pdf.~~

~~4. Massey E, Harding K, Kahan BC, Llewelyn C, Wynn R, Moppett J, Robinson SP, Green A, Lucas G, Sadani D, Liakopoulou E, Bolton-Maggs P, Marks DI, Stanworth S (2012). The granulocytes in neutropenia 1 (GIN 1) study: a safety study of granulocytes collected from whole blood and stored in additive solution and plasma. Transfusion Medicine, 22, 277–284.~~

~~5. British Committee for Standards in Haematology Blood Transfusion Task Force (2004). Transfusion guidelines for neonates and older children. British Journal of Haematology, 124, 433–453.~~

«7.2: Whole Blood Components

Whole blood components are collected from UK donors as described in chapter 5. These components undergo primary processing to separate the blood constituents into red cell, platelet, granulocyte and plasma components.

7.2.1: Whole Blood, Leucocyte Depleted

Currently in the UK whole blood components are not routinely used for transfusion, although provisional component specifications for use in clinical trials are described in Annexe 3.»

«7.2.1» ~~7.4~~: Whole Blood, Leucocyte Depleted

A unit of blood collected into an anticoagulant, containing less than 1×10^6 leucocytes.

«7.2.1.1» ~~7.4.1~~: Technical information

- A unit of whole blood «is» collected in the UK ~~currently consists of 450 mL ±10% of blood~~ from a suitable donor (see «Chapters 3 and 5» ~~Chapter 3~~)~~, plus 63 mL of anticoagulant, which is then leucocyte depleted, and stored in an approved container~~. The «International Blood Pack specification» ~~Eurobloodpack~~ contains 66.5 mL of anticoagulant and is suitable for the collection of 475 mL ±10%~~, although in the UK a volume of 495 mL will not be exceeded~~.
- Whole Blood, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.2.1.2» ~~7.4.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Whole Blood, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.2.1.3» ~~7.4.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C if an adenine-supplemented anticoagulant is used, otherwise the maximum period of storage is 28 days at a core temperature of 4 ±2°C.

- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre to cover such eventualities
    - adequate records of the incident are compiled and retained.

«7.2.1.4» ~~7.4.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.2.1» ~~7.1~~ shall meet the specified values.

Table «7.2.1» ~~7.1~~ Whole Blood, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	«475 mL ±10%» ~~470 ±50 mL~~
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Haemoglobin content	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	≥40 g/unit
Leucocyte count [2]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. After volume losses resulting from leucodepletion		
2. Methods validated for counting low numbers of leucocytes must be used		

«7.2.1.5» ~~7.4.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.3: Red Cell Components

Red cell components are manufactured from whole blood or apheresis donations and suspended in additive solution and/or plasma. All red cell components are leucocyte depleted. Some components undergo additional processing steps described.

«7.3.1» ~~7.5~~: Red Cells, Leucocyte Depleted

A red cell component containing less than 1×10^6 leucocytes.

«7.3.1.1» ~~7.5.1~~: Technical information

- A red cell component prepared by removing a proportion of the plasma from leucocyte-depleted whole blood or by leucodepleting plasma reduced red cells.
- Red Cells, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

«7.3.1.2» ~~7.5.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.3.1.3» ~~7.5.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C if an adenine supplemented anticoagulant is used, otherwise the maximum period of storage is 28 days at a core temperature of 4 ±2°C.

- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature change has not exceeded 5 hours
    - a documented system is available in each Blood Centre or hospital to cover such eventualities
    - adequate records of the incident are compiled and retained.

«7.3.1.4» ~~7.5.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.3.1» ~~7.2~~ shall meet the specified values.

Table «7.3.1» ~~7.2~~ Red Cells, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	280 ±60 mL
Haemoglobin content		≥40 g/unit
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count [1]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. Methods validated for counting low numbers of leucocytes must be used		

«7.3.1.5» ~~7.5.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.3.1.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

If possible, time out of a controlled temperature environment should be restricted to under 30 minutes

- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.3.2» ~~7.6~~: Red Cells in Additive Solution, Leucocyte Depleted

A red cell component «derived from whole blood or collected by apheresis» containing less than 1 × 10^6 leucocytes and suspended in an approved additive solution.

«7.3.2.1» ~~7.6.1~~: Technical information

- A red cell component prepared by removing a proportion of the plasma from leucocyte-depleted whole blood and suspending in an approved additive solution «, or by collection using apheresis technology». Leucodepletion may be carried out on either the whole blood starting material or on the final component.
- «Red Cells in Additive Solution, Leucocyte Depleted may be collected by a variety of apheresis systems using different protocols and anticoagulants. Each procedural protocol must be fully validated so that the resulting red cells meet the required specifications.»
- Red Cells in Additive Solution, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- May be produced by remanufacture of Red Cells for Exchange Transfusion, Leucocyte Depleted (section «7.3» ~~7.24~~) up to «7» ~~6~~ days after donation.

«7.3.2.2» ~~7.6.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells in Additive Solution, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number* «and if collected via apheresis technology and divided, sub-batch number»
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the additive solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.3.2.3» ~~7.6.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre or hospital to cover such eventualities

- adequate records of the incident are compiled and retained.

«7.3.2.4» ~~7.6.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.3.2» ~~7.3~~ shall meet the specified values.

Table «7.3.2» ~~7.3~~ Red Cells in Additive Solution, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	280 ±60 mL ~~2~~
Haemoglobin content «2»		≥40 g/unit ~~3~~
«Haematocrit 3,4»		«0.50 – 0.70»
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count «5»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1»~~2~~. Units measured and found to be «<210 mL or» >375 mL should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2»~~3~~. Units measured and found to have <30 g/unit should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«3. Units measured and found to have haematocrit <0.40 or >0.70 should only be issued for transfusion under concessionary release»		
«4. A minimum of 90% of those components tested shall meet the specified value»		
«5»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.3.2.5» ~~7.6.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.3.2.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes

- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.3.3» ~~7.7~~: Red Cells, Washed, Leucocyte Depleted

A red cell component, containing less than 1 × 10^6 leucocytes, which has been washed with 0.9% w/v sodium chloride for injection (BP) or other validated solution. The Red Cells, Washed, Leucocyte Depleted may then be suspended in an approved solution.

«7.3.3.1» ~~7.7.1~~: Technical information

- The amount of residual protein will depend on the washing protocol. Washing can be performed by interrupted or continuous flow centrifugation.
- The use of validated «closed system» washing procedures that incorporate chilled ~~saline or other~~ validated solution for suspension is recommended. This will minimise the risk of bacterial growth and help to produce a component that meets the transit temperature requirements. ~~Use of an automated, closed washing system would be preferable.~~
- If the washing process results in the transfer of the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation identification number is put on the component pack of Red Cells, Washed, Leucocyte Depleted.
- Red Cells, Washed, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.3.3.2» ~~7.7.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells, Washed, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the suspending solution
- the date and time of preparation
- the expiry date and time*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.3.3.3» ~~7.7.3~~: Storage

For general guidelines, see section 6.7.

- ~~The component should be used as soon as possible if produced in an open system.~~ Where the component has been produced in a closed system and storage is required the component should be stored at a core temperature of 4 ±2°C and used «up to 14 days if stored in SAGM. Where alternative additive solutions are used, storage will be defined through validation.» ~~within 24 hours of production if suspended in saline or a defined validated period if suspended in an approved additive solution.~~

«7.3.3.4» ~~7.7.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table

«7.3.3» ~~7.4~~ shall meet the specified values. Provided the component is prepared from a process that is validated for leucocyte removal, testing of washed red cells for residual leucocytes is not required.

Table «7.3.3» ~~7.4~~ Red Cells, Washed, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	100% unless the process capability by SPC demonstrates otherwise	Within locally specified volume range
Haemoglobin content «2»		≥40 g/unit
Haematocrit «3»		0.50 – 0.70
Residual protein «4»~~2~~		«≤0.5 g/unit» ~~<0.5 g/unit~~
Leucocyte count «5»~~1~~ (pre-wash)	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1. Units measured and found to be <210 mL or >375 mL should only be issued for transfusion under concessionary release»		
«2. Units measured and found to be <30 g/unit should only be issued for transfusion under concessionary release»		
«3. Units measured and found to have haematocrit <0.40 or >0.70 should only be issued for transfusion under concessionary release»		
«4»~~2~~. Units measured and found to have >0.5 g/unit should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«5»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.3.3.5» ~~7.7.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.3.4» ~~7.8~~: Red Cells, Thawed and Washed, Leucocyte Depleted

A red cell component that contains less than 1 × 10^6 leucocytes, frozen in the presence of a cryoprotectant (preferably within 5 days of collection), and washed before use. Red Cells, Thawed and Washed, Leucocyte Depleted may then be suspended in an approved additive solution.

«7.3.4.1» ~~7.8.1~~: Technical information

- The concentration and nature of the cryoprotectant must provide appropriate protection of the red cells at the intended storage temperature. The entire process of freezing, thawing and washing must be validated and documented.
- The use of validated washing procedures that incorporate chilled saline or other validated solution for suspension is recommended. This will minimise the risk of bacterial contamination and helps to produce a component that meets the transit temperature requirements. Use of an automated, closed washing system would be preferable.
- The target minimum haemoglobin content is 36 g.
- If the washing process results in the transfer of the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation identification number is put on the pack in which the component is frozen and the pack in which the final component is presented.
- Red Cells, Thawed and Washed, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.3.4.2» ~~7.8.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells, Thawed and Washed, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the suspending solution
- the date and time of preparation
- the expiry date and time*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
«Where possible administer by gravity only»
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.3.4.3» ~~7.8.3~~: Storage

For general guidelines, see section 6.7.

- Maintenance of a constant storage temperature is important, particularly if a low-glycerol cryoprotectant system is used. Storage should be controlled to ensure the temperature is:
    - –60°C to –80°C if stored in an electrical freezer, when a high-glycerol method is used
    - –140°C to –150°C if stored in vapour phase liquid nitrogen, when a low-glycerol method is used.
- Storage may be extended to 30 years if the correct storage temperature is guaranteed.

- The thawed component should be used as soon as possible if produced in an open system. Where the component has been produced in a closed system and storage is required the component should be stored at a core temperature of 4 ±2°C and used within 24 hours of production if suspended in saline or a defined validated period if suspended in an approved additive solution.

«7.3.4.4» ~~7.8.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.3.4» ~~7.5~~ shall meet the specified values. Provided the component is prepared from a process that is validated for leucocyte removal, testing of washed red cells for residual leucocytes is not required.

Table «7.3.4» ~~7.5~~ Red Cells, Thawed and Washed, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	All	Within locally defined nominal volume range
Supernatant haemoglobin «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	«<0.2 g/unit» ~~≤2 g/unit~~
Red cell haemoglobin		≥36 g/unit
Leucocyte count «2»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~2~~
«1. Testing to be carried out prior to issue on all units as a product release criterion. Units measured and found to have ≥0.5 g/unit should not be issued for transfusion except under clinical concession on a named patient basis. This may apply to some units of rare red cell phenotype associated with a known red cell membrane defect causing increased fragility (such as Rh_{null} and K_o).»		
«2»~~1~~. Methods validated for counting low numbers of leucocytes must be used. «Pre-freeze testing.»		
~~2. Pre-freeze~~		

«7.3.4.5» ~~7.8.5~~: Transportation

For general guidelines, see section 6.11.

- The transport requirements for red cells in the frozen state will be influenced by the nature and concentration of cryoprotectant used: e.g. a component containing <20% glycerol requires a refrigerant colder than dry ice, such as the vapour phase of liquid nitrogen.
- For thawed red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:
    - the validation exercise should be repeated periodically
    - if melting ice is used, it should not come into direct contact with the components
    - dead air space in packaging containers should be minimised
    - as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
    - transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.4: Platelet Components

Platelet components are manufactured from pooling whole blood-derived buffy coats or directly from apheresis collections. They are suspended in plasma with or without a platelet additive solution.

«7.4.1» ~~7.9~~: Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted

A pool of platelets, derived from buffy coats, which contains less than 1×10^6 leucocytes.

«7.4.1.1» ~~7.9.1~~: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for platelet production.
- The buffy coats must be prepared at ambient temperature from whole blood where the surface temperature of packs has not dropped below 18°C.
- Initial separation of buffy coat must occur within 24 hours of venepuncture (unless supported by additional validation), with a minimum buffy coat rest period of 2 hours before secondary pooling and processing of buffy coats to produce the final component, which is generally completed before the end of Day 1.
- The volume of suspension medium must be sufficient to maintain the pH «at ≥6.4» ~~within the range 6.4–7.4~~ at the end of the shelf life of the component.
- The production process transfers the final component into a pack that was not part of the original pack assembly. Therefore a secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.
- Where the production method requires the use of a single unit of plasma for resuspension, the plasma from group O donors should be tested for high-titre anti-A and anti-B and 'high-titre negative' units labelled. The testing method and acceptable limits should be defined (see also Chapter 9). Plasma should be selected from male donors as a TRALI risk reduction strategy.
- Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted, should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.4.1.2» ~~7.9.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing platelet units*
- the ABO group*
- the RhD group stated as positive or negative*
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.4.1.3» ~~7.9.3~~: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.
- Packs currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 5 days in a closed system. Appropriate pack and platelet concentration combinations may allow storage up to 7 days, but due to concerns over bacterial contamination requires either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.
- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.
- Platelets should be gently agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided «that» ~~the interruptions are for no longer than a total of 24 hours and~~ no single interruption lasts for more than eight hours «, and the total length of all interruptions is no longer than 24 hours».

«7.4.1.4» ~~7.9.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.4.1» ~~7.6~~ shall meet the specified values.

Table «7.4.1» ~~7.6~~ Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range ~~2~~
Platelet count «2»		≥240 × 10^9/pool ~~3~~
pH at end of shelf life «3»~~4~~		≥6.4
Leucocyte count «4»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/pool
«1»~~2~~. Units measured and found to be «<150 mL or >380 mL» ~~outside of the range 150 to 380 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2»~~3~~. Units measured and found to have <160 × 10^9/pool «, or more than the maximum recommended by the manufacturer of the storage pack where stated,» should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«3»~~4~~. A minimum of 95% of those components tested shall meet the specified values		
«4»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.4.1.5» ~~7.9.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.4.2» ~~7.10~~: Platelets, Apheresis, Leucocyte Depleted

A single-donor platelet component containing less than 1 × 10^6 leucocytes.

«7.4.2.1» ~~7.10.1~~: Technical information

- Platelets, Apheresis, Leucocyte Depleted may be collected by a variety of apheresis systems using different protocols. Since platelet yields may vary, each procedural protocol must be fully validated, documented and specifications set accordingly.
- If a double or triple dose is collected the platelet concentrate must be temporarily split, as a continuous part of the collection process, into the storage packs integral to the collection set so that the capacity of an individual pack is not exceeded.
- If filtration is used the recommended capacity of the filter should not be exceeded.
- The volume of suspension medium must be sufficient to maintain the pH «at ≥6.4» ~~within the range 6.4–7.4~~ at the end of the shelf life of the component.
- If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.
- The plasma from group O donors should be tested for high-titre anti-A and anti-B, and 'high-titre negative' units labelled. The testing method and acceptable limits should be defined (see also Chapter 9). Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy.
- Platelets, Apheresis, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.4.2.2» ~~7.10.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, Apheresis, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.4.2.3» ~~7.10.3~~: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets and whether an open or closed system is used.
- Packs currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 5 days in a closed system. Appropriate pack and platelet concentration combinations may allow

storage up to 7 days, but due to concerns over bacterial contamination requires either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.

- Where any manufacturing step involves an open system the platelets should be used as soon as possible after collection. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.
- Platelets should be gently agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided «that» ~~the interruption is for no longer than a total of 24 hours and~~ no single interruption lasts for more than eight hours «, and the total length of all interruptions is no longer than 24 hours».

«7.4.2.4» ~~7.10.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.4.2» ~~7.7~~ shall meet the specified values.

Table «7.4.2» ~~7.7~~ Platelets, Apheresis, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range ~~2~~
Platelet count «2»		≥240 × 10^9/«unit» ~~pool~~ ~~3~~
pH at end of shelf life «3» ~~4~~		≥6.4
Leucocyte count «4» ~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1» ~~2~~. Units measured and found to be «<150 mL or >380 mL» ~~outside of the range 150 to 380 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2» ~~3~~. Units measured and found to have <160 × 10^9/«unit» ~~pool~~ «, or more than the maximum recommended by the manufacturer of the storage pack where stated,» should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«3» ~~4~~. A minimum of 95% of those components tested shall meet the specified values		
«4» ~~1~~. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.4.2.5» ~~7.10.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.4.3» ~~7.11~~: Platelets, Pooled, Buffy Coat Derived, in Additive Solution and Plasma, Leucocyte Depleted

A platelet concentrate, derived from buffy coats, which contains less than 1 × 10^6 leucocytes and where the suspending medium comprises approximately 30% plasma and 70% additive solution.

«7.4.3.1» ~~7.11.1~~: Technical Information

- The component is manufactured as a primary component and not as a remanufactured secondary component.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for platelet production.
- The buffy coats must be prepared at ambient temperature from whole blood where the surface temperature of packs has not dropped below 18°C.
- Initial separation of buffy coat must occur within 24 hours of venepuncture (unless supported by additional validation), with a minimum buffy coat rest period of 2 hours before secondary pooling and processing of buffy coats to produce the final component, which is generally completed before the end of Day 1.
- The proportion of plasma carried over into the final component should be determined by validation and will depend upon the type of additive solution and platelet storage pack. Re-validation of the proportion of plasma carried over must be performed at least annually on a minimum of 25 units and after any changes to production method.
- The volume of suspension medium must be sufficient to maintain the pH «at ≥6.4» ~~within the range 6.4–7.4~~ at the end of the shelf life of the component.
- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the audit trail and the correct identification number is put on the final component pack.
- Platelets, Pooled, Buffy Coat Derived, in Additive Solution and Plasma, Leucocyte Depleted, should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.4.3.2» ~~7.11.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets in Additive Solution and Plasma, Leucocyte Depleted * and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing platelet units*
- the RhD group stated as positive or negative*
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.4.3.4» ~~7.11.3~~: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets and on whether an open or closed system is used.
- Packs currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 5 days in a closed system. Appropriate pack and platelet concentration combinations may allow

storage up to 7 days, but due to concerns over bacterial contamination would require either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen reduction procedure.

- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours. If platelet agitation is interrupted due to equipment breakdown or prolonged transportation, platelets are suitable for use provided that no single interruption lasts for more than eight hours, and the total length of all interruptions is no longer than 24 hours.

«7.4.3.4» ~~7.11.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 and leucocyte counting (see section 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown at Table «7.4.3» ~~7.8~~ shall meet the specified values.

Table «7.4.3» ~~7.8~~ Platelets «, Pooled, Buffy Coat Derived,» in Additive Solution and Plasma «, Leucocyte Depleted» – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count «2»		≥240 × 10^9/pool
pH at end of shelf life «3»	If less than 10 per month, every available component	≥6.4
Leucocyte count «4»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/pool ~~1~~
«1. Units measured and found to be <150 mL or >380 mL should only be issued for transfusion under concessionary release»		
«2. Units measured and found to have <160 × 10^9/pool, or more than the maximum recommended by the manufacturer of the storage pack where stated, should only be issued for transfusion under concessionary release»		
«3. A minimum of 95% of those components tested shall meet the specified values»		
«4»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.4.3.5» ~~7.11.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.4.4» ~~7.12~~: Platelets in Additive Solution, Leucocyte Depleted

A platelet concentrate derived from buffy coats or apheresis, which contains less than 1 × 10^6 leucocytes and where the suspending medium is additive solution. This component is indicated for patients with reactions to plasma-containing components.

«7.4.4.1» ~~7.12.1~~: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for platelet production.
- Where prepared from buffy coats, the buffy coats must be prepared at ambient temperature from whole blood where the surface temperature of packs has not dropped below 18°C.
- Where prepared from buffy coats, initial separation of buffy coat must occur within 24 hours of venepuncture (unless supported by additional validation), with a minimum buffy coat rest period of 2 hours before secondary pooling and processing of buffy coats to produce the final component, which is generally completed before the end of Day 1.
- The volume of suspension medium must be sufficient to maintain the pH «at ≥6.4» ~~within the range 6.4–7.4~~ at the end of the shelf life of the component.
- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.
- Platelets in Additive Solution, Leucocyte Depleted, should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.4.4.2» ~~7.12.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets in Additive Solution, Leucocyte Depleted* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing platelet units*
- the ABO group*
- the RhD group stated as positive or negative*
- the expiry date and time*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.4.4.3» ~~7.12.3~~: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets, the additive solution used and whether an open or closed system is used.
- Platelets in Additive Solution, Leucocyte Depleted, should be used within 24 hours of production.

- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.

«7.4.4.4» ~~7.12.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.4.4» ~~7.9~~ shall meet the specified values.

Table «7.4.4» ~~7.9~~ Platelets in Additive Solution, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count «1»		≥200 × 10^9/unit
pH at end of shelf life «2»		≥6.4
Leucocyte count «3» ~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1. Units measured and found to have <160 × 10^9/unit, or more than the maximum recommended by the manufacturer of the storage pack where stated, should only be issued for transfusion under concessionary release»		
«2. A minimum of 95% of those components tested shall meet the specified values»		
«3» ~~1~~. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.4.4.5» ~~7.12.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.5: Plasma Components

Plasma components are manufactured from whole blood or apheresis collections. These components a rapidly frozen to retain labile clotting factors. All plasma components are leucocyte depleted. Some components undergo additional processing steps described.

«7.5.1» ~~7.15~~: Fresh Frozen Plasma, Leucocyte Depleted

~~*"To align these guidelines with the Blood Safety and Quality Regulations (BSQR) specifications while providing reassurance on likely minimum FVIII content, the following changes have been made to section 7.15.4."*~~

Plasma that has been obtained from whole blood or by apheresis ~~*(as defined in section 7.3)*~~. The plasma contains less than 1 × 10^6 leucocytes per component and has been rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

«7.5.1.1» ~~7.15.1~~: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII~~:C~~ yields will be obtained when the plasma is separated as soon as possible after venepuncture and rapidly frozen to –25°C or below.
- The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII~~:C~~ concentration.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII~~:C~~ levels between ABO blood groups.
- Fresh Frozen Plasma, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

«7.5.1.1» ~~7.15.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Fresh Frozen Plasma, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*

- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing if maintained at 22 ±2°C, or up to a maximum of 120 hours of thawing if stored at 4 ±2°C, depending on indication
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.5.1.3» ~~*7.15.3*~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~*daily*~~ and maintained to minimise the risk of bacterial contamination. After thawing, and at the time of administration, the content should be inspected to ensure that no insoluble ~~*cryo*~~precipitate is visible and that the container is intact. If to be stored thawed for an extended period (>24 hours from thawing), thawing methods that do not directly expose units to water must be used to minimise bacterial contamination.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C or up to a maximum of 120 hours if stored at 4 ±2°C, but it should be borne in mind that extended post-thaw storage will result in a decline in the content of labile coagulation factors.
- Pre-thawed FFP that is out of a controlled temperature environment (4 ±2°C), can be accepted back into temperature controlled storage if this occurs on one occasion only of less than 30 minutes. Transfusion of FFP should be completed within 4 hours of issue out of a controlled temperature environment.
- For indications other than unexpected major haemorrhage, the component should be used within 24 hours of thawing.

«7.5.1.4» ~~*7.15.4*~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~*7.1*~~), a minimum of 75% of those components tested for the parameters shown in Table «7.5.1» ~~*7.12*~~ shall meet the specified values ~~*with the exception of FVIII:C*~~.

Table «7.5.1» ~~7.12~~ Fresh Frozen Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Stated volume ±10% ~~2~~
Total protein		≥50 g/L
Platelet count «2,3»		<30 × 10^9/L ~~3~~
Red cell count «3»		<6 × 10^9/L ~~3~~
FVIII ~~:C~~ «4,5» ~~4,5~~		Mean ≥0.70 IU/mL
Leucocyte count «3,6» ~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~3~~
«1» ~~2~~. Units measured and found to be «<200 mL or >340 mL» ~~outside of the range 200 to 340 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2. Units with residual platelet count >100 × 10^9/L should only be issued for transfusion under concessionary release»		
3. Pre-freeze in starting component		
4. Units measured and found to have <0.30 IU/mL should «only» ~~not~~ be issued for transfusion «under concessionary release»		
5. A minimum of 90% of those components tested should have ≥0.50 IU/mL		
«6» ~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.5.1.5» ~~7.15.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.5.2» ~~7.16~~: Fresh Frozen Plasma, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted

~~This component is intended for use in children and is made from plasma from a country with a low risk of variant Creutzfeldt-Jakob Disease (vCJD).~~

Fresh Frozen Plasma, «Pathogen Reduced» ~~Methylene Blue Treated (MBT) and Removed~~, Leucocyte Depleted, is plasma that has been obtained from whole blood or by apheresis ~~from a previously tested donor (as defined in section 7.3)~~, contains less than 1×10^6 leucocytes and has been treated with «a pathogen inactivation (PI) system.» ~~methylene blue and exposure to visible light to inactivate pathogens.~~ «The PI system must be approved (CE/UKCA/UKNI marked) for this use, and must have been validated by the Blood Service.»

Following «PI treatment» ~~methylene blue treatment and removal~~, the plasma is rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

«7.5.2.1» ~~7.16.1~~: Technical information

- ~~Where the starting component is sourced outside the UK, a detailed and agreed specification must be available.~~
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- «Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted may be prepared from small pools of up to 12 individual donations if validated by the blood service and if in accordance with the specifications of the manufacturer of the PI system.»
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII~~:C~~ yields will be obtained when the plasma is separated as soon as possible after venepuncture, «pathogen reduced» ~~methylene blue treated~~ and rapidly frozen to –25°C or below.
- The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII~~:C~~ concentration.
- «It contains, on average, greater than 60% of the labile coagulation factors and naturally occurring inhibitors present in standard fresh frozen plasma.
- The PI system typically reduces the risk of infection from enveloped viruses (e.g. HBV, HCV, HIV) by at least one thousand-fold.»
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- «The level of removal of the activating agent prior to final storage should be validated, if such a step is included in the PI system.»
- ~~The MBT process reduces the FVIII:C content by approximately 30% when compared to standard fresh frozen plasma.~~
- Intact white blood cells in the plasma should be reduced to less than 1×10^6 per unit prior to exposure to «the PI process.» ~~methylene blue and visible light.~~
- ~~The process for methylene blue removal should be validated to give components with a methylene blue concentration ≤0.30 µmol/L (less than approximately 30 µg per unit).~~
- Fresh Frozen Plasma, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.5.2.2» ~~7.16.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Fresh Frozen Plasma, «Pathogen Reduced» ~~*Methylene Blue Treated and Removed*~~, Leucocyte Depleted* and «the» volume
- «the name of the PI system used»
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component should be used within 4 hours of thawing if maintained at 22 ±2°C and 24 hours if maintained at 4 ±2°C
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection «including vCJD and allergy to the compounds used for, or derived from, PI treatment»

«7.5.2.3» ~~7.16.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~*daily*~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~*cryo*~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C or 24 hours if stored at 4 ±2°C, but it should be borne in mind that extended post-thaw storage will result in a decline in the content of labile coagulation factors.

«7.5.2.4» ~~7.16.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.5.2» ~~7.13~~ shall meet the specified values.

Table «7.5.2» ~~7.13~~ Fresh Frozen Plasma, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range and within any limits specified for the «PI» ~~MBT~~ process used
Platelet count «1,2»		<30 × 10^9/L ~~2~~
FVIII ~~:C~~		≥0.50 IU/mL
Leucocyte count «2,3» ~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~2~~
«1. Units with residual platelet count >100 × 10^9/L should only be issued for transfusion under concessionary release»		
2. Pre-freeze in starting component		
«3» ~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.5.2.5» ~~7.16.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.5.3» ~~7.17~~: Cryoprecipitate, Leucocyte Depleted

The component «provides a concentrated source of» ~~represents a source of concentrated~~ FVIII~~:C~~, and von Willebrand factor, fibrinogen, FXIII and fibronectin ~~from a unit of fresh frozen plasma~~. «It is derived from a unit of Fresh Frozen Plasma, Leucocyte Depleted.» The plasma from which the «Cryoprecipitate, Leucocyte Depleted is» ~~cryoprecipitate was~~ produced contains less than 1×10^6 leucocytes per component.

«7.5.3.1» ~~7.17.1~~: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing a single donation of Fresh Frozen Plasma, Leucocyte Depleted (see section «7.5.1» ~~7.15~~) at 4 ±2°C.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- For storage, Cryoprecipitate, Leucocyte Depleted should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII~~:C~~ levels between ABO blood groups.
- Cryoprecipitate, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.5.3.2» ~~7.17.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.5.3.3» ~~7.17.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

«7.5.3.4» ~~7.17.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.5.3» ~~7.14~~ shall meet the specified values.

Table «7.5.3» ~~7.14~~ Cryoprecipitate, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal range
Fibrinogen		≥140 mg/unit
FVIII~~:C~~		≥70 IU/unit
Leucocyte count [1«,2»]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit [~~2~~]
1. Methods validated for counting low numbers of leucocytes must be used		
2. Pre-freeze in starting component		

«7.5.3.5» ~~7.17.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.5.4» ~~7.18~~: Cryoprecipitate, Pooled, Leucocyte Depleted

The pooled component «provides a concentrated source of» ~~represents a source of concentrated~~ FVIII~~:C~~, von Willebrand factor, fibrinogen, FXIII and fibronectin ~~from primary cryoprecipitate components derived from units of fresh frozen plasma~~. «It is derived from units of Fresh Frozen Plasma, Leucocyte Depleted.» The plasma from which the «Cryoprecipitate, Pooled, Leucocyte Depleted is» ~~cryoprecipitate was~~ produced contains less than 1×10^6 leucocytes per primary component.

«7.5.4.1» ~~7.18.1~~: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate, Pooled, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing and pooling five single «Cryoprecipitate, Leucocyte Depleted» ~~cryoprecipitate~~ components or pooling five single «Cryoprecipitate, Leucocyte Depleted» ~~cryoprecipitate~~ components immediately after production from thawed fresh frozen plasma.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- For storage, Cryoprecipitate Pooled, Leucocyte Depleted should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Initial process validation must ensure that for a minimum of 20 tested Cryoprecipitate, Pooled, Leucocyte Depleted components a minimum of 75% of those components tested for the parameters shown in Table «7.5.4» ~~7.15~~ shall meet the specified values.
- Annual process validation is acceptable for quality monitoring purposes, provided that the primary components, Fresh Frozen Plasma, Leucocyte Depleted and/or Cryoprecipitate, Leucocyte Depleted are separately monitored as part of monthly testing. If this is not the case, test monthly 1% or as determined by statistical process control (if ≤10 components produced per month then test every available component), of Cryoprecipitate Pooled, Leucocyte Depleted components. A minimum of 75% of those components tested for the parameters shown in Table «7.5.4» ~~7.15~~ shall meet the specified values.
- A secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.
- Cryoprecipitate Pooled, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.5.4.2» ~~7.18.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate, Pooled, Leucocyte Depleted* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing units*
- the ABO group*
- the RhD group stated as positive or negative*
- ~~the date of collection~~
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing
- the name, composition and volume of anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.5.4.3» ~~7.18.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

«7.5.4.4» ~~7.18.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in «Chapter 9» ~~Annex 4~~, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown at Table «7.5.4» ~~7.15~~ shall meet the specified values.

Table «7.5.4» ~~7.15~~ Cryoprecipitate, Pooled, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component) Refer to Technical information (section «7.5.4.1» ~~17.18.1~~) above	100 – 250 mL
Fibrinogen		≥700 mg/unit
FVIII~~:C~~		≥350 IU/unit
Leucocyte count «1»	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit in the starting component ~~1~~
1. Pre-freeze methods validated for counting low numbers of leucocytes must be used		

«7.5.4.5» ~~7.18.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.5.5» ~~7.33~~: Cryoprecipitate, Pooled, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted

~~This component is intended for use for patients born on or after 1st January 1996.~~

The component «provides a concentrated source of» ~~represents a source of concentrated~~ FVIII, and von Willebrand factor, fibrinogen, Factor XIII and fibronectin ~~produced from units of Fresh Frozen Plasma, Methylene Blue Treated and Removed~~. «It is derived from units of Fresh Frozen Plasma, Pathogen Reduced, Leucocyte Depleted.» The plasma from which the Cryoprecipitate, «Pooled, Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted «is» ~~was~~ produced contains less than 1 × 10^6 leucocytes per component ~~and is from a country with a low risk of vCJD~~.

«7.5.5.1» ~~7.33.1~~: Technical information

- ~~Where the starting component is sourced outwith the UK, a detailed and agreed specification must be available.~~
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate, Pooled, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing and pooling «between 6 and 12 single Cryoprecipitate for Neonates and Infants, Pathogen Reduced, Leucocyte Depleted components.» ~~six single Cryoprecipitate, Methylene Blue Treated and Removed plasma components.~~
- Plasma should be selected from male donors or screening of female donors for HLA/HNA antibodies should be considered, as a TRALI risk reduction strategy.
- ~~The process for methylene blue removal should be validated to give components with a methylene blue concentration ≤0.30 µM (< approximately 30 µg per unit) in the starting components.~~
- For storage, Cryoprecipitate, Pooled, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted should be rapidly frozen to a core temperature of –25 °C or below within 2 hours of preparation.
- Component samples collected for the Quality Monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Annual process validation is acceptable for leucodepletion quality monitoring purposes, provided that the primary components, ~~Methylene Blue Treated and Removed~~ Fresh Frozen Plasma, «Pathogen Reduced,» Leucocyte Depleted are separately monitored as part of monthly testing. If this is not the case, test monthly 1% or as determined by statistical process control (if ≤10 components produced per month then test every available component), of Cryoprecipitate, Pooled, «Pathogen Reduced,» ~~Methylene Blue Treated and Removed~~ Leucocyte Depleted components. A minimum of 75% of those components tested for the parameters shown at Table «7.5.5» ~~7.26~~ below shall meet the specified values.
- A secure system must be in place to ensure a full audit trail and the correct identification number is put on the final component pack.
- Cryoprecipitate, Pooled, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted, should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.5.5.2» ~~7.33.2~~: Labelling

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format.)

- Cryoprecipitate Pooled, «Pathogen Reduced» ~~Methylene Blue Treated and Removed~~, Leucocyte Depleted * and volume
- «the name of the PI system used»
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing units*
- the ABO group*
- the RhD group stated as positive or negative*
- ~~the date of collection~~

- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within «4» ~~four~~ hours of thawing
- the name, composition and volume of the anticoagulant ~~or additive solution~~.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection «including vCJD and allergy to the compounds used for, or derived from, PI treatment.»

«7.5.5.3» ~~7.33.3~~: Storage

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a water bath or other equipment designed for the purpose, within a vacuum sealed over wrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33-37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimize the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within «4» ~~four~~ hours.

«7.5.5.4» ~~7.33.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see Sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.5.5» ~~7.26~~ shall meet the specified values.

Table «7.5.5» ~~7.26~~ Cryoprecipitate, Pooled, «Pathogen Reduced» ~~methylene blue treated and removed~~, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	100 – 300 mL
Fibrinogen	Refer to Technical information (section «7.5.5.1» ~~17.18.1~~) above	≥700 mg/unit
FVIII~~:C~~		≥250 IU/unit
Leucocyte count [1«,2»]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit [2]
1. Methods validated for counting low numbers of leucocytes must be used		
2. Pre-freeze in starting component		

«7.5.5.5» ~~7.33.5~~: Transportation

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straight away it should be transferred immediately to storage at the recommended temperature.

«7.5.6» ~~7.37~~: Human Plasma for Fractionation, Leucocyte Depleted

Plasma that has been obtained from whole blood or by apheresis (as defined in section «7.1.4» ~~7.3~~), containing less than 1×10^6 leucocytes per unit.

UK derived plasma may be used for the manufacture of immunoglobulins for domestic use provided all relevant vCJD risk mitigation measures currently in place for blood components for transfusion are applied and manufacturers submit an application to the MHRA to register the use of UK-sourced plasma including a product specific risk assessment. Manufacture of other blood products such as clotting factors or albumin is not currently permitted.

«7.5.6.1» ~~7.37.1~~: Technical information

- All aspects of collection and manufacture, testing and storage should satisfy the requirements defined in the current British Pharmacopoeia monograph on Human Plasma for Fractionation.
- See chapters 3, 4, 5, 9 and 12 for specific details on donor selection, care and testing for Human Plasma for Fractionation, Leucocyte Depleted.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for clinical use.
- Plasma with a volume below 200 mL is not suitable for use.
- Plasma may be selected from both male and female donors. Female donors do not need additional screening for anti-HLA and anti-HNA antibodies.
- When obtained by plasmapheresis, plasma intended solely for the recovery of proteins that are not labile in plasma is frozen using validated conditions by cooling rapidly in a chamber at –20°C or below as soon as possible and at the latest within 24 h of collection.
- When obtained from whole blood, plasma intended solely for the recovery of proteins that are not labile in plasma is separated from cellular elements and frozen using validated conditions in a chamber at −20°C or below as soon as possible and at the latest within 72 h of collection.
- Human Plasma for Fractionation, Leucocyte Depleted must not be transfused directly to patients.

«7.5.6.2» ~~7.37.2~~: Labelling

For general guidelines, see section 6.6. The following shall be included on the label in eye readable format:

(* = also in UKBTS approved barcode format)

- Human Plasma for Fractionation, Leucocyte Depleted*
- Recovered or Source plasma
- the component volume
- the blood component producer's name
- the donation number and, if divided, sub-batch number*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- the name, composition and volume of the anticoagulant.
- Not for transfusion

«7.5.6.3» ~~7.37.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –20°C or below for a maximum of 36 months.
- Although frozen storage temperatures improve the preservation of labile and non-labile proteins, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.

«7.5.6.4» ~~7.37.4~~: Testing

- In addition to the mandatory and other tests required for blood donations for Human Plasma for Fractionation, Leucocyte Depleted described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), components should be tested for the parameters shown in Table «7.5.6» ~~7.37~~.
- Total protein testing will be undertaken according to the British Pharmacopeia 2021 – Plasma for Fractionation (*Human Plasma for Fractionation, Ph. Eur. 10.3 monograph 0853*) or using equivalent, validated assays.

Table «7.5.6» ~~7.37~~ Human Plasma for Fractionation, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Stated volume ±10% ~~2~~
Total protein		Mean ≥50 g/L
Platelet count «1,2»		<50 × 10^9/L ~~2,3~~
Red cell count «1,2»		<6 × 10^9/L ~~2,3~~
Leucocyte count «2,3»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~3~~
«1»~~2~~. A minimum of 90% of units tested should meet the required value		
«2»~~3~~. Pre-freeze in starting component		
«3»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

More than 90% of leucocyte-depleted components from relevant processes must have less than 1 × 10^6 leucocytes per unit and more than 99% of components must contain less than 5 × 10^6 leucocytes per unit, both with 95% confidence.

Where plasma is collected into one container for final frozen storage the specification must be assessed based on volume ranges of 200 mL to ≤400 mL for a single unit equivalent, >400 mL to ≤680 mL for a double unit equivalent, and >680 mL for a triple unit equivalent collection.

«7.5.6.5» ~~7.37.5~~: Transportation

For general guidelines, see section 6.11.

The frozen plasma should be stored and transported under conditions validated to maintain a temperature of –20°C or below. Temperature fluctuations in the plasma should be kept to a minimum during storage or transportation. A plasma temperature record during storage and transit of frozen plasma shall be available for inspection.

Short excursions of up to 30 minutes whilst preparing plasma for shipping are permissible.

Exceptional temperature deviations above –20°C, e.g. in the case of equipment failure, on one or more occasions are acceptable so long as the following conditions are met:

- the total period of time above –20°C does not exceed 72 hours
- the temperature does not exceed –15°C on more than one occasion
- the temperature does not exceed –5°C

Where plasma has been subject to temperature deviations during storage or transportation this must be recorded and reported to any third party receiving the plasma.

The following specifications have been moved from **Chapter 7** to **Annexe 4: Redundant Components**

~~***7.19: Cryoprecipitate, Methylene Blue Treated and Removed, Leucocyte Depleted***~~

~~***7.20: Plasma, Cryoprecipitate Depleted, Leucocyte Depleted***~~

«7.6: Granulocyte Components

Granulocyte components are manufactured from whole blood-derived buffy coats and are not leucodepleted.

7.6.1: Granulocytes, Pooled, Buffy Coat Derived, in Platelet Additive Solution and Plasma»

«7.6.1» ~~7.14~~: Granulocytes, Pooled, Buffy Coat Derived, in Platelet Additive Solution and Plasma

A pool of granulocytes, derived from buffy coats, with retention of neutrophils as the major cellular product, suspended in a portion of the plasma and platelet additive solution.

«7.6.1.1» ~~7.14.1~~: Technical information

- The component is not leucodepleted.
- The component contains red cells and requires compatibility testing.
- CMV seronegative granulocytes should be considered for CMV seronegative recipients.
- The component contains 2.0 adult transfusion doses (ATDs) of platelets«4»~~2~~ and additional platelet transfusion is therefore unlikely to be required.
- The component must not be agitated during storage.
- The component must be irradiated before use.
- Granulocytes should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- The component must be stored in a pack that allows gas exchange (i.e. a platelet pack).
- The production process transfers the final component into a pack that was not part of the original pack assembly. Therefore a secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.
- Recommended dose for adults is 1-2 packs daily and for a child 10-20 mL/kg.
- A clinical study has been undertaken in 30 human patients using this component. Leucocyte antibody formation occurred at a rate similar to historical multiply transfused controls (3 of 29 patients assessed).«5»~~4~~

«7.6.1.2» ~~7.14.2~~: Labelling

For general guidelines, see section 6.6.

The following should be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Granulocytes, Pooled, Buffy Coat Derived, in Platelet Additive Solution and Plasma* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing units*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date and time*
- the temperature of storage
- the statement 'Do not agitate'
- the blood pack lot number*
- the name, composition and volume of the anticoagulant solution
- the name, composition and volume of the platelet additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.6.1.3» ~~7.14.3~~: Storage

For general guidelines, see section 6.7.

- Granulocytes should be used as soon as possible after their preparation. If storage is unavoidable, provided the component is produced using a closed system, the component should be stored, without agitation, at a core temperature of 22 ±2°C and transfusion should commence by midnight on Day 1 (the day following donation).

«7.6.1.4» ~~7.14.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, «95% or more of» ~~all~~ components tested for the parameters shown in Table «7.6.1» ~~7.11~~ shall meet the specified values. «Where a unit is tested and found to have a granulocyte yield <3.8 × 10^9/unit the production process should be reviewed.»

Table «7.6.1» ~~7.11~~ Granulocytes, Pooled, Buffy Coat Derived, in Additive Solution and Plasma

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	175 – 250 mL ~~1~~
Total granulocyte count «1»		>5 × 10^9/unit ~~1~~
1. Based on production from ten whole blood donations		

«7.6.1.5» ~~7.14.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting granulocytes should be equilibrated at room temperature before use. During transportation the temperature of the component must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C without agitation.
- Plastic overwraps should be removed prior to storage.

~~7.13: Granulocytes, Apheresis~~

~~This component is now redundant and has been moved to Annexe 4: Redundant Components.~~

«7.7» ~~7.21~~: Components suitable for use in Intrauterine transfusion, Neonates and Infants under 1 year

~~7.21.1:~~ General requirements

- Unless they are subjected to a validated pathogen inactivation process, components for use in intrauterine transfusion, neonates and infants under 1 year must be prepared from previously tested donors who fulfil the following criteria:
    - have given at least one donation in the last 2 years, which was either negative for all mandatory markers, or if repeat reactive, has been confirmed to be non-specifically reactive and the donor reinstated in accordance with section 9.4, Reinstatement of blood donors
    - negative results were obtained for mandatory microbiology markers with the current donation.
- Red cell and platelet components should be negative for CMV antibodies although leucodepleted components may be used if CMV antibody negative components are not available.
- Components should be tested and shown to be free of clinically significant, irregular blood group antibodies including high-titre anti-A and anti-B.
- It is good practice to provide neonates, who are likely to be repeatedly transfused, with components in which the original donation has been split, thereby providing the potential to reduce donor exposures in this vulnerable group of recipients.
- When a component is to be split for neonatal use, the original pack must first be mixed thoroughly by a validated procedure to ensure that the contents are homogeneous.
- When a component is split for neonatal use, it is sufficient to undertake leucocyte counting on the parent pack or process.
- When a component is split for neonatal use, each ‘split’ must be identified by a unique number to ensure all splits can be accounted for.

«7.7.1» ~~7.22~~: Red Cells for Intrauterine Transfusion ~~(IUT)~~, Leucocyte Depleted

A component for intrauterine transfusion «(IUT)», prepared by removing a proportion of the plasma from fresh whole blood. The component should be leucocyte depleted to less than 1×10^6 leucocytes per unit.

«7.7.1.1» ~~7.22.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for intrauterine transfusion and use in neonates and infants under 1 year.»
- The component must be prepared and used for IUT by the end of Day 5, should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B (see Chapter 12), and should be negative for antibodies to CMV.
- «Whenever possible the component should be selected from male donors as a TRALI risk reduction measure.»
- The component must be irradiated and should be transfused within 24 hours of irradiation. See the «British Society for Haematology (BSH) 'Guidelines on transfusion for fetuses, neonates and older children'.[6]» ~~*British Committee for Standards in Haematology* (BCSH) 'Transfusion guidelines for neonates and older children'.[5]~~
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.
- Red Cells for Intrauterine Transfusion, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

«7.7.1.2» ~~7.22.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells for Intrauterine Transfusion, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.1.3» ~~7.22.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 5 days at a core temperature of 4 ±2°C.
- The component must be used within 24 hours of irradiation and within the overall maximum 5-day shelf life.
- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.

- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre or hospital to cover such eventualities
    - adequate records of the incident are compiled and retained.

«7.7.1.4» ~~7.22.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.1» ~~7.17~~ shall meet the specified values.

Table «7.7.1» ~~7.17~~ Red Cells for Intrauterine Transfusion ~~(IUT)~~, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range ~~2~~
Haematocrit «2»		0.70 – 0.85 ~~3~~
Haemoglobin content «3»		Locally defined ~~4~~
Leucocyte count «4»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1»~~2~~. Units measured and found to be «<150 mL or >350 mL» ~~outside of the range 150 to 350 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2»~~3~~. Units measured and found to be «<0.70 or >0.85» ~~outside of the range 0.70 to 0.85~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«3»~~4~~. Units measured and found to have «<40 g/unit» ~~<30 g/unit~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«4»~~1~~. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

«7.7.1.5» ~~7.22.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.7.1.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes
- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.7.2» ~~7.23~~: Whole Blood for Exchange Transfusion, Leucocyte Depleted

A component for exchange or large-volume transfusion of neonates, containing less than 1×10^6 leucocytes per unit.

«7.7.2.1» ~~7.23.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component must be prepared and used for exchange transfusion by the end of Day 5, should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B (see Chapter 12) and should be negative for antibodies to CMV.
- «Whenever possible the component should be selected from male donors as a TRALI risk reduction measure.»
- The component should be irradiated and transfused within 24 hours of irradiation. See the «BSH 'Guidelines on transfusion for fetuses, neonates and older children'.[6]» ~~BCSH 'Transfusion guidelines for neonates and older children'.[5]~~
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.
- Whole Blood for Exchange Transfusion, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- If not required for exchange transfusion, the component may be remanufactured into Red Cells in Additive Solution, Leucocyte Depleted (see section «7.3.2» ~~7.6~~), up to 6 days after donation, with a shelf life of up to 35 days in total.

«7.7.2.2» ~~7.23.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Whole Blood for Exchange Transfusion, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.2.3» ~~7.23.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 5 days at a core temperature of 4 ±2°C.
- The component should be used within 24 hours of irradiation and within the overall maximum 5-day shelf life.
- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre to cover such eventualities
    - adequate records of the incident are compiled and retained.
- If Whole Blood for Exchange Transfusion, Leucocyte Depleted is unused within its specified shelf life, the Blood Centre may return the component to stock provided that:
    - the component was stored within specification
    - the component is appropriately relabelled as Whole Blood Leucocyte Depleted and, if necessary, 'irradiated'
    - the storage restrictions of irradiated red cells are observed, i.e. use within 14 days of irradiation.

«7.7.2.4» ~~7.23.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.2» ~~7.18~~ shall meet the specified values.

Table «7.7.2» ~~7.18~~ Whole Blood for Exchange Transfusion, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Haematocrit		0.4 – 0.5
Haemoglobin content		≥40 g/unit
Leucocyte count [1]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

«7.7.2.5» ~~7.23.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- «for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours»
- ~~transport time normally should not exceed 12 hours.~~

In some instances, it is necessary to issue red cell components «from the blood supplier to hospitals» that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.7.2.6: Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes
- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within four hours of issue out of a controlled temperature environment.»

«7.7.3» ~~7.24~~: Red Cells for Exchange Transfusion, Leucocyte Depleted

A component for exchange or large-volume transfusion of neonates prepared by leucodepleting fresh whole blood to less than 1 × 10^6 leucocytes per component and removing a proportion of the plasma.

«7.7.3.1» ~~7.24.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component must be prepared and used by the end of Day 5, should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B (see Chapter 12), and should be negative for antibodies to CMV.
- «Whenever possible, the component should be selected from male donors as a TRALI risk reduction measure.»
- The component should be irradiated and transfused within 24 hours of irradiation. See the «BSH 'Guidelines on transfusion for fetuses, neonates and older children'.[6]» ~~BCSH 'Transfusion guidelines for neonates and older children'.[3]~~
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.
- Red Cells for Exchange Transfusion, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- If not required for exchange transfusion, the component may be remanufactured into Red Cells in Additive Solution, Leucocyte Depleted (see section «7.3.2» ~~7.6~~), up to «7» ~~6~~ days after donation, with a shelf life of up to 35 days in total.

«7.7.3.2» ~~7.24.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells for Exchange Transfusion, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.3.3» ~~7.24.3~~: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 5 days at a core temperature of 4 ±2°C.
- Transfusion of this component should commence within 24 hours of irradiation and within the overall maximum 5-day shelf life.

- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre or hospital to cover such eventualities
    - adequate records of the incident are compiled and retained.
- If Red Cells for Exchange Transfusion, Leucocyte Depleted are unused within their specified shelf life, the Blood Centre may return them to stock provided that:
    - the component was stored within specification
    - the component is appropriately relabelled as Red Cells, Leucocyte Depleted and, if necessary, 'irradiated'
    - the storage restrictions of irradiated red cells are observed, i.e. use within 14 days of irradiation.

«7.7.3.4» ~~7.24.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.3» ~~7.19~~ shall meet the specified values.

Table «7.7.3» ~~7.19~~ Red Cells for Exchange Transfusion, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range ~~2~~
Haematocrit «2»		0.50 – 0.60 ~~3~~
Haemoglobin content «3»		≥40 g/unit ~~4~~
Leucocyte count «4»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1»~~2~~. Units measured and found to be «<220 mL or >420 mL» ~~outside of the range 220 to 420 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2»~~3~~. Units measured and found to be «<0.50 or >0.60» ~~outside of the range 0.50 to 0.60~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«3»~~4~~. Units measured and found to have «<40 g/unit» ~~<30 g/unit~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«4»~~1~~. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

«7.7.3.5» ~~7.24.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised

- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.7.3.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes
- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.7.4» ~~7.25~~: Red Cells for Neonates and Infants, Leucocyte Depleted

A red cell component suitable for neonates and infants under 1 year that contains less than 1 × 10^6 leucocytes (per starting component). The Red Cells for Neonates and Infants, Leucocyte Depleted may be divided into approximately equal volumes using a closed system.

«7.7.4.1» ~~7.25.1~~: Technical information

- «Section 7.7 provides guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- Red Cells for Neonates and Infants, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.

«7.7.4.2» ~~7.25.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells for Neonates and Infants, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.4.3» ~~7.25.3~~: Storage

For general guidelines, see section 6.7.

- For top-up transfusions of neonates and infants under 1 year, this component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C if an adenine-supplemented anticoagulant is used, otherwise (e.g. with CPD anticoagulant) the maximum period of storage is 28 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- For large-volume transfusion of neonates, this component should be used within 24 hours of irradiation and before the end of Day 5.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:

- the component has been exposed to such a temperature change on one occasion only
- the duration of the temperature excursion has not exceeded 5 hours
- a documented system is available in each Blood Centre or hospital to cover such eventualities
- adequate records of the incident are compiled and retained.

«7.7.4.4» ~~7.25.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.4» ~~7.20~~ shall meet the specified values.

Table «7.7.4» ~~7.20~~ Red Cells for Neonates and Infants, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Haemoglobin content		Locally defined
Haemolysis (only required if produced as a primary component)	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count [1]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/starting component
1. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

«7.7.4.5» ~~7.25.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.7.4.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes
- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C

- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.7.5» ~~7.26~~: Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted

A red cell component suitable for top-up or large-volume transfusion of neonates and infants under 1 year containing less than 1×10^6 leucocytes (per starting component). The red cells are suspended in an additive solution and may be divided into approximately equal volumes using a closed system.

«7.7.5.1» ~~7.26.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~
- Unless the Blood Centre recommends screening is unnecessary, the donor should be Haemoglobin S screen negative.

«7.7.5.2» ~~7.26.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the additive solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.5.3» ~~7.26.3~~: Storage

For general guidelines, see section 6.7.

- Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted for top-up transfusion of neonates and infants under 1 year may be stored for a maximum of 35 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- For large-volume transfusion of neonates and infants under 1 year, this component should be transfused within 24 hours of irradiation and before the end of Day 5.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:

- the component has been exposed to such a temperature change on one occasion only
- the duration of the temperature excursion has not exceeded 5 hours
- a documented system is available in each Blood Centre or hospital to cover such eventualities
- adequate records of the incident are compiled and retained.

«7.7.5.4» ~~7.26.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.5» ~~7.21~~ shall meet the specified values.

Table «7.7.5» ~~7.21~~ Red Cells in Additive Solution for Neonates and Infants, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	280 ±60 mL
Haemoglobin content «1»		≥40 g/unit «2»
«Haematocrit 2»		«0.50 – 0.70»
Haemolysis (only required if produced as a primary component)	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count «3»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/starting component
«1»~~2~~. Units measured and found to have <30 g«/unit» prior to splitting «(or 30 g/no. of units for split units)» should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2. Units measured and found to have haematocrit <0.40 or >0.70 should only be issued for transfusion under concessionary release»		
«3»~~1~~. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

«7.7.5.5» ~~7.26.5~~: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

«7.7.5.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes

- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

«7.7.6» ~~7.29~~: Platelets for Intrauterine Transfusion, Leucocyte Depleted

A hyperconcentrated platelet component for intrauterine transfusion, prepared by apheresis, that contains less than 1×10^6 leucocytes per donation.

«7.7.6.1» ~~7.29.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for intrauterine transfusion and use in neonates and infants under 1 year.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- The component must be used by the end of Day 1.
- The component must be irradiated. See the «BSH 'Guidelines on transfusion for fetuses, neonates and older children'.[6]» ~~*BCSH 'Transfusion guidelines for neonates and older children'.*[5]~~
- The component should contain a concentration of platelets between 2 and 4×10^{12}/L in a collected volume generally in the range of 50-100 mL. «The volume of suspension medium must be sufficient to maintain the pH at ≥6.4 at the end of the shelf life of the component.»
- All components should be quality monitored and achieve the specified requirements. The testing need not necessarily be performed before component release.
- Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy. If platelets are to be issued as HPA-matched (e.g. HPA-1a or HPA-5b negative) then donors should be screened and found negative for all clinically significant HLA and HPA antibodies (as defined in Chapters 16 and 18). This screening can be done on an initial sample and does not need repeating at each donation unless the donor has been transfused or pregnant since the last antibody screen.
- A record which demonstrates that the donor has not been transfused since the initial negative screen for antibodies and in case of female donors that the donor has not been pregnant since the initial negative screen for antibodies needs to be maintained.
- Platelets for Intrauterine Transfusion, Leucocyte Depleted should «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*be transfused through a 170–200 µm filter.*~~

«7.7.6.2» ~~7.29.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets for Intrauterine Transfusion, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the relevant HPA and HLA type, if necessary
- the date of collection
- the expiry date and time*
- the temperature of storage and a comment that continuous gentle agitation during storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.6.3» ~~7.29.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 22 ±2°C for use up to the end of Day 1.
- The component should be gently and continuously agitated during storage.

«7.7.6.4» ~~7.29.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.7.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B and antibodies to CMV. Furthermore, all components tested for the other parameters shown in Table «7.7.6» ~~7.24~~ shall meet the specified values.

Table «7.7.6» ~~7.24~~ Platelets for Intrauterine Transfusion, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	Every component	Within locally defined range ~~3~~
Platelet concentration		$2 – 4 \times 10^{12}$/L
pH at end of shelf life «2»~~1~~		≥6.4
Leucocyte count «3,4»~~2~~	As per sections 6.3 and «7.7.1» ~~7.1~~	$<1 \times 10^{6}$/unit ~~4~~
«1»~~3~~. Units measured and found to be «<50 mL or >120 mL» ~~outside of the range 50 to 120 mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
«2»~~1~~. The shelf life of this hyperconcentrated platelet component has been set to reflect validation data. Therefore, once this has been validated locally, there is no need to measure pH at expiry on a routine basis		
«3»~~2~~. Methods validated for counting low numbers of leucocytes must be used		
4. Units measured and found to have «≥2.5 × 10^{6}/unit» ~~>2.5 × 10^{6}/unit~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.7.6.5» ~~7.29.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.7.7» ~~7.30~~: Platelets for Neonatal Use, Leucocyte Depleted

An apheresis platelet component for neonatal use that contains less than 1 × 10^6 leucocytes per starting component.

«7.7.7.1» ~~7.30.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- The component may be prepared by splitting Platelets, Apheresis, Leucocyte Depleted (see section «7.4.2» ~~7.10~~) using a closed system.
- The component should contain >40 × 10^9 platelets in sufficient plasma to maintain the pH «at ≥6.4» ~~between 6.4 and 7.4~~ at the end of the shelf life of the component.
- The component may be leucodepleted as part of an apheresis process or by subsequent filtration of the platelet component.
- Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy. If platelets are to be issued as HPA-matched (e.g. HPA-1a or HPA-5b negative) then donors should be screened and found negative for all clinically significant HLA and HPA antibodies (as defined in Chapters 16 and 18). This screening can be done on an initial sample and does not need repeating at each donation unless the donor has been transfused or pregnant since the last antibody screen.
- A record which demonstrates that the donor has not been transfused since the initial negative screen for antibodies and in the case of female donors that the donor has not been pregnant since the initial negative screen for antibodies needs to be maintained.
- Platelets for Neonatal Use, Leucocyte Depleted should «administered through a CE/UKCA/UKNI marked transfusion set.» ~~be transfused through a 170–200 µm filter.~~

«7.7.7.2» ~~7.30.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets for Neonatal Use, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.7.3» ~~7.30.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 22 ±2°C for up to 5 days. Appropriate pack and platelet concentration combinations may allow storage up to 7 days, but due to concerns over bacterial contamination would require either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.
- Platelets should be agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided the interruption is for no longer than a total of 24 hours.

«7.7.7.4» ~~7.30.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.7» ~~7.25~~ shall meet the specified values.

Table «7.7.7» ~~7.25~~ Platelets for Neonatal Use, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined range
Platelet count «2»		≥40 × 10^9/unit
pH at end of shelf life «3,4»~~1~~		≥6.4
Leucocyte count «5»~~2~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/starting component
«1. Units measured and found to be <30 mL or >95 mL should only be issued for transfusion under concessionary release»		
«2. Units measured and found to have <40 × 10^9/unit, or more than the maximum recommended by the manufacturer of the storage pack where stated, should only be issued for transfusion under concessionary release»		
«3»~~1~~. If producing low numbers, use of most units is likely to make testing of outdated units impossible. In this situation periodic checks to ensure end-of-shelf-life quality should be undertaken with the combination of blood pack platelet concentration and storage conditions in routine use.		
«4. A minimum of 90% of components tested shall meet the specified value»		
«5»~~2~~. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.7.7.5» ~~7.30.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.7.8» ~~7.34~~: Platelets in Plasma and Additive Solution for Neonatal Use, Leucocyte Depleted

An apheresis platelet component for neonatal use which contains less than 1 × 10^6 leucocytes per starting component and where the suspending medium comprises approximately 80% plasma and 20% additive solution.

«7.7.8.1» ~~7.34.1~~: Technical information

- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B and should be negative for antibodies to CMV.
- The component is manufactured as a secondary component by splitting Platelets, Apheresis, Leucocyte Depleted (see section «7.4.2» ~~7.10~~) after the sterile addition of a controlled volume of an approved platelet additive solution. Splitting must be performed using a closed system.
- The volume of additive solution added should be determined by validation and will depend upon the type of additive solution and platelet storage pack. Re-validation of the proportion of plasma / PAS must be performed at least annually on a minimum of 25 units and after any changes to production method.
- The volume of additive solution should be sufficient to maintain the pH ≥6.4 at the end of the shelf life of the component.
- The component should contain ≥40 × 10^9 platelets.
- The component may be leucodepleted as part of an apheresis process or by subsequent filtration of the platelet component.
- Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy. If platelets are to be issued as HPA-matched (e.g. HPA-1a or HPA-5b negative) then donors should be screened and found negative for all clinically significant HLA and HPA antibodies (as defined in Chapters 16 and 18). This screening can be done on an initial sample and does not need repeating at each donation unless the donor has been transfused or pregnant since the last antibody screen.
- A record which demonstrates that the donor has not been transfused since the initial negative screen for antibodies and in the case of female donors that the donor has not been pregnant since the initial negative screen for antibodies needs to be maintained.
- Platelets in Plasma and Additive Solution for Neonatal Use, Leucocyte Depleted should be administered through a «CE/UKCA/UKNI» ~~CE~~ marked transfusion set.

«7.7.8.2» ~~7.34.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets in Plasma and Additive Solution for Neonatal Use Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name of the anticoagulant and additive solution

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.8.3» ~~7.34.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 22 ±2°C for up to 5 days. Appropriate pack and platelet concentration combinations may allow storage up to 7 days, but due to concerns over bacterial contamination would require either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.
- Platelets should be agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided the interruption is for no longer than a total of 24 hours and no single interruption lasts for more than eight hours.

«7.7.8.4» ~~7.34.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B, and antibodies to CMV.

Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.8» ~~7.27~~ shall meet the specified values.

Table «7.7.8» ~~7.27~~ Platelets in Plasma and Additive Solution for Neonatal Use, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined range
Platelet count [1]		≥40 × 10^9/unit
pH at end of shelf life [2,3]		≥6.4
Leucocyte count [4]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/starting component
1. Units measured and found to have <40 × 10^9/unit, or more than the maximum recommended by the manufacturer of the storage pack, where stated, should «only» ~~not~~ be issued for transfusion «under concessionary release»		
2. If producing low numbers, issue of most units is likely to make testing of outdated units impossible. In this situation periodic checks to ensure end-of-shelf-life quality should be undertaken with the combination of blood pack platelet concentration and storage conditions in routine use.		
3. A minimum of 90% of components tested shall meet the specified value		
4. Methods validated for counting low «numbers» ~~levels~~ of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

«7.7.8.5» ~~7.34.5~~: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

«7.7.9» ~~7.35~~: Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted

Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted is plasma that has been obtained from whole blood or by apheresis. The plasma contains less than 1×10^6 leucocytes per component.

Using a closed system the component may be subdivided into approximately equal volumes and rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

«7.7.9.1» ~~7.35.1~~: Technical information

- Section «7.7» ~~7.21~~ provides general guidance on the requirements for components for use in neonates and infants under 1 year.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B. Testing for CMV antibodies is not required.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII~~:C~~ yields will be obtained when the plasma is separated as soon as possible after venepuncture and rapidly frozen to -25°C or below.
- The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII~~:C~~ concentration.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted should be transfused through a «CE/UKCA/UKNI» ~~CE~~ marked transfusion set.

«7.7.9.2» ~~7.35.2~~: Labelling

For general guidelines, see section 6.6

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component should be used within 4 hours of thawing if maintained at 22 ±2oC or up to a maximum of 24 hours of thawing if stored at 4 ±2°C
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.9.3» ~~7.35.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, and at the time of administration, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C, or up to a maximum of 24 hours if stored at 4 ±2°C.
- Transfusion of FFP should be completed within 4 hours of issue out of a controlled temperature environment.

«7.7.9.4» ~~7.35.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.9» ~~7.35~~ shall meet the specified values with the exception of FVIII~~:C~~.

Table «7.7.9» ~~7.35~~ Fresh Frozen Plasma for Neonates and Infants, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Stated volume ±10%
Total protein		≥50 g/L
Platelet count «1,2»		<30 × 10^9/L ~~2~~
Red cell count «2»		<6 ×10^9/L ~~2~~
FVIII~~:C~~ 3,4		Mean ≥0.70 IU/mL
Leucocyte count «2,5»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~2~~
«1. Units with a residual platelet count >100 × 10^9/L should only be issued for transfusion under concessionary release»		
2. Pre-freeze in starting component		
3. Units measured and found to have «<0.30 IU/mL» ~~<0.3 IU/mL~~ should «only» ~~not~~ be issued for transfusion «under concessionary release»		
4. A minimum of 90% of those components tested should have ≥0.50 IU/mL		
«5»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.7.9.5» ~~7.35.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.7.10» ~~7.27~~: Fresh Frozen Plasma~~,~~ «for Neonates and Infants, Pathogen Reduced» ~~Neonatal Use, Methylene Blue Treated and Removed~~, Leucocyte Depleted

«This component» ~~Fresh Frozen Plasma, Neonatal Use, Methylene Blue Treated (MBT) and Removed, Leucocyte Depleted~~ is plasma that has been obtained from whole blood or by apheresis ~~from a country with a low risk of vCJD~~, contains less than 1×10^6 leucocytes and has been treated with «a pathogen inactivation (PI) system. The PI system must be approved (CE/UKCA/UKNI marked) for this use, and must have been validated by the Blood Service.» ~~methylene blue and exposure to visible light to inactivate pathogens, and processed to remove residual methylene blue.~~

«Following PI treatment,» using a closed system the component may be subdivided into approximately equal volumes «. The treated component is» ~~and~~ rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

«7.7.10.1» ~~7.27.1~~: Technical information

- ~~Where the starting component is sourced outside the UK, a detailed and agreed specification must be available.~~
- «Section 7.7 provides guidance on the requirements for components for use in neonates and infants under 1 year.»
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- «Fresh Frozen Plasma for Neonates and Infants, Pathogen Reduced, Leucocyte Depleted, may be prepared from small pools of up to 12 individual donations if validated and risk-assessed by the blood service and if in accordance with the specifications of the manufacturer of the PI system.»
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B. Testing for CMV antibodies is not required.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- The plasma should be separated before the red cell component is cooled to its storage temperature. Greater FVIII~~:C~~ yields will be obtained when the plasma is separated as soon as possible after venepuncture and rapidly frozen to –25°C or below.
- The method of preparation should ensure the component has the maximum level of labile coagulation factors with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII~~:C~~ concentration.
- «It contains, on average, greater than 60% of the labile coagulation factors and naturally occurring inhibitors present in standard fresh frozen plasma.»
- «The PI system typically reduces the risk of infection from enveloped viruses (e.g. HBV, HCV, HIV) by at least one thousand-fold.»
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- ~~The MBT process reduces the FVIII:C content by approximately 30% when compared to standard fresh frozen plasma.~~
- ~~Intact white blood cells in the plasma should be reduced to less than 1 × 106 per unit prior to exposure to methylene blue and visible light.~~
- «The level of removal of the photo-sensitising agent prior to final storage should be validated, if such a step is included in the PI system.» ~~The process for methylene blue removal should be validated to give components with a methylene blue concentration ≤0.30 µmol/L. The methylene blue content of the final component is the initial content of the unsplit starting component (less than approximately 30 µg per unit) divided by the number of split components produced.~~
- «Intact white blood cells in the plasma should be reduced to less than 1×10^6 per unit prior to the PI process.»
- Fresh Frozen Plasma~~,~~ «for Neonates and Infants, Pathogen Reduced» ~~Neonatal Use, Methylene Blue Treated and Removed~~, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.7.10.2» ~~7.27.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Fresh Frozen Plasma~~,~~ «for Neonates and Infants, Pathogen Reduced» ~~*Neonatal Use, Methylene Blue Treated and Removed*~~, Leucocyte Depleted * and volume
- «the name of the PI system used»
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component should be used within 4 hours of thawing
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection «including vCJD and allergy to the compounds used for, or derived from, PI treatment»

«7.7.10.3» ~~7.27.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~*daily*~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~*cryo*~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C or 24 hours if stored at 4 ±2°C, but it should be borne in mind that extended post-thaw storage will result in a decline in the content of labile coagulation factors.

«7.7.10.4» ~~7.27.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), the component shall be free from clinically significant irregular blood group antibodies and high-titre anti-A and/or anti-B. Furthermore, a minimum of 75% of those components tested for the other parameters shown in Table «7.7.10» ~~7.22~~ shall meet the specified values.

Table «7.7.10» ~~7.22~~ Fresh Frozen Plasma~~,~~ «for Neonates and Infants, Pathogen Reduced» ~~Neonatal Use, Methylene Blue Treated and Removed~~, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range and within any limits specified for the «PI» ~~MBT~~ process used
Platelet count «1,2»		<30 × 10^9/L ~~2~~
FVIII~~:C~~		≥0.50 IU/mL
Leucocyte count «2,3»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~2~~
«1. Units with residual platelet count >100 × 10^9/L should only be issued for transfusion under concessionary release»		
2. Pre-freeze in starting component		
«3»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

«7.7.10.5» ~~7.27.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.7.11» ~~7.36~~: Cryoprecipitate for Neonates and Infants, Leucocyte Depleted

The component represents a source of concentrated FVIII, and von Willebrand factor, fibrinogen, FXIII and fibronectin from a unit of fresh frozen plasma. The plasma from which the cryoprecipitate was produced contains less than 1 × 10^6 leucocytes per component.

«7.7.11.1» ~~7.36.1~~: Technical information

- Section «7.7» ~~7.21~~ provides general guidance on the requirements for components for use in neonates and infants under 1 year.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate for Neonates and Infants, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing a single donation of Fresh Frozen Plasma, Leucocyte Depleted (see section «7.5.1» ~~7.15~~), fulfilling the requirements for neonates and infants, at 4 ±2°C.
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B. Testing for CMV antibodies is not required.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- For storage, Cryoprecipitate for Neonates and Infants, Leucocyte Depleted should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Cryoprecipitate for Neonates and Infants, Leucocyte Depleted should be administered through a «CE/UKCA/UKNI» ~~CE~~ marked transfusion set.

«7.7.11.2» ~~7.36.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate for Neonates and Infants, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within «4» ~~four~~ hours of thawing
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

«7.7.11.3» ~~7.36.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

«7.7.11.4» ~~7.36.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.7.11» ~~7.36~~ shall meet the specified values.

Table «7.7.11» ~~7.36~~ Cryoprecipitate «for Neonates and Infants», Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal range
Fibrinogen		≥140 mg/unit
FVIII		≥70 IU/unit
Leucocyte count [1«,2»]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit [2]
1. Methods validated for counting low numbers of leucocytes must be used		
2. Pre-freeze in starting component		

«7.7.11.5» ~~7.36.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

«7.7.12» ~~7.28~~: Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted

The component «provides» ~~represents~~ a source of concentrated FVIII~~:C~~, and von Willebrand factor, fibrinogen, FXIII and fibronectin ~~from a unit of Fresh Frozen Plasma, Methylene Blue Treated and Removed~~. «It is derived from a unit of Fresh Frozen Plasma for Neonates and Infants, Pathogen Reduced, Leucocyte Depleted.» The plasma from which «this component is» ~~the Cryoprecipitate, Methylene Blue Treated and Removed, Leucocyte Depleted was~~ produced contains less than 1 × 10^6 leucocytes per component ~~and is from a country with a low risk of vCJD~~.

«7.7.12.1» ~~7.28.1~~: Technical information

- ~~Where the starting component is sourced outside the UK, a detailed and agreed specification must be available.~~
- «Section 7.7 provides general guidance on the requirements for components for use in neonates and infants under 1 year.»
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted is the cryoglobulin fraction of plasma obtained by thawing a single donation of Fresh Frozen Plasma, Neonatal Use, Methylene Blue Treated and Removed, Leucocyte Depleted (see section «7.7.10» ~~7.27~~) at 4 ±2°C.
- «The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B. Testing for CMV antibodies is not required.»
- Plasma should be selected from male donors or screening of female donors for HLA/HNA antibodies should be considered, as a TRALI risk reduction strategy.
- ~~The process for methylene blue removal should be validated to give components with a methylene blue concentration ≤0.30 µmol/L (less than approximately 30 µg per unit) in the starting component.~~
- For storage, Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~transfused through a 170–200 µm filter.~~

«7.7.12.2» ~~7.28.2~~: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted* and volume
- «the name of the pathogen inactivation (PI) system used»
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing

- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection «including vCJD and allergy to the compounds used for, or derived from, PI treatment»

«7.7.12.3» ~~7.28.3~~: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be used immediately. If delay is unavoidable, the component should be stored at ambient temperature and used within 4 hours.

«7.7.12.4» ~~7.28.4~~: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table «7.7.12» ~~7.23~~ shall meet the specified values.

Table «7.7.12» ~~7.23~~ Cryoprecipitate «for Neonates and Infants, Pathogen Reduced»~~, Methylene Blue Treated and Removed~~, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal range
Fibrinogen		≥140 mg/unit
FVIII~~:C~~		≥50 IU/unit
Leucocyte count [1«,2»]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit [~~2~~]
1. Methods validated for counting low numbers of leucocytes must be used		
2. Pre-freeze in starting component		

«7.7.12.5» ~~7.28.5~~: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

Annexe 3 Provisional components

A3.1: Platelets in Additive Solution and Plasma, Leucocyte Depleted, Pathogen Reduced

A platelet concentrate, derived from buffy coats or apheresis, which contains less than 1 × 10^6 leucocytes and where the suspending medium comprises approximately 30-50% plasma and 50-70% additive solution. Subsequently the component is subjected to treatment using a licensed pathogen inactivation system prior to storage.

A3.1.1: Technical Information

- The primary platelet component prior to pathogen-reduction must meet the specifications set by the manufacturer of the pathogen-reduction system.
- Provided the pathogen reduction system used has been validated to inactivate lymphocytes, irradiation of the component to prevent transfusion-associated graft versus host disease is not required.
- The level of removal of the photo-sensitising agent prior to final storage should be validated, if such a step is included in the pathogen-reduction system.
- Provided the pathogen reduction system used has been validated to inactivate CMV, CMV testing of the component to prevent transfusion-associated CMV infection is not required.
- The component is manufactured as a primary component and not as a remanufactured secondary component.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for platelet production.
- Where prepared from buffy coats, the buffy coats must be prepared at ambient temperature before the whole blood is cooled to below 20°C.
- Where prepared from buffy coats, initial separation of buffy coat must occur within 24 hours of venepuncture (unless supported by additional validation), with a minimum buffy coat rest period of 2 hours before secondary pooling and processing of buffy coats to produce the final component, which is generally completed before the end of Day 1.
- Screening of female apheresis donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy.
- The volume of suspension medium must be sufficient to maintain the pH «at ≥6.4» ~~*within the range 6.4-7.4*~~ at the end of the shelf life of the component.

- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the audit trail and the correct identification number is put on the final component pack.
- Platelets in Additive Solution and Plasma, Leucocyte Depleted, Pathogen Reduced should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

A3.1.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, (pooled or apheresis) in Additive Solution and Plasma, Leucocyte Depleted, Pathogen-Reduced (name of PR method)* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing platelet units*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant and platelet additive solution
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.1.3: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the pathogen inactivation system, additive solution and storage container.
- Systems currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 7 days in a closed system.
- If any production stage involves an open system, after preparation the component should be used as soon as possible. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.

A3.1.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 and leucocyte counting (see section 6.3 and «7.1.1» ~~*7.1*~~), a minimum of 75% of those components tested for the parameters shown at Table A3.1 shall meet the specified values.

Table A3.1 Platelets in Additive Solution and Plasma, «Leucocyte Depleted,» Pathogen Reduced – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count «1»		≥240 × 10^9/pool ~~2~~
pH at end of shelf life	If less than 10 per month, every available component	«≥6.4» ~~6.4 – 7.4~~
Leucocyte count «2»	As per section 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/pool ~~1~~
«1»~~2~~. Units measured and found to have <160 × 10^9/pool should not be issued for transfusion		
«2»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

A3.1.5: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.

A3.2: Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced

A red cell component containing less than 1×10^6 leucocytes and suspended in an approved additive solution. Subsequently the component is subjected to treatment using a pathogen inactivation system prior to storage.

A3.2.1: Technical information

- The primary red cell component prior to pathogen-reduction must meet the specifications set by the manufacturer of the pathogen-reduction system.
- Provided the pathogen reduction system «CE/UKCA/UKNI» ~~*CE*~~ mark states that it may be used as an alternative to irradiation to prevent transfusion-associated graft versus host disease, irradiation of the component is not required.
- Provided the pathogen reduction system «CE/UKCA/UKNI» ~~*CE*~~ mark states that it may be used as an alternative to serological testing for the prevention of transfusion-associated CMV infection, CMV testing of the component is not required.
- The component is manufactured as a secondary component from red cells in additive solution, leucocyte depleted. The primary component (red cells in additive solution) must not have been previously remanufactured from red cells for exchange transfusion.
- Where the production process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the audit trail and the correct identification number is put on the final component pack.
- Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

A3.2.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the additive solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.2.3: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 35 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been prepared in a closed system and exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre to cover such eventualities
    - adequate records of the incident are compiled and retained.

A3.2.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table A3.2 shall meet the specified values.

Table A3.2 Red Cells in Additive Solution, Leucocyte Depleted, Pathogen Reduced – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	190 – 330 mL
Haemoglobin content «1»		≥40 g/unit ~~2~~
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count «2»~~1~~	As per section 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1»~~2~~. Units measured and found to have <30 g/unit should not be issued for transfusion		
«2»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

A3.2.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

A3.3: Liquid Plasma, Leucocyte Depleted

Plasma that has been obtained from whole blood from a previously tested donor (as defined in section «7.1.4» ~~7.3~~). The plasma contains less than 1 × 10^6 leucocytes per component.

A3.3.1: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Plasma should be selected from male donors only.
- The plasma should be separated before the red cell component is cooled to its storage temperature.
- The method of preparation should ensure minimum cellular contamination. The plasma should be placed at 2-6°C as soon as possible after separation from the red cell component. The production process should be validated to ensure that components meet the specified limits for FVIII~~:C~~ concentration at the end of expiry.
- Liquid Plasma, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~

A3.3.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Liquid Plasma, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the component*
- the temperature of storage
- the blood pack lot number*
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.3.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of 4 ±2°C for a maximum of 7 days
- The component must not be frozen and should be transfused as soon as possible. It should be borne in mind that the content of labile coagulation factors declines with the duration of storage.

A3.3.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table A3.3 shall meet the specified values.

Table A3.3 Liquid Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Stated volume ±10% 2
Platelet count «2»		<30 × 10^9/L 3
Red cell count «2»		<0.2 × 10^9/L 3
FVIII ~~.C~~ «3»		[≥X IU/mL]
Leucocyte count «2,4»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit 3
«1»~~2~~. Units measured and found to be outside of the range 200 to 360 mL should not be issued for transfusion		
«2»~~3~~. Pre-freeze in starting component		
«3»~~4~~. Units measured and found to have <0.3 IU/mL should not be issued for transfusion		
«4»~~1~~. Methods validated for counting low numbers of leucocytes must be used		
[To be defined following operation validations]		

A3.3.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be used straight away it should be transferred immediately to storage at the recommended temperature.

For liquid plasma components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

A3.4: Red Cells, Rejuvenated and Washed, Leucocyte Depleted

A red cell component, containing less than 1 × 10^6 leucocytes, which has been rejuvenated, washed, and resuspended in a validated additive solution (SAGM). The component is intended to be used as part of the REDJUVENATE clinical study only, with a maximum of 6 units to be transfused in any 24 hours.

A3.4.1: Technical information

- The starting material is Red Cells in Additive Solution, Leucocyte Depleted, on or after Day 7 and no later than Day 32.
- To reduce the risk of bacterial growth, periods where Red Cells in Additive Solution, Leucocyte Depleted for the trial are removed from controlled storage must not exceed 30 min on each occasion prior to receipt in NHSBT.
- Rejuvenation of red cells occurs via the addition of 50 mL rejuvesol® Red Blood Cell Processing Solution (rejuvesol Solution) and incubation at 37 ±2°C for 60 mins ±5 mins.
- The time that red cells are removed from controlled temperature storage for rejuvenation prior to placement in transport containers and cooling towards 10°C must be kept to a minimum and should not exceed 4 hours.
- Each 50 mL of rejuvesol Solution contains sodium pyruvate 0.550 g, inosine 1.34 g, adenine 0.034 g, dibasic sodium phosphate (heptahydrate) 0.730 g, and monobasic sodium phosphate (monohydrate) 0.311 g, in water for injection, pH 6.7-7.4.
- A validated closed manual washing procedure should be used following rejuvenation. The washing protocol used must be validated to ensure effective removal of the rejuvenating solution.
- Monitoring of component volumes and temperatures must be used to assure that the washing process has taken place on every unit rejuvenated.
- If the washing process results in the transfer of the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct donation identification number is put on the component pack of Red Cells, Rejuvenated and Washed, Leucocyte Depleted.
- Red Cells, Rejuvenated, Washed, Leucocyte Depleted should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a CE marked transfusion set.*~~

A3.4.2: Labelling

For general guidelines, see section 6.6 ~~*of the Red Book*~~.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- REDJUVENATE trial Red Cells, Leucocyte Depleted* and volume (note the trial is blinded and therefore control and treatment arms are labelled the same but that they can be differentiated through PULSE).
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the suspending solution
- the date and time of preparation
- the expiry date and time*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.4.3: Storage

The component should be used as soon as possible. Where the component has been produced in a closed system and storage is required the component should be stored at a core temperature of 4 ±2°C and used within 72 hours of rejuvenation if suspended in SAGM.

A3.4.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9 of the Red Book, and leucocyte counting (see sections 6.3 and «7.1.1» ~~*7.1 of the Red Book*~~), a minimum of 75% of those components tested for the parameters shown in Table A3.4 shall meet the specified values. Provided the component is prepared from a process that is validated for leucocyte removal, testing of washed red cells for residual leucocytes is not required.

Table A3.4 Red Cells, Rejuvenated and Washed, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	100% (all tests are on the day after manufacture and are retrospective quality monitoring, not pre-release criteria)	Within locally specified volume range
Haemoglobin content		≥40 g/unit
Haematocrit		0.50 – 0.70
Haemolysis [1]		<0.3%
ATP and/or 2,3-DPG		ATP: >6 µmol/g Hb 2,3-DPG: >9 µmol/g Hb
Supernatant potassium (as a marker of washing efficiency)		<3.5 mmol/L
Leucocyte count [2] (pre-wash)	As per sections 6.3 and «7.1.1» ~~*7.1 in the Red Book*~~	<1 × 10^6/unit
1. Note: this measurement is not at end of shelf-life as for standard red cell components		
2. Methods validated for counting low numbers of leucocytes must be used. Since the starting material Red Cells in Additive Solution are monitored and controlled for LD performance, the final component does not require a leucocyte count.		

A3.4.5: Transportation

For general guidelines, see section 6.11 ~~*in the Red Book*~~.

- For red cell components, transit containers, packing materials and procedures must have been validated to ensure the component core temperature can be maintained between 2°C and 6°C during transportation between trial sites, and NHSBT prior to rejuvenation.
- Following rejuvenation and washing, red cells must be placed in transport containers with packing materials and procedures that are validated to reduce the core temperature of red cells to below 10°C within 3 hours and maintain a temperature below 10°C for at least 10 hours. Red Cells, Rejuvenated and Washed, Leucocyte Depleted should be returned to controlled storage at 2-6°C as soon as possible thereafter, and no later than 10 hours from being placed in the transport container to ensure that the core temperature does not exceed 10°C.

«A3.4.6:» Removal from and return to 2-6°C controlled storage within hospitals

For occasions when Red Cells, Rejuvenated and Washed, Leucocyte Depleted are removed from 2-6 °C controlled storage (e.g., when issued to a clinical area immediately prior to transfusion) then:

- The unit should not be returned to the issue location refrigerator for re-issue.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

A3.5: Red Cells and Plasma, Leucocyte Depleted

A unit of blood collected into CPD anticoagulant, containing less than 1×10^6 leucocytes.

A3.5.1: Technical information

- Red Cells and Plasma, Leucocyte Depleted (LD) is intended for the treatment of major traumatic haemorrhage with transfusion of a maximum of 4 units (or weight-related equivalent for children) prior to switching to standard component therapy.
- A unit of whole blood collected in the UK currently consists of 470 mL ±10% of blood from a suitable donor (see Chapter 3), plus 63 mL of CPD anticoagulant, which is then LD, and stored in an approved container. The Eurobloodpack contains 66.5 mL of anticoagulant and is suitable for the collection of 475 mL ±10%, although in the UK a volume of 495 mL will not be exceeded.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for direct clinical use.
- Donations should be selected from male donors as a TRALI risk reduction measure.
- The component should be made from group O RhD negative, Kell negative donations.
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B
- Red Cells and Plasma, LD, should be administered through a CE/UKCA/UKNI marked transfusion set.

A3.5.2: Labelling

For general guidelines, see section 6.6 ~~*of the Red Book*~~.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells and Plasma, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.5.3: Storage

For general guidelines, see section 6.7 ~~*of the Red Book*~~.

- The component may be stored for a maximum of 14 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:

- the component has been exposed to such a temperature change on one occasion only
- the duration of the temperature excursion has not exceeded 5 hours
- a documented system is available in each Blood Centre to cover such eventualities
- adequate records of the incident are compiled and retained.

A3.5.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1 of the Red Book~~), a minimum of 75% of those components tested for the parameters shown in Table A3.5 shall meet the specified values. Table A3.5 does not include plasma quality monitoring parameters as the Red Cells and Plasma, Leucocyte Depleted component will not be within the Blood Service at the end of shelf-life and as plasma quality at the point of production is already monitored as part of the process of manufacturing Fresh Frozen Plasma, Leucocyte Depleted from whole blood, using the same filtration process.

Table A3.5 Red Cells and Plasma, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control	470 ±50 mL
Haemoglobin content	(if ≤10 components produced per month then test every available component)	≥40 g/unit
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count [2]	As per section 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. After volume losses resulting from leucodepletion		
2. Methods validated for counting low numbers of leucocytes must be used		

A3.5.5: Transportation

For general guidelines, see section 6.11 ~~of the Red Book~~.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

A3.5.6: Removal from and return to 2-6°C controlled storage within hospitals / pre-hospital clinical environment

For occasions when Red Cells and Plasma, Leucocyte Depleted are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- the time out of a controlled temperature environment should be restricted to under 30 minutes and on one occasion only.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

A3.6: Whole Blood, Leucocyte Depleted, for Clinical Studies

A unit of blood collected into CPD anticoagulant, containing red cells, plasma and platelets as well as less than 1×10^6 leucocytes.

A3.6.1: Technical information

- Whole Blood, Leucocyte Depleted (LD), for Clinical Studies is intended for the treatment of major haemorrhage only, and currently only as part of clinical studies, initially in the pre-hospital situation, with transfusion of a maximum of 4 units (or weight-related equivalent for children) prior to switching to standard component therapy.
- A unit of whole blood collected in the UK currently consists of 470 mL ±10% of blood from a suitable donor (see Chapter 3), plus 63 mL of CPD anticoagulant, which is then LD, and stored in an approved container. The Eurobloodpack contains 66.5 mL of anticoagulant and is suitable for the collection of 475 mL ±10%, although in the UK a volume of 495 mL will not be exceeded.
- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for direct clinical use.
- Donations should be selected from male donors as a TRALI risk reduction measure.
- The component should be produced from group O RhD negative, Kell negative donations
- The component should be free from clinically significant irregular blood group antibodies including high-titre anti-A and anti-B
- Whole Blood, Leucocyte Depleted, for Clinical Studies should be administered through a «CE/UKCA/UKNI» ~~*CE*~~ marked transfusion set.

A3.6.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Whole Blood, Leucocyte Depleted, for Clinical Studies* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the anticoagulant solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.6.3: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 21 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C must be kept to a minimum during storage and restricted to any short period necessary for examining, labelling or issuing the component.

- Exceptionally, i.e. due to equipment failure at a Blood Centre, red cell components which have been exposed to a core temperature not exceeding 10°C and not less than 1°C may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre to cover such eventualities
    - adequate records of the incident are compiled and retained.

A3.6.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~*7.1 of the Red Book*~~), a minimum of 75% of those components tested for the parameters shown in Table A3.6 shall meet the specified values. Table A3.6 does not include plasma quality monitoring parameters as the component will not be within the Blood Service at the end of shelf-life. This should be revalidated annually.

Table A3.6 Whole Blood, Leucocyte Depleted, for Clinical Studies – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal range
Platelet count		
Haemoglobin content		≥40 g/unit
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count [2]	As per section 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. After volume losses resulting from leucodepletion		
2. Methods validated for counting low numbers of leucocytes must be used. 100% of units must be monitored for residual leucocytes and any units measured and found to be >5 × 10^6/Unit must not be issued for clinical use.		

A3.6.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- transport time normally should not exceed 12 hours.

In some instances, it is necessary to issue red cell components that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

A3.6.6: Removal from and return to 2-6°C controlled storage within hospitals / pre-hospital clinical environment

For occasions when units of Whole Blood, Leucocyte Depleted, for Clinical Studies are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- the time out of a controlled temperature environment should be restricted to under 30 minutes and on one occasion only.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

A3.7: Convalescent Plasma (COVID-19), FFP, Leucocyte Depleted

This specification is now redundant and has been moved to Annexe 4: Redundant Components.

A4.2: Convalescent Plasma (COVID-19), FFP, Leucocyte Depleted

A3.8: Convalescent Plasma (COVID-19), FFP, for Neonates and Infants, Leucocyte Depleted

This specification is now redundant and has been moved to Annexe 4: Redundant Components.

A4.3: Convalescent Plasma (COVID-19), FFP, for Neonates and Infants, Leucocyte Depleted

A3.9: Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw

The pooled component represents a source of concentrated FVIII~~:C~~, von Willebrand factor, fibrinogen, FXIII and fibronectin from primary cryoprecipitate components derived from units of fresh frozen plasma. The plasma from which the cryoprecipitate was produced contains less than 1×10^6 leucocytes per primary component.

A3.9.1: Technical information

- Donations of whole blood where the bleed time exceeded 15 minutes are not suitable for the production of plasma components for direct clinical use.
- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw is the cryoglobulin fraction of plasma obtained by thawing and pooling five single cryoprecipitate components or pooling five single cryoprecipitate components immediately after production from thawed fresh frozen plasma.
- Plasma should be selected from male donors or consideration should be given to screening female donors for HLA/HNA antibodies, as a TRALI risk reduction measure.
- For storage, Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw should be rapidly frozen to a core temperature of –25°C or below within 2 hours of preparation.
- Component samples collected for the quality monitoring assessment of FVIII~~:C~~ should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Initial process validation must ensure that for a minimum of 20 tested Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw components a minimum of 75% of those components tested for the parameters shown in Table A3.9 shall meet the specified values.
- Annual process validation is acceptable for quality monitoring purposes, provided that the primary components, Fresh Frozen Plasma, Leucocyte Depleted and/or Cryoprecipitate, Leucocyte Depleted, Extended Shelf-life Post-thaw are separately monitored as part of monthly testing. If this is not the case, test monthly 1% or as determined by statistical process control (if ≤10 components produced per month then test every available component), of Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw components. A minimum of 75% of those components tested for the parameters shown in Table A3.9 shall meet the specified values.
- A secure system must be in place to ensure a full audit trail and that the correct identification number is put on the final component pack.
- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw should be transfused through a «CE/UKCA/UKNI» ~~CE/UKCA~~ marked transfusion set.

A3.9.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the component label:

(* = in eye-readable and UKBTS approved barcode format)

- Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-life Post-thaw* and volume
- the blood component producer's name*
- a unique pool or batch number or the donation number of all contributing units*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within 4 hours of thawing if maintained at 22 ±2°C, or up to a maximum of 120 hours of thawing if stored at 4 ±2°C
- the name, composition and volume of anticoagulant.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.9.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a waterbath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~*daily*~~ and maintained to minimise the risk of bacterial contamination. After thawing, the content should be inspected to ensure that no insoluble ~~*cryo*~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component should either be used or returned to 4 ±2°C within a maximum of 4 hours if maintained below 24°C. Extended Shelf-life Post-thaw cryoprecipitate may be stored up to 120 hours at 4 ±2°C following thawing. Following storage at 4 ±2°C, Extended Shelf-life Post-thaw cryoprecipitate must be briefly warmed using a plasma thawing device at 33-37°C until any precipitate has gone back into solution (through visual inspection). This should occur in the majority of units within 5 minutes, and should not exceed 20 minutes. Once re-warmed, Extended Shelf-life Post-thaw cryoprecipitate should not be placed back in the refrigerator.
- Transfusion of Extended Shelf-life Post-thaw cryoprecipitate should be completed within 4 hours of issue out of a controlled temperature environment unless it fulfils the criteria to be returned to storage at 4 ±2°C and if this occurs on one occasion only.

A3.9.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~*7.1*~~), a minimum of 75% of those components tested for the parameters shown at Table A3.9 shall meet the specified values.

Table A3.9 Cryoprecipitate Pooled, Leucocyte Depleted, Extended Shelf-Life Post-Thaw – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	100 – 250 mL
Fibrinogen	Refer to Technical information (section A3.9.1) above	≥700 mg/unit
FVIII ~~:C~~		≥350 IU/unit
Leucocyte count «1»	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit ~~1~~ in the starting component
1. Pre-freeze methods validated for counting low numbers of leucocytes must be used		

A3.9.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

A3.10: Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted

Plasma that has been obtained by apheresis from vaccinated donors who have very high titre antibodies (Roche Elisa of at least 20,000 units/ml or equivalent), for the treatment of patients with COVID-19. The plasma contains less than 1×10^6 leucocytes per component and has been rapidly frozen to a temperature that will maintain the activity of labile coagulation factors.

A3.10.1: Technical information

- Plasma can be selected from male or female donors. Female donors must be screened and negative for HLA/HNA antibodies, as a TRALI risk reduction measure. Plasma should only be selected as CP for treatment of patients with COVID-19 if it is validated to contain a minimum concentration of SARS-CoV-2 antibody levels according to national clinical guidelines.
- Greater FVIII yields will be obtained when the plasma is rapidly frozen to –25°C or below.
- The method of preparation should be validated to ensure there is no evidence of significant activation at 24 hours shelf life, with minimum cellular contamination. The production process should be validated to ensure that components meet the specified limits for FVIII concentration. If plasma collected for CP were to be re-manufactured for any other purpose these procedures must be fully validated and in accordance with the specification of the alternative component.
- Component samples collected for the quality monitoring assessment of FVIII should be from an equal mix of group O and non-O donations due to the difference in FVIII levels between ABO blood groups.
- Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted should be administered through a «CE/UKCA/UKNI» ~~*CE/UKCA*~~ marked transfusion set.

A3.10.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the date of collection
- the expiry date of the frozen component*
- the temperature of storage
- the blood pack lot number*
- a warning that the component must be used within four hours of thawing if maintained at 22 ±2°C, or up to a maximum of 24 hours of thawing if stored at 4 ±2°C.
- the name, composition and volume of the anticoagulant.

In addition, the following statements should be made

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A3.10.3: Storage

For general guidelines, see section 6.7.

- The component should be stored at a core temperature of –25°C or below for a maximum of 36 months.
- Although a storage temperature below –25°C improves the preservation of labile coagulation factors, lower temperatures increase the fragility of plastic. Particular care must be taken when handling such packs.
- The component should be thawed in a water bath or other equipment designed for the purpose, within a vacuum-sealed overwrap bag according to a validated procedure. The optimal temperature at which the component should be thawed is 37°C; temperatures between 33°C and 37°C are acceptable.
- Protocols must be in place to ensure that the equipment is «regularly» cleaned ~~daily~~ and maintained to minimise the risk of bacterial contamination. After thawing, and at the time of administration, the content should be inspected to ensure that no insoluble ~~cryo~~precipitate is visible and that the container is intact.
- Once thawed, the component must not be refrozen and should be transfused as soon as possible. If delay is unavoidable, the component may be stored and should be used within 4 hours if maintained at 22 ±2°C or up to a maximum of 24 hours if stored at 4 ±2°C.
- Transfusion of Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted should be completed within 4 hours of issue out of a controlled temperature environment.

A3.10.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~ and Table A3.10), a minimum of 75% of those components tested for the parameters shown in Table A3.10 shall meet the specified values with the exception of FVIII~~:C~~.

Table A3.10 Convalescent Plasma (VCOV-19), FFP, Leucocyte Depleted – additional tests

Parameter	Frequency of test	Specification
Volume	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Stated volume ±10%
Total protein		≥50 g/L
Platelet count «1,2»		<30 × 10^9/L ~~3,6~~
Red cell count «1»		<6 × 10^9/L ~~3~~
FVIII «3,4»~~4,5~~		Mean ≥ 0.70 IU/mL
Leucocyte count «1,5,6»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~ (but see «6.» ~~2.~~ below for leucocyte count)	<1 × 10^6/unit ~~2,3~~
«1»~~3~~. Pre-freeze in starting component		
«2»~~6~~. Units measured and found to have a platelet count >100 × 10^9/L should not be issued for transfusion		
«3»~~4~~. Units measured and found to have <0.3 IU/mL should not be issued for transfusion		
«4»~~5~~. A minimum of 90% of those components tested should have ≥0.50 IU/mL		
«5»~~1~~. Methods validated for counting low numbers of leucocytes must be used		
«6»~~2.~~ 90% units should have less than 1 × 10^6 leucocytes and more than 99% of units should contain less than 5 × 10^6 leucocytes, both with 95% confidence		

A3.10.5: Transportation

For general guidelines, see section 6.11.

Every effort should be made to maintain the core storage temperature during transportation. Unless the component is to be thawed and used straightaway it should be transferred immediately to storage at the recommended temperature.

Annexe 4 Redundant components

The specifications for **Cryoprecipitate, Methylene Blue Treated and Removed, Leucocyte Depleted** (previously 7.19) and **Plasma, Cryoprecipitate Depleted, Leucocyte Depleted** (previously 7.20) have now been moved from Chapter 7 to Annexe 4. The text of each specification remains unchanged.

This section contains information for reference regarding redundant components

A4.1 Granulocytes, Apheresis

A4.2 Convalescent Plasma (COVID-19), FFP, Leucocyte Depleted

A4.3 Convalescent Plasma (COVID-19), FFP, for Neonates and Infants, Leucocyte Depleted

«A4.4: Cryoprecipitate, Methylene Blue Treated and Removed, Leucocyte Depleted

A4.5: Plasma, Cryoprecipitate Depleted, Leucocyte Depleted»

Annexe 5 Blood components for contingency use

This section contains specifications for blood components used for contingency for a limited time, which will be posted here for the applicable period. Use will be at the discretion of each UK Blood Service.

Guidance notes for use when implementing components for contingency use

This guidance has been produced in order to provide Blood Establishments with a checklist of items to be considered before implementing components for contingency use, or reactivation of components after they have been archived.

The findings may then inform any further validation work that is required prior to activation of a component.

Guidance

Before implementing or reactivating a component, the following should be considered:

- Any changes that individual Blood Establishments have since made to the way blood or blood components have been collected, including by whole blood or component donation. This must include blood bag material/plasticiser and anticoagulant etc.
- Any changes that individual Blood Establishments have since made to their manufacturing processes, as these may impact on component quality
- A review of any new scientific or clinical data in the context of the specification
- A review of the original validation data and output report, including any caveats or stipulations around use or application
- A review of the specification to ensure that the content remains current and accurate (this might also include a comparison with a similar or relevant component in Chapter 7)
- A review of any other, or new, specific clinical indications for use
- Approval from JPAC for use of the component in the context of the relevant situation (i.e. subject to a case by case review).

A5.1: Red Cells in Additive Solution, Leucocyte Depleted, Extended Shelf Life

A red cell component containing less than 1×10^6 leucocytes and suspended in an approved additive solution.

A5.1.1: Technical information

- A red cell component prepared by removing a proportion of the plasma from leucocyte-depleted whole blood and suspending in an approved additive solution. Leucodepletion may be carried out on either the whole blood starting material or on the final component.
- Red Cells in Additive Solution, Leucocyte Depleted, Extended Shelf Life should be «administered through a CE/UKCA/UKNI marked transfusion set.» ~~*transfused through a 170–200 µm filter.*~~
- May be produced by remanufacture of Red Cells for Exchange Transfusion, Leucocyte Depleted (section «7.7.3» ~~*7.24*~~) up to 6 days after donation.

A5.1.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Red Cells in Additive Solution, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number*
- the ABO group*
- the RhD group stated as positive or negative*
- the name, composition and volume of the additive solution
- the date of collection
- the expiry date*
- the temperature of storage
- the blood pack lot number.*

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A5.1.3: Storage

For general guidelines, see section 6.7.

- The component may be stored for a maximum of 42 days at a core temperature of 4 ±2°C.
- Variation from the core temperature of 4 ±2°C of the finished component must be kept to a minimum during storage at all stages of the blood supply chain and restricted to any short period necessary for examining, labelling or issuing the component.
- Exceptionally, i.e. due to equipment failure at a Blood Centre or hospital, for temperature excursions where the core temperature has not exceeded 10°C or fallen below 1°C, components may be released for transfusion provided that:
    - the component has been exposed to such a temperature change on one occasion only
    - the duration of the temperature excursion has not exceeded 5 hours
    - a documented system is available in each Blood Centre or hospital to cover such eventualities
    - adequate records of the incident are compiled and retained.

A5.1.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.1.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table A5.1 shall meet the specified values.

Table A5.1 Red Cells in Additive Solution, Leucocyte Depleted, Extended Shelf Life – additional tests

Parameter	Frequency of test	Specification
Volume «1»	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	280 ±60 mL ~~2~~
Haemoglobin content «2»		≥40 g/unit ~~3~~
Haemolysis	As per section «7.1.3» ~~7.2~~	<0.8% of red cell mass
Leucocyte count «3»~~1~~	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
«1»~~2~~. Units measured and found to be >375 mL should not be issued for transfusion		
«2»~~3~~. Units measured and found to have <30 g/unit should not be issued for transfusion		
«3»~~1~~. Methods validated for counting low numbers of leucocytes must be used		

A5.1.5: Transportation

For general guidelines, see section 6.11.

For red cell components, transit containers, packing materials and procedures should have been validated to ensure the component surface temperature can be maintained between 2°C and 10°C during transportation. Additionally:

- the validation exercise should be repeated periodically
- if melting ice is used, it should not come into direct contact with the components
- dead air space in packaging containers should be minimised
- as far as is practicable, transit containers should be equilibrated to their storage temperature prior to filling with components
- for transportation between blood supplier and hospital an upper limit of 10°C surface temperature is acceptable but should be limited to one occasion, not exceeding 12 hours

In some instances, it is necessary to issue red cell components from the blood supplier to hospitals that have not been cooled to their storage temperature prior to placing in the transit container. The transport temperature specified above is not applicable for such consignments.

A5.1.6: Removal from and return to 2-6°C controlled storage within hospitals

For occasions when red cells are removed from 2-6°C controlled storage (e.g. when issued to a clinical area immediately prior to transfusion) and returned then:

- If possible, time out of a controlled temperature environment should be restricted to under 30 minutes
- if 30 minutes is exceeded the unit should not be returned to the issue location in the refrigerator, but returned to the transfusion laboratory or quarantined remotely using electronic blood tracking
- up to 60 minutes out of controlled temperature is acceptable, provided the unit is then quarantined by placing in a secure refrigerator for at least 6 hours prior to reissue, to allow the unit to return to 2-6°C
- Hospitals will need to identify such units so that they are not subject to being out of controlled temperature storage for between 30 and 60 minutes on more than three occasions.

Transfusion should be completed within 4 hours of issue out of a controlled temperature environment.

A5.2: Platelets, Apheresis, Leucocyte Depleted, at Reduced Dose as a Contingency

A single-donor platelet component containing less than 1×10^6 leucocytes.

A5.2.1: Technical information

- Platelets, Apheresis, Leucocyte Depleted, at Reduced Dose as a Contingency may be collected by a variety of apheresis systems using different protocols. Since platelet yields may vary, each procedural protocol must be fully validated, documented and specifications set accordingly.
- If a double or triple dose is collected the platelet concentrate must be temporarily split, as a continuous part of the collection process, into the storage packs integral to the collection set so that the capacity of an individual pack is not exceeded.
- If filtration is used the recommended capacity of the filter should not be exceeded.
- The volume of suspension medium must be sufficient to maintain the pH at ≥6.4 at the end of the shelf life of the component.
- If the leucodepletion process transfers the final component into a pack that was not part of the original pack assembly, a secure system must be in place to ensure the correct identification number is put on the final component pack.
- The plasma from group O donors should be tested for high-titre anti-A and anti-B, and 'high-titre negative' units labelled. The testing method and acceptable limits should be defined (see also Chapter 9). Screening of female donors for HLA/HNA antibodies should be considered as a TRALI risk reduction strategy.
- Platelets, Apheresis, Leucocyte Depleted, at Reduced Dose as a Contingency should be administered through a «CE/UKCA/UKNI» ~~CE~~ marked transfusion set.

A5.2.2: Labelling

For general guidelines, see section 6.6.

The following shall be included on the label:

(* = in eye-readable and UKBTS approved barcode format)

- Platelets, Apheresis, Leucocyte Depleted* and volume
- the blood component producer's name*
- the donation number and, if divided, sub-batch number*
- the ABO group*
- the RhD group stated as positive or negative*
- the expiry date*
- the temperature of storage and a comment that continuous gentle agitation throughout storage is recommended
- the blood pack lot number*
- the name, composition and volume of the anticoagulant or additive solution.

In addition, the following statements should be made:

INSTRUCTION
Always check patient/component compatibility/identity
Inspect pack and contents for signs of deterioration or damage
Risk of adverse reaction/infection, including vCJD

A5.2.3: Storage

For general guidelines, see section 6.7.

- The storage period depends on a number of factors including the nature of the container, the concentration of platelets and whether an open or closed system is used.
- Packs currently in use for this purpose allow for storage at a core temperature of 22 ±2°C with continuous gentle agitation for up to 5 days in a closed system. Appropriate pack and platelet concentration combinations may allow

storage up to 7 days, but due to concerns over bacterial contamination requires either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.

- Where any manufacturing step involves an open system the platelets should be used as soon as possible after collection. If storage is unavoidable, the component should be stored at a core temperature of 22 ±2°C with continuous agitation and used within 6 hours.
- Platelets should be gently agitated during storage. If agitation is interrupted, for example due to equipment failure or prolonged transportation, the components are suitable for use, retaining the same shelf life, provided that no single interruption lasts for more than eight hours, and the total length of all interruptions is no longer than 24 hours.

A5.2.4: Testing

In addition to the mandatory and other tests required for blood donations described in Chapter 9, and leucocyte counting (see sections 6.3 and «7.7.1» ~~7.1~~), a minimum of 75% of those components tested for the parameters shown in Table A5.2 shall meet the specified values.

Table A5.2 Platelets, Apheresis, Leucocyte Depleted, at Reduced Dose as a Contingency – additional tests

Parameter	Frequency of test	Specification
Volume [1]	1% or as determined by statistical process control (if ≤10 components produced per month then test every available component)	Within locally defined nominal volume range
Platelet count [2]		≥150 × 10^9/unit
pH at end of shelf life [3]		≥6.4
Leucocyte count [4]	As per sections 6.3 and «7.1.1» ~~7.1~~	<1 × 10^6/unit
1. Units measured and found to be outside of the range 100 to 380 mL should not be issued for transfusion		
2. Units measured and found to have <120 × 10^9/unit or more than the maximum recommended by the manufacturer of the storage pack, where stated, should not be issued for transfusion		
3. A minimum of 95% of components tested shall meet the specified value		
4. Methods validated for counting low numbers of leucocytes must be used		

Note: Visual inspection of platelet components for the swirling phenomenon, clumping, excessive red cell contamination and abnormal volume is a useful pre-issue check.

A5.2.5: Transportation

For general guidelines, see section 6.11.

- Containers for transporting platelets should be equilibrated at room temperature before use. During transportation the temperature of platelets must be kept as close as possible to the recommended storage temperature and, on receipt, unless intended for immediate therapeutic use, the component should be transferred to storage at a core temperature of 22 ±2°C with continuous gentle agitation.
- Plastic overwraps should be removed prior to storage.