Guidelines for the Blood Transfusion Services

7.1: Introduction

http://www.transfusionguidelines.org/red-book/chapter-7/7-1

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:

- **7.2: Whole Blood Components**
- **7.3: Red Cell Components**
- **7.4: Platelet Components**
- **7.5: Plasma Components**
- **7.6: Granulocyte Components**
- **7.7: Components suitable for use in Intrauterine Transfusion, Neonates and Infants under 1 year**

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**

Introduction contents

7.1.1: 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], 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: 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) Guidelines on the Use of Irradiated Blood Components.[2]

- 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: Description

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

7.1.2.2: 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 (±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 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: Labelling

- Irradiated components must be identified by the applied labelling and include any reduction in shelf life.

- Labels which are sensitive to irradiation and undergo a visual change are available and are considered a useful indicator of exposure to irradiation. The dose at which the label changes to indicate irradiated status 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: Storage

For general guidelines, see section 6.7.

- Red cell components, other than washed red cells and those for intrauterine transfusion, exchange transfusion, or largevolume 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 5 days after irradiation if irradiated on the day of washing, or 48 hours if irradiated after the day of washing.

7.1.3: 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) achieve the specifications.

Allowing for losses due to material retained in the associated tubing, 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: 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) 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: 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.