

Guidelines for the Blood Transfusion Services

6.4: Component processing

<http://www.transfusionguidelines.org/red-book/chapter-6/6-4>

6.4: Component processing

6.4.1: Premises

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

- the ambient temperature of blood component processing areas should be maintained within a range that would not be expected to adversely affect component viability/shelf life
- where appropriate, steps should be taken to ensure that air quality in the blood component processing environment does not increase the bioburden to which blood components are exposed.

6.4.2: The starting material

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

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

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

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

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

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

6.4.3: Prevention of microbial contamination

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

- Creating and maintaining the highest level of awareness among all personnel of the constant care and attention to detail needed to minimise microbial contamination, e.g. validation of the effectiveness of venepuncture site preparation and re-validation of process change.
- Using validated procedures designed to minimise microbial contamination of the environment and prevent microbial contamination of components.
- Diverting the first part of the donation into a sample pouch, to avoid entry into the primary donation. This may be used for mandatory screening tests.
- Monitoring the microbial load in equipment and in the environment of component preparation areas. Assessing the contamination rate in outdated components may provide additional, indirect evidence of processing cleanliness.

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

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

6.4.4: Closed system

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

6.4.4.1: Venting

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

6.4.4.2: Sealing

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

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

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

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

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

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

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

Pressure or tensile testing the strength of welds should be performed during the validation or qualification of equipment.^{4,5}

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

6.4.4.3: Pre-donation sampling

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

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

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

6.4.5: Open system

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

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

Blood components prepared by an open system should be used as soon as possible. If storage is unavoidable, components with a recommended storage temperature of $22 \pm 2^{\circ}\text{C}$ should be used within 6 hours. Components with a recommended storage temperature of $4 \pm 2^{\circ}\text{C}$ 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.