Guidelines for the Blood Transfusion Services

8.8: Further guidance on the evaluation of blood packs and apheresis collection systems containing new plasticisers and additive solutions, where they are combined

http://aws-lon-jpac.targetservers.uk/red-book/chapter-8-evaluation-of-novel-blood-components-production-processes-and-blood-packs-generic-protocols/8-8-further-guidance-on-the-evaluation-of-blood-packs-and-apheresis-collection-systems-containing-new-plasticisers-and-additive-solutions-where-they-are-combined

8.8: Further guidance on the evaluation of blood packs and apheresis collection systems containing new plasticisers and additive solutions, where they are combined

8.8.1 Basic information about the Blood pack / Additive solution

The manufacturer must provide the following information for review:

- Instruction for use
- Information on composition and relative weights/volumes of the plastic / plasticiser of the bag and additive solution
- The minimum and maximum volume of whole blood or component that can be stored in the bag
- The shelf-life and storage conditions of incoming goods
- Evidence that the blood bag / additive solution or combination is CE/UKCA marked as a Medical Device
- Quantification of leaching of plasticisers into blood components. Manufacturers may work with Blood Services on these studies
- Studies on toxicology should be supplied by the manufacturer or be available from peer-reviewed scientific journal and should support the safety for use as a medical device. Where the toxicology data has been supplied by a manufacturer, there must be evidence of independent review by relevant external bodies with toxicology expertise.

8.8.2 Phase 0: Evaluation

This phase covers the initial assessment. Transfusion services may work alongside manufacturers to complete developmental work.

- Control data from routinely used blood bags should be included within the study
- The minimum number of units tested should be 16
- Due to the fact that plastics/plasticisers are under investigation, pool and split study designs may not be possible and where possible whole systems should be evaluated. Intermediate bags, tubing and needle assemblies will themselves contain plasticisers that could leach into components and thereby influence results; this must be taken into account during study design. Advice from SACBC should be sought where required.

The following information should be recorded:

- Whole blood collection or Apheresis
- Conditions of overnight hold (if applicable)

- Collection volumes
- Mix of ABO groups (for plasma studies)
- Gender mix of donors
- Additive solutions used.

Data should be provided as close as possible to provide starting levels, mid-point and end of storage shelf-life measures being assessed. Plasma components should be sampled prior to freezing to allow assessment of the percentage recovery of coagulation factors. Further samples will be taken during storage and/or at the expiry of the component. This allows assessment of the impact of the novel system over the shelf-life of the components.

The phase 0 parameters to be validated are summarised in Tables 8.2, 8.3b and 8.4. The basis for acceptance criteria should be 'no worse than current' available systems, comparing against specifications where available and routine control data and where necessary published data. Advice from SACBC should be sought where required.

- Table 8.2 provides guidance on the specific tests recommended for assessing Red Cell components. For novel plasticisers, the tests specified for novel additive solutions are all relevant, with the additional parameter of '*Recovered plasticiser in supernatant and cells*'.
- Tables 8.3a and 8.3b provides guidance on the specific tests recommended for assessing platelet components. For novel plasticisers, the tests specified for novel additive solutions are all relevant, with the additional parameter of '*Recovered plasticiser in supernatant and cells*'. Plasma content and Plasma:PAS ratio are not required.
- Table 8.4 provides guidance on the specific tests recommended for assessing plasma components. For novel plasticisers, the tests specified for novel filter are all relevant, with the additional parameter of '*Recovered plasticiser in supernatant and cells*'.

For platelet components, there are three possibilities to consider:

- A new plasticiser for the whole blood system
- A new plasticiser for the platelet storage bag
- A new plasticiser for the apheresis collection set.

Where the whole blood system is novel, then the final platelet product derived from whole blood via buffy coat or PRP must be tested to demonstrate that it is similar (or no worse) to current platelet components. Some test parameters, for example '*Recovered plasticiser in supernatant and cells*' may have already been completed under red cell testing and this would not change for platelet storage.

For plasma components, there are three possibilities to consider:

- A new plasticiser for the whole blood system
- A new plasticiser for the plasma storage bag
- A new plasticiser for the apheresis collection set.

Where the whole blood system is novel, then the final plasma product derived from whole blood must be tested to demonstrate that it is similar (or no worse) to current product. Some test parameters, for example '*Recovered plasticiser in supernatant and cells*' may have already been completed under red cell testing and this would not change for plasma storage.

8.8.3 Plasticiser Analysis

Blood bag manufacturers or external laboratories may be required for chemical analysis of plasticisers. The chosen methodology will be specific to the plasticiser under investigation, but likely to be by liquid chromatography-mass spectrometry. It is important to have a validated analytical method for the detection of the plasticiser(s), with high sensitivity for the plasticiser and its major metabolites. Advice can be sought

from manufacturers, SACBC and peer-reviewed literature. It is important to consider metabolites that may also influence product quality and may have toxicological effects. Concentrations in the supernatant (and cellular content for red cells and platelets) should be measured at the beginning, during and at end of storage to assess leaching and potential patient exposure. Consideration must be given to the effects of irradiation on the bag and subsequent leaching potential. Suppliers must undertake toxicology studies as part of CE/UKCA/UKNI marking. Suppliers must provide evidence of an independent review of toxicology data; this data will then be reviewed by SACBC.

8.8.4 Routine Process Evaluation

There is specific guidance on the evaluation required in section 8.7. Only specific points relevant to novel plasticisers are highlighted here:

- Due to the inclusion of a new plasticiser, label adhesion for base label and processing labels (donation number, component type, ABO or full face labels) should be confirmed
- The manufacturer should provide evidence to support the safety of glue and ink from base label migration across the bag as this migration may be affected by new plasticisers
- Collection and Processing teams should assess the pack assembly for general suitability and defects as per routine processes. If the needle assembly and tubing includes novel plasticisers, then special attention should be placed on suitability of use.

During phases 1 and 2, Processing teams should record processing faults, with special emphasis on:

- Breakage rates particularly following freezing, thawing and centrifugation
- Heat seal failures
- Flexibility of tubing and bag material with consideration for apheresis collection systems
- Transparency/opacity of tubing bags- this can affect sensors on automated separators
- Cannula breakage
- Ability to sterile dock: integrity of joint; compatibility with other tubing and docking machine
- Blast freezing and packaging of frozen components compatibility
- Irradiation of components: opacity/transparency; increased fragility.

8.8.5 Clinical Data

During phases 1 and 2, consideration should be given for the collection of clinical data on red cell, platelet and plasma components. This may include measures of haemostatic effect, *in vivo* recovery and survival and corrected count increment following transfusion.

Clinical studies/observations should include human data on transfusion reactions, other safety considerations, and efficacy. Clinical studies comparing blood components from existing and novel blood bag systems are required and advice can be sought from SACBC.

Observational data and post marketing surveillance data including national haemovigilance data must be available or in collection.