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Vox Sanguinis

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Response to Zimmermann *et al*

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Dear Editor,

We appreciate the opportunity to respond to Zimmermann *et al*. They refer to publications by Vamvakas [1] and Heuft *et al*. [2]. Both base their conclusion on mathematical models. Vamvakas presents calculations for additional transfusion transmitted infections (TTI) contracted through platelet transfusions in the United States (US) if pooled platelet concentrate (PPC) would completely replace single-donor apheresis platelet concentrates (APC)[1]. These calculations are based on assumptions which do not all apply for Europe. The calculation is based on the risk of TTI in the US today (1 per 2 135 000 donations for HIV, 1 per 1 935 000 for HCV and 1 per 280 000 for HBV [1]). For the German Red Cross Blood Donor Services, the residual risk for TTI is substantially lower (data 1997–2005): 1 per 4 300 000 donations for HIV, 1 per 10 880 000 for HCV and 1 per 360 000 for HBV [3]. This analysis does not account the effect of anti-HBc testing, which became mandatory in Germany since 2006 and will most likely reduce the risk for HBV.

The 'worst-case scenario' of Vamvakas who carefully confines the conclusions to the United States assumes that a PPC contains platelets from six whole blood (WB) donations [1]. In many European countries, PPC is pooled from five or four donations. The risk calculation is substantially different if assuming six or four donor exposures per PPC [1]. A significant proportion of APC represents split products so that an infected donor can infect two or even three recipients by one donation and in addition further recipients by subsequent donations during the 'window period' because of the potentially short interval of APC donations [4].

A model on GBV-C virus infections takes into account that pooling of a GBV-C RNA positive buffy coat (BC) with a BC containing a GBV-C neutralizing antibody could lead to a non-infectious PPC. A careful sensitivity analysis demonstrates that the number of theoretical GBV-C transmissions depends on the assumed frequency of neutralizing antibodies in the donor population [2]. Many assumptions affect the results of mathematical models and delimit their conclusions [4].

Zimmermann *et al*. argue that the preparation of PPC affects the quality of red blood cell concentrates (RCC) resulting 'in a remarkable proportion of underfilled RCC'. The binding German Haemotherapy Guidelines [5] and the 'Guide to the preparation, use and quality assurance of blood components' [6] stipulate that at least 95% of the leucocyte-depleted RCC must contain ≥ 40g haemoglobin/unit. The mean haemoglobin of RCC produced by our Blood Service using RCC filtration after BC-removal is 56·4 g, and only 0·2% of RCC had haemoglobin content below 40 g/unit, and there is no difference when comparing haemoglobin content in RCC produced from donations without or with concomitant preparation of a PPC. For our Blood Service, we can decline that preparation of PPC by the BC method results in a remarkable proportion of underfilled RCC – and this applies also to other blood services obliged to meet regulatory requirements.

Zimmermann *et al*. refer to the loss of 2,3-DPG during overnight storage at 22°C [7]. Several aspects need to be considered in interpretation of this surrogate parameter: Rapid cooling slowed the loss of 2,3-DPG levels but 2,3-DPG levels were undetectable by day 21 irrespective of the initial storage temperature [7]. Wilsher *et al*. [7] compared processing within 8h versus storage for 24 h at 22°C. In practice, the actual interval between donation and start of processing in most institutions is shorter than 24 h even if overnight storage at 22°C is involved. It has been shown that 2,3-DPG levels return to near normal levels after transfusion [8]. The clinical significance of the observed difference needs to be studied further. Overnight storage at 22°C can increase the efficiency of separation of platelets from WB donations and can reduce bacterial contamination.

Zimmermann *et al*. argue that the processing method affects the levels of platelet-derived cytokines in RCC [9]. It is important to take into account all details of the processing. A high concentration of platelet-derived cytokines was measured in PC prepared with the dock-in Sepacell RBC filter or with platelet-saving WB filters before removing plasma or platelet-rich plasma. In this study, the plasma-reduced RCC (still containing platelets) were held overnight at 4°C. Neither a storage at 4°C nor a storage overnight *after* removal of plasma nor the use of platelet-saving WB filters can be considered as standard procedure for PPC

preparation by the BC method. Also, we need more information on the clinical significance of platelet-derived cytokines in RCC.

Last, but not least, we must respect donor safety. The frequency of adverse events of WB donation as well as apheresis donation is low but not completely negligible. Plateletpheresis implies additional recruitment of donors, additional risk and additional cost if there is no compelling medical reason not to use the available platelets from WB donations [4].

Zimmermann *et al*. conclude that 'PPC should be replaced by APC'. However, there is a bunch of data demonstrating equivalence of PPC and APC in terms of quality, safety and clinical efficacy in non-allosensitized patients [4]. Considering the available evidence, we refuse reasoning that one product type should 'replace' the other one. In contrast to this view, which does not take into account all aspects, and in particular neglects the donor's point of view we re-emphasize that both product types should be available. This controversy fulfills an important purpose if more thoughtfulness also about the donor's perspective is induced. New developments, e.g. pathogen inactivation, necessitate reassessment of the comparison.

References

1 Vamvakas EC: Relative safety of pooled whole blood-derived versus single-donor (apheresis) platelets in the United States: a systematic review of disparate risks. *Transfusion* 2009; **49**(12): 2743–2758

2 Heuft HG, Mende W, Blasczyk R: A general change of the platelet transfusion policy from apheresis platelet concentrates to pooled platelet concentrates is associated with a sharp increase in donor exposure and infection rates. *Transfus Med Hemother* 2008; **35**:106–113

3 Hourfar MK, Jork C, Schottstedt V *et al.*: Experience of German Red Cross blood donor services with nucleic acid testing: results of screening more than 30 million blood donations for human immunodeficiency virus-1, hepatitis C virus, and hepatitis B virus. *Transfusion* 2008; **48**(8):1558–1566

4 Schrezenmeier H, Seifried E: Buffy-coat-derived pooled platelet concentrates and apheresis platelet concentrates: which product type should be preferred? *Vox Sang* 2010; **99**:1–15

5 Wissenschaftlicher Beirat der Bundesärztekammer: Richtlinien zur Gewinnung von Blut und Blutbestandteilen und zur Anwendung von Blutprodukten (Hämotherapie); Köln, Deutscher Ärzteverlag, 2007

6 Council of Europe: Council of Europe Guide to the Preparation, Use and Quality Assurance of Blood Components, 15th edn. Council of Europe Publishing, Strasbourg, France, 2009

7 Wilsher C, Garwood M, Sutherland J *et al.*: The effect of storing whole blood at 22 degrees C for up to 24 hours with and without rapid cooling on the quality of red cell concentrates and fresh-frozen plasma. *Transfusion* 2008; **48**(11):2338–2347

8 Beutler E, Wood L: The in vivo regeneration of red cell 2,3 diphosphoglyceric acid (DPG) after transfusion of stored blood. *J Lab Clin Med* 1969; **74**(2):300–304

9 Glenister KM, Sparrow RL: Level of platelet-derived cytokines in leukoreduced red blood cells is influenced by the processing method and type of leukoreduction filter. *Transfusion* 2010; **50**(1):185–189

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