

## Joint UKBTS Professional Advisory Committee <sup>(1)</sup> Summary Sheet

1. Paper for the JPAC meeting on:	23 June 2016
2. Date submitted:	07 June 2016
3. Title (including version no.):	Extended Storage of Frozen Red Cells
4. Author(s):	Gina MacLaren, National Frozen Blood Bank
5. Brief summary:	<p>Currently there are red cell units of extremely rare phenotype within the national frozen blood bank that exceed the current maximal shelf-life of 10 years. They are currently issued under concession, but have to be labelled manually as the current label printed by Pulse is for a 10 year shelf-life. The process and audit trail for this is not ideal as units have no electronic audit trail after 10 years and manually labelled units do not appear to the professional standards to which UKBTS usually issue components.</p> <p>Data suggest that the quality of red cells when frozen with the high glycerol method used by the NFFB is acceptable for 30 years.</p> <p>One issue in relation to the use of older units of frozen red cells is improvements in microbiology testing with time. As and when additional testing requirements are introduced the NFBB systems will be updated to warn that this should be considered non-compliant and form part of a concessionary release with authorisation from a medical consultant and QA and full knowledge and acceptance from the hospital's requesting consultant.</p> <p>It is important to note that in the UK, unlike other countries, frozen red cells are only used for the provision of blood of rare phenotypes.</p>
<b>6. Action required by JPAC:</b> (What do you want JPAC to do in response to this paper?) e.g. <ul style="list-style-type: none"> <li>• endorse a specific recommendation</li> <li>• advise where there is a choice of possible actions</li> <li>• advise on priorities within the work plan</li> <li>• provide a steer on policy</li> </ul>	<p>Endorse the recommendation to change the shelf life of 7.8: Red Cells, Thawed and Washed, Leucocyte Depleted from</p> <p>'The storage may be extended to at least 10 years, if the correct storage temperature is guaranteed'</p> <p>To</p> <p>'Storage may be extended to 30 years if the correct storage temperature is guaranteed'</p>
7. Any other relevant information:	

<sup>(1)</sup> Joint United Kingdom Blood Transfusion Services Professional Advisory Committee

## Extended Storage of Frozen Red Cells

### **Request for the extended storage of frozen red cells beyond 10 years to be considered for inclusion within UK Guidelines.**

By Gina MacLaren, on behalf of the NFBB Steering Group.  
May 2015

#### Summary

Frozen red cells are currently processed using the high glycerol method (40% glycerol) and stored between -60°C and -82°C in upright mechanical freezers. They are discarded after 10 years frozen storage. However, BSQR permits storage for up to 30 years, and UK and European Guidelines permit storage for 'at least 10 years'. There is no published evidence to show adverse effect of extended storage and the literature supports the storage of frozen red cells at -80°C beyond 10 years. The NFBB recommends that NHSBT procedures and UK guidelines be updated to permit the storage of frozen red cells for up to 30 years.

#### Background

The National Frozen Blood Bank (NFBB) processes, freezes and stores donations of red cells from donors with very rare phenotypes. The current UK Guidelines (1) and the 17<sup>th</sup> Edition of Council of Europe Guidelines (2) state the following regarding the storage life of frozen red cells,

- *The storage may be extended to at least 10 years, if the correct storage temperature is guaranteed.*

The NHSBT Pulse system gives frozen red cells a shelf life of exactly 10 years from the date bled. Units reaching expiry are discarded and replaced with fresh stock. Occasionally it is not possible, or a very difficult and lengthy process, to replace units reaching 10 year expiry. In these circumstances the unit is reviewed by the NFBB consultant and may be recommended for continued storage via deviation procedures. There are currently 28 donations being kept under deviation. These units are of a type with either no current UK donors, or just 1 current UK donor. These units are labelled and issued manually via concession, with the joint authorisation of an NHSBT consultant and a Responsible Person from Quality Assurance.

The NFBB Steering Group seeks approval from SACBC to update the UK Guidelines to give a clear statement allowing the extended storage of exceedingly rare units for up to 30 years. It is hoped that this may authorise the creation of a Pulse location that could be used to maintain an audit trail for very rare donations that have been approved for extended storage through consideration of evidence and risk assessment by the NFBB consultant.

#### Justification

The wording of both UK and Council of Europe Guidelines indicate that 10 years is the minimum acceptable storage period, implying that storage beyond 10 years is already a reasonable option if storage temperatures are guaranteed.

The AABB Technical Manual (3) states that frozen red cells will expire after 10 years, however it goes on to state the following,

- *Rare frozen units may be used beyond the expiration date, but only after medical review and approval that are based on the patient's needs and the availability of other rare compatible units.*

An extended expiry would allow us to manage very rare units beyond 10 years, with a clear audit trail and labelling of the final product prior to issue.

For the purpose of this request a very rare unit is defined as a donation of frozen red cells that is of a phenotype with 3 or less known UK donors.

### Literature Search

Below are 6 references with the findings paraphrased.

- I) Commission Directive 2004/33/EC, Annex IV page L91/35

Storage of frozen red cells is acceptable up to 30 years, according to processes used for collection, processing and storage.

- II) The Blood Safety and Quality Regulations 2005, Schedule Part 4, 1.2 Cryopreservation page 28

Storage duration for cryopreserved red cells is up to 30 years according to processes used for collection, processing and storage

- III) Transfusion, 2004; 44:1306-1313

AABB permit development of an institutional policy for exceptionally rare frozen units beyond 10 years. RBCs can be stored at -80°C beyond 10 years with acceptable in-vitro quality.

- IV) Vox Sang, 2000; 79:168-174

Thawed red cells that have been stored beyond 10 years are acceptable for transfusion. The only issue is retrospective mandatory testing.

- V) Transfusion, 2004; 44(7), 990-995

Units stored at -80°C for up to 14 years had acceptable in-vitro quality.

- VI) Vox Sanguinis, 2000; 79(3), 168-174

Red cells frozen with 40% W/V glycerol can be stored at -80°C for up to 37 years with acceptable in vitro results.

- VII) Immunohematology, 2009; 25(1), 13-17

France regularly transfuse units frozen for longer than 10 years (118 over 13 year period), with no reported problems that could be related to long-term storage beyond 10 years.

## NHSBT Evidence

In 2013 the NFBB carried out an evaluation of factors affecting the supernatant haemoglobin (SNHb) of reconstituted red cells for therapeutic use (4). Data was analysed in a study examining 559 deglycerolised red blood cell units. One variable studied was the length of frozen storage. The results showed that data were not normally distributed upon initial analysis of SNHb and duration of frozen storage. The Spearman's Rank-Order Correlation test indicated that there was a weak statistically significant positive correlation between the duration of frozen storage and its affect on the SNHb result ( $p < .001$ ).

This result may seem in favour of a 10 year cut-off, however all units are sampled to test the SNHb, with units above 2g/unit being issued on concession (out of hours this procedure needs completing next working day).

To date, three units have been issued post expiry. Data for these units is shown below.

Donation Number	Rarity	Expiry date	Issue date	Hb g/unit	SNHb g/unit
G073 599 344 970 E	Ko	14/12/09	04/04/13	44.7	0.19
G073 501 117 107 7	Ko	16/05/11	04/04/13	42.6	0.2
G074 602 333 900 F	I-	22/10/12	31/03/14	31.5	0.04

The two Ko units were issued for the same patient. In each of the two cases above there was no alternative product available at the time of request.

All units that are held beyond 10 year expiry are managed under deviation (Qpulse reference INC25096) and their continued storage is reviewed at least 12 monthly by the NFBB manager, NFBB consultant and Quality manager. This is recorded at the NFBB Operations Group meetings. If an extension to storage within guidelines and Pulse is put in place, these units will continue to be reviewed at regular intervals by this group.

The NFBB does not have archive samples for units currently stored; therefore retrospective testing will not be possible. Should a new test be introduced then the continued storage of units would be reviewed and risk assessed.

The storage of archive samples is currently being discussed, with a possibility of beginning a program of sample storage going forward.

## Conclusion

NFBB recommends that NHSBT procedures and the UK guidelines be updated to permit the storage of frozen red cells for up to 30 years, in particular for exceedingly rare frozen red cells.

## References

- 1) Guidelines for the Blood Transfusion Services in the United Kingdom, 8<sup>th</sup> Edition, 2013, p82.
- 2) Council of Europe Guide to the preparation, use and quality assurance of blood components, 17<sup>th</sup> Edition, p295.

3) AABB Technical Manual, Chapter 6, Whole Blood Collection and Component Processing at Blood Collection Centers, p208.

4) MacLaren, G., Healy, D., Seeney, F., King, M.J., Procter, S., Nicholson, G., Nightingale, M. (2013). Factors Affecting Residual Haemoglobin Content in Supernatant of Deglycerolised Frozen Red Cells for Therapeutic Use. *Transfusion Medicine*, 23(2), 33.

I) Commission Directive 2004/33/EC, Annex IV page L91/35.

II) The Blood Safety and Quality Regulations 2005 No. 50 Health and Safety, p28

III) Lecak, J., Scott, K., Young, C., Hannon, J., Acker, J.P. (2004). Evaluation of red blood cells stored at  $-80^{\circ}\text{C}$  in excess of 10 years. *Transfusion*, 44(9), 1306-1313. DOI: 10.1111/j.1537-2995.2004.03271.x.

IV) Vox Sang, 2000; 79:168-174.

V) Valeri, C. R., Srey, R, Tilahun, D., & Ragno, G. (2004). The in vitro quality of red blood cells frozen with 40 percent (wt/vol) glycerol at  $-80^{\circ}\text{C}$  for 14 years, deglycerolized with the Haemonetics ACP 215, and stored at  $4^{\circ}\text{C}$  in additive solution-1 or additive solution-3 for up to 3 weeks. *Transfusion*, 44(7), 990-995.

VI) Valeri, C. R., Ragno G., Pivacek L. E., Cassidy G. P., Srey R., Hansson-Wicher, M., Leavy, M. E. (2000). An Experiment with Glycerol-Frozen Red Blood Cells Stored at  $-80^{\circ}\text{C}$  for up to 37 Years. *Vox Sanguinis*, 79(3), 168-174.