NHS
Blood and Transplant

Platelets:
what storage deviations are acceptable?

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BBTS Spotlight on Platelets – 11 November 2015

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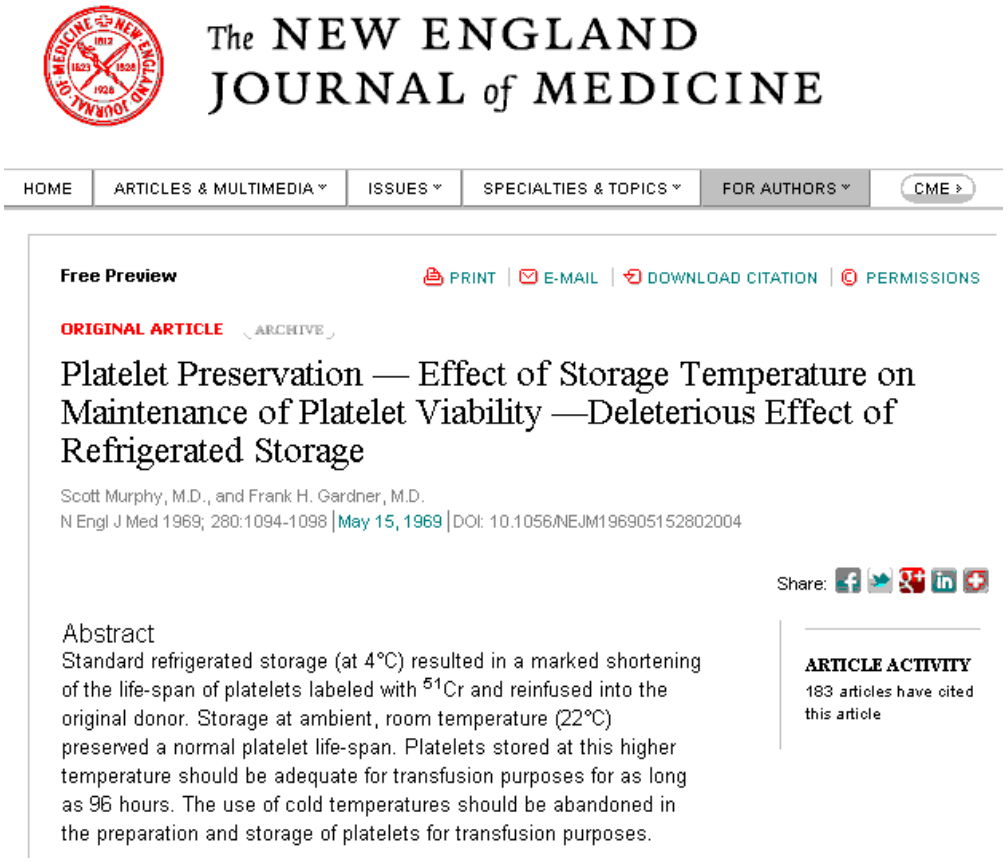
Guidelines

- 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…
- …requires either an assay to exclude bacterial contamination prior to transfusion or application of a licensed pathogen inactivation procedure.

Temperature

- Red Book: storage at a core temperature of 22 ± 2 °C
- Originally based on a paper by Murphy and Gardner NEJM 1969
- Platelets made by newer methods and stored in improved packs will be similarly affected by temperature.



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ORIGINAL ARTICLE ARCHIVE

Platelet Preservation — Effect of Storage Temperature on Maintenance of Platelet Viability —Deleterious Effect of Refrigerated Storage

Scott Murphy, M.D., and Frank H. Gardner, M.D.

N Engl J Med 1969; 280:1094-1098 | May 15, 1969 | DOI: 10.1056/NEJM196905152802004

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Abstract

Standard refrigerated storage (at 4°C) resulted in a marked shortening of the life-span of platelets labeled with ^{51}Cr and reinfused into the original donor. Storage at ambient, room temperature (22°C) preserved a normal platelet life-span. Platelets stored at this higher temperature should be adequate for transfusion purposes for as long as 96 hours. The use of cold temperatures should be abandoned in the preparation and storage of platelets for transfusion purposes.

ARTICLE ACTIVITY

183 articles have cited this article

In vivo assessment

- Count increments or haemostatic efficacy
- Recovery and survival of radio-labelled platelets in volunteers
  - FDA requirement for stored platelets to have at least:
    67 % of the recovery, and
    50% of the survival of fresh platelets.

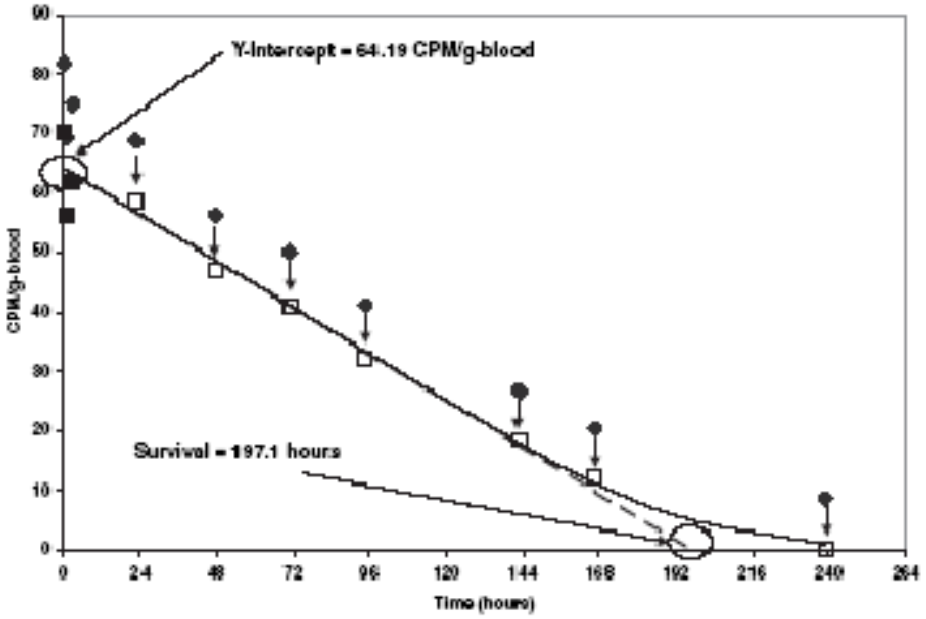


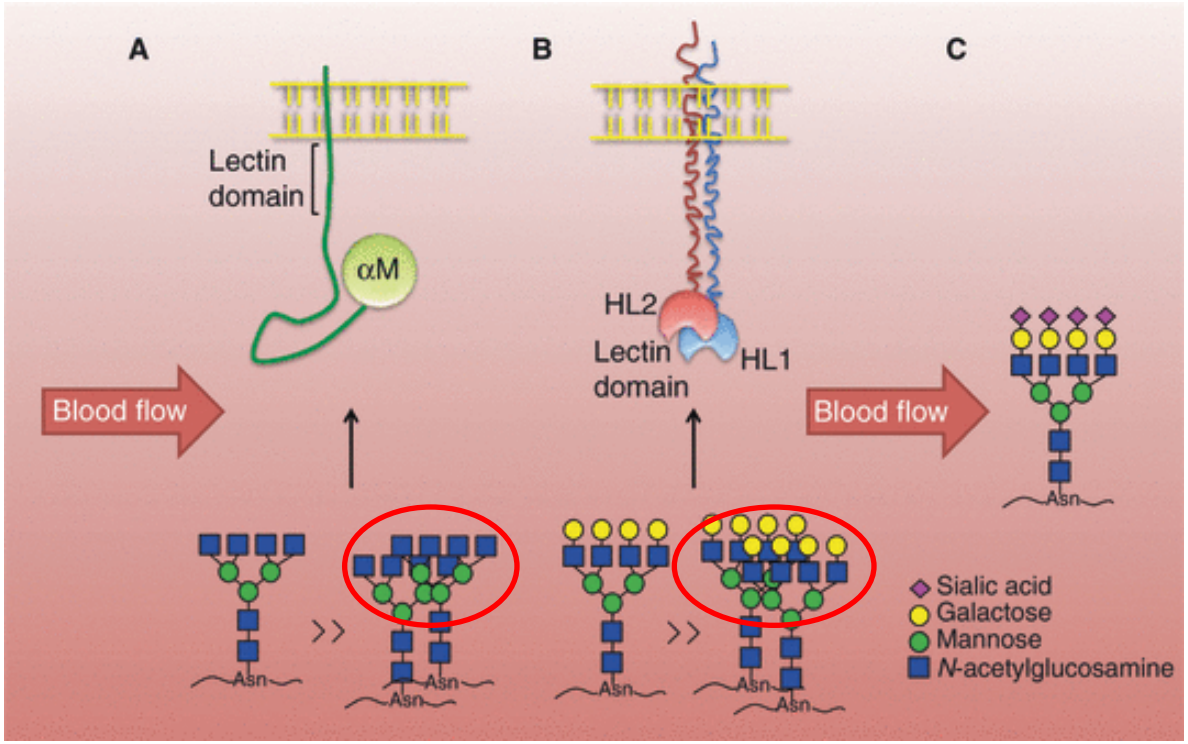
Fig. 2. Unadjusted counts from a subject (◆) are plotted versus time in hours. Full adjustment for cell-bound fraction and baseline is indicated by downward arrows and plotted as squares. (■) Points less than 24 hours were omitted from multiple-hit regression. The regression curve (COST solution) is plotted as solid line. The tangent to the fitted curve at Time 0 is plotted as a dashed line. Survival is indicated as the *x*-intercept of the tangent line (197.1 hr). Recovery is 64.19 CPM per g divided by the expected count at Time 0 for this subject, 114.7 CPM per g (adjusted for elution), or 56.0 percent.

Slichter 2006

Key reports

- Gottschall *et al* Transfusion 1986
  - –72 hours storage at: 21 19.5 18 °C
  - –little effect on recovery: 47 47 48 %
  - –survival reduced: 8.1 5.2 1.9 days
- Moroff *et al* Transfusion 1994
  - –paired controls at 20 – 24 °C
  - –stored to 5d
  - –17 hours storage at: 22 16 12 °C
  - –effect on recovery: 49 43 38 %
  - –survival reduced: 6.5 3.5 2.0 days
- Why / how?

The role of lectins and glycans in platelet clearance



(A) Acutely chilled platelets have clustered GPIbα subunits bearing glycans with *N*-acetylglucosamine terminal structures, which engage with the αM lectin domain of the β2 integrin to initiate phagocytosis by liver macrophages.
(B) Prolonged refrigeration increases GPIbα clustering and exposure of galactose terminal glycan structures, which bind to the hepatic AMR initiating removal of long-term-refrigerated platelets from circulation.
(C) Platelets with sialylated glycan structures continue to circulate.

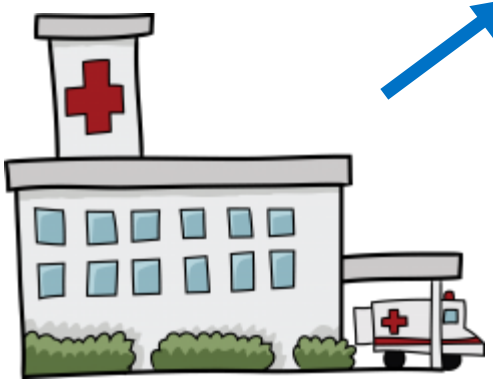
Karin Hoffmeister
Journal of Thrombosis and Haemostasis
pages 35-43, 22 JUL 2011 DOI: 10.1111/j.1538-7836.2011.04276.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1538-7836.2011.04276.x/full#f2

Conclusions on temperature

- NB There is no proposal to alter the recommended storage limits
- Conservative conclusions from the literature
  - if immediate *in vivo* recovery is the main concern:
  - deviations for up to 12 hours
  - between 18 °C and 30 °C may still yield an acceptable therapeutic product.
- Therefore, in the case of unplanned deviations, perhaps…
  - Platelets that are exposed for a cumulative period of 12 hours between 18 and 24 °C could be issued
  - Above 24 °C there is likely to be an increased risk of bacterial contamination - consider screening.
- Interestingly, function is well preserved in the cold…

Ref: Chris Prowse and Sheila MacLennan for SACBC

Post collection handling



Post-collection conditions

- Moroff *et al* (Transfusion 2011) post-collection storage without agitation
  - 4 x 10^{11} platelets
  - unagitated and tightly packed in a shipping container for eight hours after collection
  - and 24 hour interruption of agitation on Day 2

T0 → 8h → 16h → 24h → Day 3 to Day 7





pH v Recovery

- *In vivo* recovery data versus pH suggests that pH below 6.2 correlates with poor *in vivo* recovery and survival.
- Compiled by Dumont and Vandenbroeke, Transfusion 2003

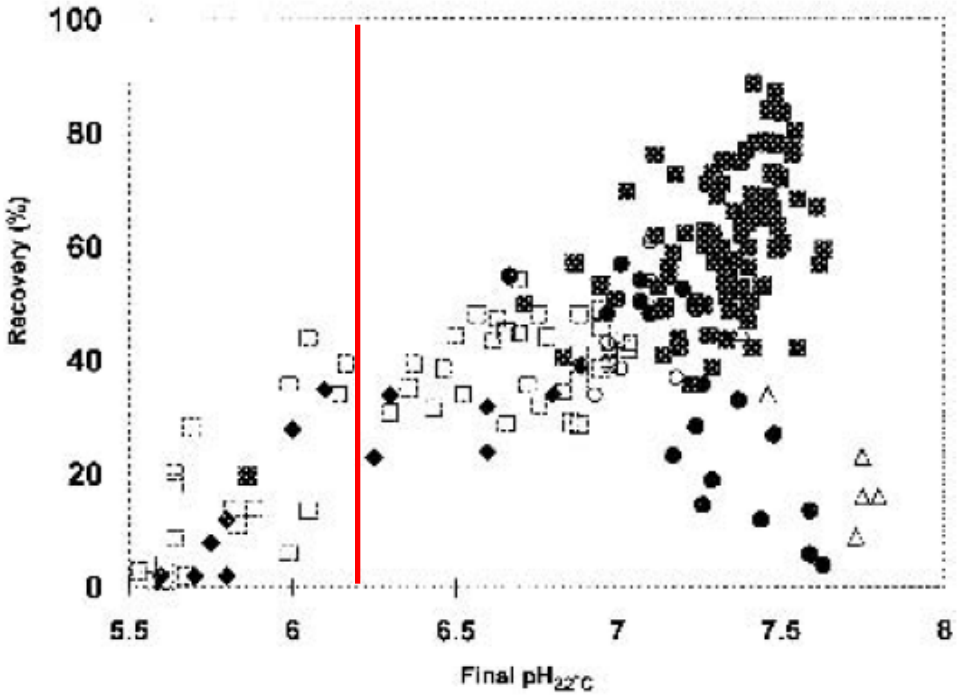


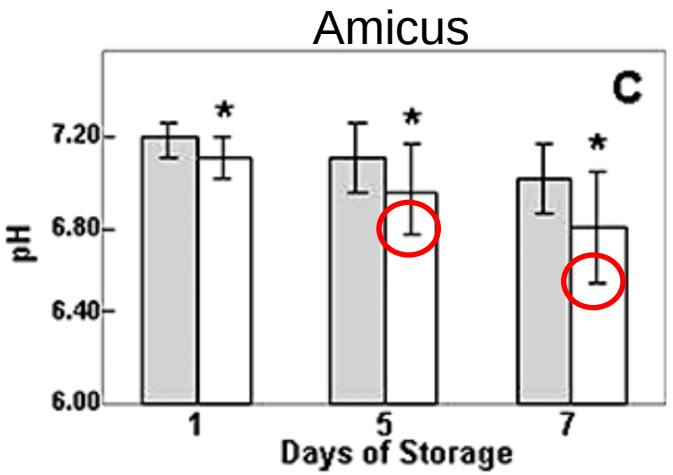
Fig. 3. In vivo recovery related to platelet pH. In vivo recoveries of platelet transfusions are shown for several studies as a function of the pH of the platelet component on the day of transfusion. Transfusions were performed from Day 3

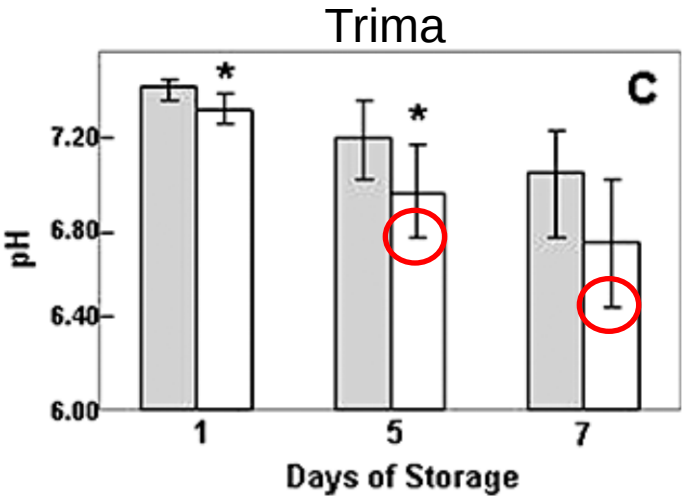
What affects pH?

- Active metabolism of platelets at room temperature
- Aerobic metabolism uses acetate, via the citric acid cycle to generate ATP
- Anaerobic metabolism uses glucose and glycolysis generates lactate
- So low pH is a symptom of lack of oxygen, exhaustion of fuel, and stressed metabolism of platelets
- Low pH possibly implicated in loss of sialic acid…

Results

- By Day 5 the unagitated units from Amicus and Trima collections had minimum pH of 6.58 and 6.75 respectively, compared with 6.78 / 6.83 with continuous agitation
- Continued decline in pH to Day 7, with increasing differences between agitated and unagitated platelets,
  - lower error bars (mean – 1 sd) appear to approach 6.4 for unagitated platelets collected with either machine.





Shipping of finished components

Paper	Machine	Platelet content	Day and length of interruption	Finding
Wagner 2008a	Amicus & Trima Plasma	4 x 10^{11} /unit	24 or 30 hours on Day 2	

Shipping of finished components - PAS

Paper	Machine	Platelet content	Study length	Day and length of interruption	Finding
Moroff 2012	Amicus 65% PASIII	4 x 10^{11}/unit	5d	Multiple scenarios	Platelets in plasma cope better (pH, HSR, ESC) than those in 65% PASIII (phosphate, no bicarb).
Hirayama 2012	Trima 100% Msol	Not stated	7d	24h interruption on Days 1 – 2.	pH remains >7 Msol contains bicarb but no phosphate

Conclusions on agitation

- After a 24 hour interruption of agitation, plasma platelet quality remains within acceptable limits by Day 5, but *in vitro* markers show significant and irreversible changes in some units by Day 7.
- Three periods of eight hours interruption appear to cause less damage than one period of 24 hours.
  - the impact of the reduced gas exchange is lower during short interruptions and these are therefore better tolerated.
  - With a platelet shelf life of seven days, it is particularly important to limit damage and thus the maximum length of each individual interruption of agitation.
- Platelets in additive solution may be able to withstand a 24 hour interruption of agitation and storage for 7 days, but:
  - it seems to be important that the additive solution contains bicarbonate or phosphate to regulate the pH
  - this is *in vitro* data only, and an artificially high pH may not guarantee *in vivo* efficacy.

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Bag capacity

- Is it a problem?

- Dumont and VandenBroeke; Transfusion 2003;43:143-153
- 24 apheresis PC prepared
- range of volumes and platelet concentrations
- *in vitro* study over seven days


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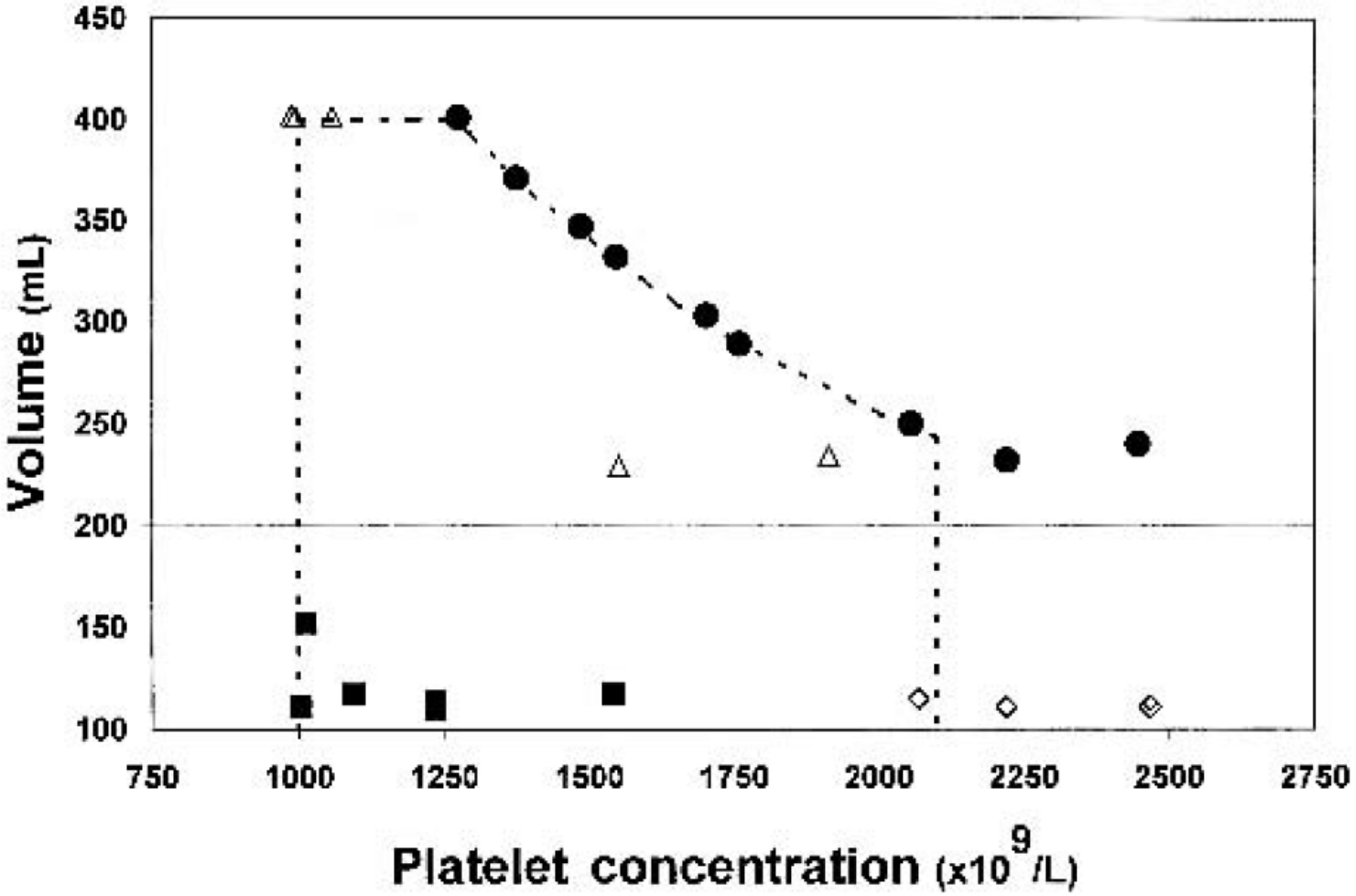


– Acceptable platelet quality was maintained ≤ 5.1 x 10^{11} platelets per bag.

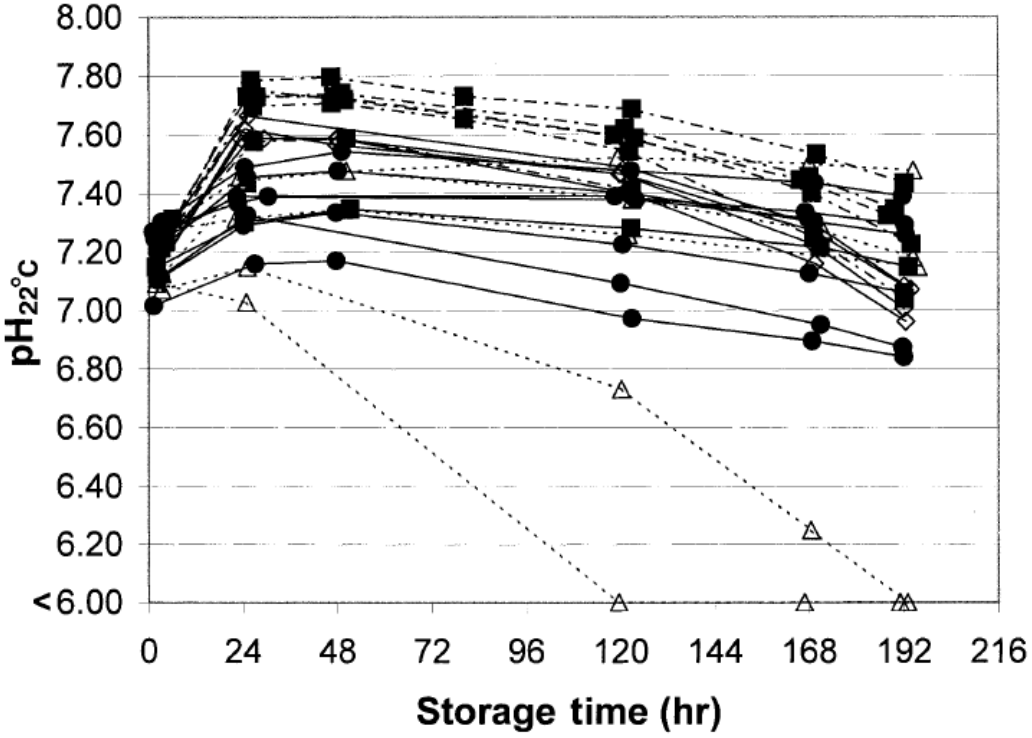
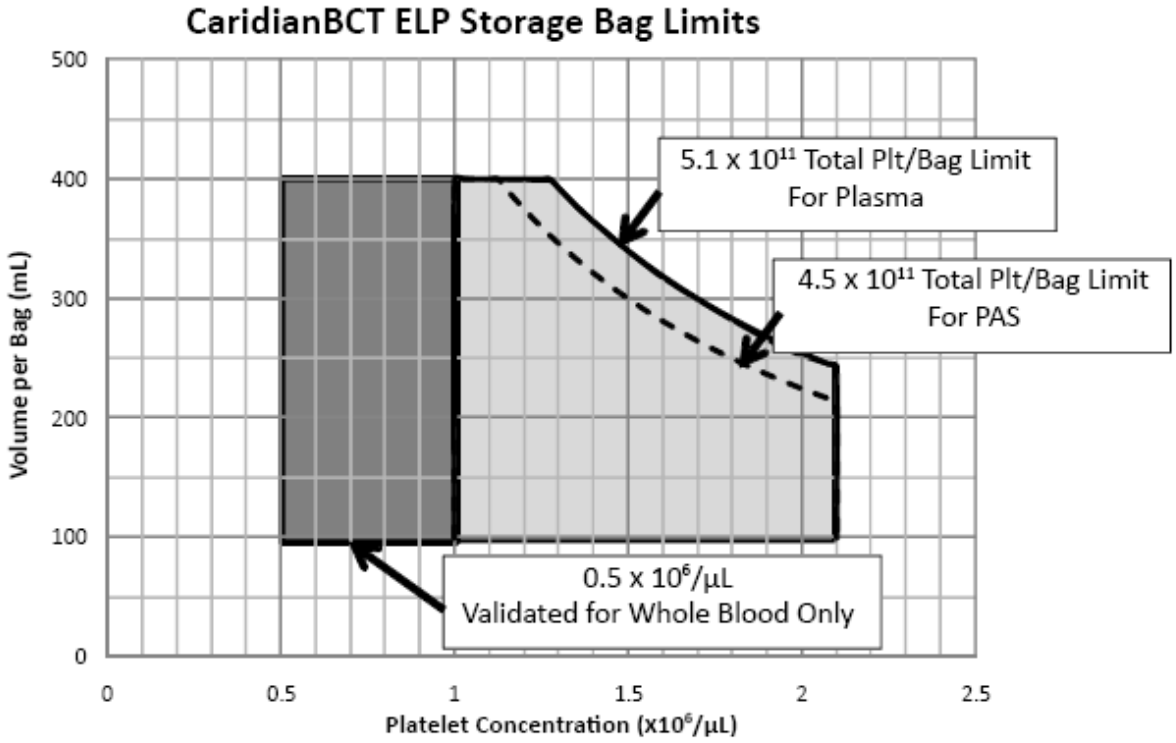


Fig. 2. Platelet component $pH_{22°C}$ over the storage period. $pH_{22°C}$ is shown for all bags in this study. See the legend to Fig. 1 for symbol definition. One component in Group 3 had a precipitous drop between Day 1 and Day 5 for unknown reasons. All others maintained a $pH_{22°C}$ value of greater than 6.2 through 7 days.

CaridianBCT Recommendations for ELP Storage Bag (continued)



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Northern Ireland Blood Transfusion Service

Scottish National Blood Transfusion Service

Welsh Blood Service

Date of publication: 09 September 2015	**Implementation:** To be determined by each Service

Change Notification UK National Blood Services No. 18 - 2015

Interruptions to agitation and testing of Platelets, Pooled, Buffy Coat Derived, Leucocyte Depleted and Platelets, Apheresis, Leucocyte Depleted

Applies to the Guidelines for the Blood Transfusion Services in the United Kingdom – 8th Edition 2013

The current guidance in relation to interruption of agitation has been changed to indicate that no single interruption may last for more than eight hours. The minimum percentage of components that must meet the specified value of 6.4-7.4 for pH at end of shelf-life has been increased to 95% and a requirement to temporarily split double or triple apheresis donations at the point of collection has been added to the specification for Platelets, Apheresis, Leucocyte Depleted.