EDQM Blood Conference

INNOVATION IN BLOOD ESTABLISHMENT PROCESSES

Abstract book

Strasbourg, France
14 - 15 January 2025

edqm
European Directorate for the Quality of Medicines & HealthCare | Direction européenne de la qualité du médicament & soins de santé

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EDQM Blood Conference
Innovation in Blood Establishment Processes

14-15 January 2025
Strasbourg, France

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European Directorate for the Quality of Medicines & Healthcare (EDQM) of the Council of Europe

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Preface

Foreword by the EDQM

The Council of Europe is the oldest and largest European international organisation, with a total of 46 member states. In the blood sector, the key principles guiding the Council of Europe's activities are the protection of blood donors and recipients, the promotion of voluntary, non-remunerated blood donation and mutual assistance among member states, as well as the optimal use of blood and blood components.

The European Directorate for the Quality of Medicines & HealthCare (EDQM), which is part of the Council of Europe, has been putting these principles into practice since 2007, under its mandate as a leading developer of internationally recognised guidelines and a provider of practical support to Blood Establishments (BEs) to improve and protect public health.

A fundamental contribution to the blood transfusion field is the EDQM's "Guide to the preparation, use and quality assurance of blood components", or "Blood Guide". This comprehensive and regularly updated guide provides technical standards that collate the latest scientific data and advances in the blood field. In addition, it addresses important ethical questions to be considered for the donation of blood and blood components to assist professionals.

In addition, the EDQM has been running two programmes to support BEs in their day-to-day work, namely the Blood Proficiency Testing Scheme (B-PTS) since 2010 and the Blood Quality Management programme (B-QM) since 2012. These programmes provide external quality assessment schemes to BE laboratories as well as on-site and virtual training and assessment schemes. Since 2013, these activities have been complemented by conferences and regular training courses for European BEs, to promote peer-exchange and cohesion in the fast-changing blood transfusion field.

As part of this programme, and with the financial support of the European Commission, we are very excited to announce the new EDQM Blood Conference to be held at the Council of Europe's Palais de l'Europe building in Strasbourg, France, on 14 and 15 January 2025. The conference will focus on "Innovation in Blood Establishment Processes – New developments in blood donation and blood component preparation in Europe" and will address the question "How can they be implemented in practice?". It will provide an invaluable opportunity for professionals in the field to discuss new challenges and to prepare for the upcoming implementation of the new Substances of Human Origin (SoHO) European Union legislation. We look forward to bringing together experts from Europe and beyond to share their in-depth knowledge, discuss practical questions from scientific, technical, and quality management points of view, and to expand their networks to strengthen the community.

In this spirit, we hope to welcome you to the beautiful city of Strasbourg soon!

Laurent Mallet
Head of Department, EDQM

Foreword by the European Commission / DG SANTE

As the European Commission's department responsible for European Union policy on health and for monitoring the implementation of related laws, the Directorate-General SANTE (DG SANTE) has the mission to make Europe a healthier and safer place. DG SANTE's goals are achieved through monitoring, listening to concerns, and then taking appropriate action. With regards to the specific theme of the Blood Conference, a key political concern is patient access to a continuous supply of safe and high-quality blood, plasma and derived therapies. European Union policy makers have therefore included specific provisions to allow actors and stakeholders to take necessary actions to ensure and improve this supply. During this conference, DG SANTE will give a presentation of these key provisions. We look forward to your attendance during this opportunity to meet other key actors in the field.

Conference programme and speakers

EDQM Blood Conference programme
Tuesday 14 January 2025

8.00 – 9.00 Registration

9.00 – 9.15 Welcome address

9.15 – 10.15 Session A1: Challenges for blood supply, donor recruitment & retention (part 1)

Room 1

Hans Vrielink: Challenges for the blood supply in Europe

Betina Samuelsen Sørensen: Donor vigilance and challenges for blood supply

10.15 – 10.45 Coffee break

10.45 – 12.15

Session A1: Challenges for blood supply, donor recruitment & retention (part 2)

Room 1

Nigar Ertuğrul Örüç: Recruitment and retention of blood donors

Rodica Popa: Mapping of AI initiatives and challenges in Europe

Norbert Niklas: Adding virtual badges to the incentive strategy of blood donation

Session B2: Risk-based approach for implementing process changes

Room 2

Simonetta Pupella: Toward a common approach to authorization of a novel blood component: GAPP-PRO experience

Dinara Samarkanova: Expanding the use of cord blood units for manufacturing platelet derived products: assessment of clinical-grade products from small units or after expiration time

Marco Amato: Stepwise process change implementation of a buffy coat pooling protocol to increase yields

Anita Siller: Using a hematology analyzer to count residual cells in blood components instead of flow cytometry

12.15 – 13.30 Lunch break (Restaurant Bleu)

13.30 – 15.00

Session B1: Innovative & novel blood components (part 1)

Room 1

Peter O'Leary: Dried plasma: current considerations in Europe

Stephen Vardy & Mike Wiltshire: Establishing spray dried plasma as a blood component in the UK - regulatory and scientific aspects

Melanie Robbins: Developing universal plasma and platelets - what challenges do we need to consider?

Luciana Teofili: Fetal haemoglobin-enriched red blood cell concentrates: an "investigational blood product" for preterm neonate transfusion

Session A2: Blood collection & apheresis

Room 2

Johanna Castrén: Blood collection and apheresis

Jan Hartmann: Hypothesis-generating analysis of active donors using a new personalized nomogram for source plasma collection

Torunn Apelseth: Emergency collection of whole blood in preparedness – an implementation guide and report from the Norwegian Civilian Walking Blood Bank Project

15.00 – 15.30 Coffee break

15.30 – 17.00 Session B1: Innovative & novel blood components (part 2)

Room 1

Torunn Apelseth: Implementation of a whole blood program for treatment of patients with massive haemorrhage – a practical guideline for blood providers

Thibaut Bocquet: Implementation and feedback of a new method for cryopreserved platelets with post-thaw minimal processing: the French experience

Beatrice Hechler: Cold-storage of amotosalen-UVA pathogen-reduced buffy-coat platelet concentrates for up to 21 days: biochemical and functional characterization, and identification of emerging platelet subpopulations

Jens Altrichter: Prolonged storage of purified granulocyte concentrates from pooled buffy coats

17.00 – 18.30 Welcome reception (Restaurant Bleu)

EDQM Blood Conference programme
Wednesday 15 January 2025

8.30 – 10.00 — **Session A3**: Donor protection

Room 1

Hans Van Remoortel: How would we decide on a good plasmapheresis frequency? Results and recommendations from the SUPPLY project

Katja van den Hurk: Whole blood donor iron management across Europe - experiences and challenges in four blood establishments

Joanne Pink: Minimising iron loss in plateletpheresis is an important component of Lifeblood's donor iron health strategy

Amber Meulenbeld: Change in hemoglobin to identify a novel threshold for iron deficiency - a study in blood donor populations

10.00 – 10.30 — Coffee break

10.30 – 12.00 — **Session A4**: Recipient protection & blood safety

Room 1

Johannes Blümel: Development of high throughput sequencing for detection of viruses in blood

Jenny Mohseni Skoglund: Risk factors for carrying *Trypanosoma cruzi* infection in non-endemic countries: a systematic review

Sandra Kurth: Assessment of travel related donor eligibility in Switzerland using the online digital tool "Travelcheck"

Susan Galel: Is antibody testing enough to protect the blood supply from transfusion-transmitted malaria?

Jeffrey Linnen: Highly sensitive nucleic acid test for detection of *Plasmodium* RNA: a potential tool to increase blood safety and availability

Session B3: Novel component development & clinical outcome monitoring

Room 2

Vanessa Agostini: Hypoxic red blood cells: an innovative blood product

Richard Benjamin: Transfusion efficacy of amustaline/glutathione pathogen-reduced red blood cells: results of a randomized, controlled clinical trial

Xavier Delabranche: Free amotosalen does not induce non-specific degranulation of basophils from healthy volunteers *in-vitro*

12.00 – 13.30 — Lunch break (Foyer)

13.30 – 15.00

Workshop: Development of innovative blood components and their authorisation/ implementation

Room 1

Linda Larsson, Ryan Evans & Simonetta Pupella

Workshop: Blood Quality Management

Room 2

Stephen Vardy & Ína Björg Hjálmarsdóttir

Workshop: Discussion regarding deferrals based on haemoglobin/ferritin levels

Room 3

Mart Janssen, Katja van den Hurk & Amber Meulenbeld

15.00 – 15.30 — Coffee break

15.30 – 17.00 — **EDQM session**: Blood Guide and blood transfusion programmes

Room 1

Interactive discussion and Q&A

The EDQM Blood Conference will feature oral presentations and practical workshops presented by 36 international experts working in the field:

- **Vanessa Agostini**, San Martino Hospital, Italy
- **Jens Altrichter**, ARTCLINE GmbH, Germany
- **Marco Amato**, Tirol Kliniken, Central Institute for Blood Transfusion and Immunology, Austria
- **Torunn Oveland Apelseth**, Department of Immunology and Transfusion Medicine, Haukeland University Hospital & Faculty of Medicine, University of Bergen, Norway
- **Richard Benjamin**, Cerus Corporation, USA
- **Ína Björg Hjálmarsdóttir**, The Blood Bank, Landspitali University Hospital, Iceland
- **Johannes Blümel**, Paul Ehrlich Institute, Germany
- **Thibaut Bocquet**, Établissement Français du Sang, France
- **Johanna Castrén**, Finnish Red Cross Blood Service, Finland
- **Xavier Delabranche**, University of Strasbourg, Établissement Français du Sang & Department of Anesthesia and Intensive Care, Strasbourg University Hospital, France
- **Nigar Ertuğrul Örüç**, Blood Transfusion Center, University of Health Sciences Diskapı Yildirim Beyazit Training and Research Hospital, Türkiye
- **Ryan Evans**, Scottish National Blood Transfusion Service (SNBTS), Scotland
- **Susan Galel**, Roche Diagnostic Solutions, USA
- **Jan Hartmann**, Haemonetics Corporation, USA
- **Beatrice Hechler**, University of Strasbourg, Établissement Français du Sang, France
- **Mart Janssen**, Sanquin Blood Supply Foundation, the Netherlands
- **Sandra Kurth**, Swiss Transfusion SRC, Switzerland
- **Linda Larsson**, National Board of Health and Welfare, Sweden
- **Jeffrey Linnen**, Grifols Diagnostic Solutions, USA
- **Amber Meulenbeld**, Donor Health, Sanquin Research & Amsterdam UMC, Dept of Public and Occupational Health, the Netherlands
- **Jenny Mohseni Skoglund**, European Centre for Disease Prevention and Control, Sweden
- **Norbert Niklas**, Red Cross Transfusion Service for Upper Austria, Austria
- **Peter O'Leary**, European Blood Alliance, Belgium
- **Joanne Pink**, Australian Red Cross Lifeblood, Australia
- **Rodica Popa**, European Blood Alliance, Belgium
- **Simonetta Pupella**, Italian National Blood Centre, Italy
- **Melanie Robbins**, NHS Blood and Transplant, England
- **Dinara Samarkanova**, Banc de Sang i Teixits & Transfusional medicine study group, Vall d'Hebron Research Institute, Spain
- **Anita Siller**, Tirol Kliniken, Central Institute for Blood Transfusion and Immunology, Austria
- **Betina Samuelsen Sørensen**, Aalborg University Hospital Department of Clinical Immunology, Denmark
- **Luciana Teofili**, Fondazione Policlinico Universitario A. Gemelli IRCCS, Italy
- **Katja van den Hurk**, Donor Health, Sanquin Research & Amsterdam UMC, Dept of Public and Occupational Health & Amsterdam Public Health Research Institute, the Netherlands
- **Hans Van Remoortel**, Belgian Red Cross-Flanders, Belgium
- **Stephen Vardy**, NHS Blood and Transplant, England

Oral presentations – topic A: blood donation

Session A1: Challenges for blood supply, donor recruitment & retention

Challenges for the blood supply in Europe

Hans Vrielink[1], Kaatje le Poole[1]

[1] *Sanquin Blood Supply Foundation, Amsterdam, the Netherlands*

Within Europe, there are ±50 sovereign states, of which 27 are members of the European Union (EU). Besides that, a number of countries are in the process of becoming EU members ("junior" members) or are negotiating to become a junior member of the EU. The EU is a supranational political and economic union with, amongst others, European Commission (EC) directives and recommendations. Directives must be transposed into national laws, generally within 2 years, otherwise the EC may intervene. Recommendations, however, are non-binding.

More than 70 years ago, member states started co-operation in the area of blood transfusion. Activities were, amongst others, inspired by the principles of promotion of voluntary, non-remunerated blood donation (VNRD), mutual assistance, optimal use of blood and blood products and protection of the donor and the recipient. Besides these principles, the European Pharmacopoeia is also important for blood establishments (BEs), since it addresses topics on the collection of whole blood or apheresis-derived donor plasma for the fractionation of plasma-derived medicinal products (PDMPs). In time, the early principles were included in EU directives which are translated into standards and specifications for implementing the quality system in BEs ('Good Practice Guidelines' (GPG)). In principle, the GPG are based on 'Good Manufacturing Practice' (GMP). To reflect the legal status of the GPG standards in the EU, the term 'must' is used in requirements derived from the EU directives. Also, in the collection of source plasma to be used for the production of PDMPs, GMP/GPG are important. BEs need to have GMP accreditation for the delivery of source plasma to the fractionation industry. Otherwise, unused collected plasma needs to be destroyed, and as is well known, Europe has a shortage of plasma.

To achieve an optimal use of blood and blood components (and no unnecessary destruction), including protection of donors and recipients in BEs and hospitals, an extensive quality system is needed. Of course, "the chain is only as strong as its weakest link" is a clincher, but it tells us that quality is the responsibility of all persons involved in the process, and not only a management issue. Quality, however, is not solely dependent on persons working in the field, but also on donor eligibility guidelines, the equipment applied in blood collection and separation, storage, etc. The BE building, but also the "lines" of work in the BE are of importance. To achieve an extensive quality system money is needed, and national authorities should allocate sufficient finances to assure quality in the blood chain. Financial status and political situations differ between European countries, but also between EU member states. Be aware, not all is in the hands of the national authorities. Local geography and climate play an important role in sustainable quality, but also in the optimal use of blood and blood components.

In accordance with World Health Assembly resolution 28.72 from 1975, the World Health Organization's goal is a global blood supply through VNRDs. This altruistic system was adopted by the EU (standard 2.1.1.1). However, despite efforts, in a number of countries or in sparsely populated regions of specific countries, insufficient numbers or even no VNRDs are available. They have to rely on family/replacement blood donors or even on paid donors to cover the blood supply. The discussion on "what is remuneration and what is not" also exists. In the national law of some countries, specific "advantages" for blood donors are listed, and since this is in the law, this is not always seen as payment.

Optimal use of blood components is an important issue in taking care of the gift of the donor. Unneeded destruction of the donated blood/blood components is unethical, but unnecessary transfusion is also a critical issue in the optimal use of blood and blood products. Implementation of patient blood management (PBM) is a valuable start. Training and with that awareness of PBM by hospital physicians prescribing blood and blood transfusion laboratories is needed.

In conclusion, to achieve a safe and reliable blood supply in and outside Europe, many challenging hurdles need to be addressed and resolved. Mutual assistance in bringing knowledge fitting the local challenges, together with co-operation of governmental and non-governmental leaders in countries, is already a step in the right direction to increase the safety of our donors and recipients.

Donor vigilance and challenges for blood supply

Betina Samuelsen Sørensen[1]

[1] *Aalborg University Hospital, Department of Clinical Immunology, Aalborg, Denmark*

Introduction

Looking in the dictionary, vigilance means more careful attention, especially to notice possible danger. In the EU Blood Directive, haemovigilance is defined as "a set of organised surveillance procedures relating to serious adverse or unexpected events or reactions in donors or recipients" (Directive 2002/98/EC). Adverse reactions have an impact on the individual donor and can have an impact on the retention of that individual donor. Donor retention is important to sustain a robust pool of donors and maintain the blood supply. One purpose of donor vigilance is protection of donors by registering and monitoring the adverse reactions in relation to blood donation. Protection of donor health is and will always be important. A sustainable blood supply is also important and should be given careful attention. Should we look more broadly at the meaning of donor vigilance in terms of challenges for blood supply and include indicators other than adverse reactions that can impact donor retention and thereby blood supply?

Study design

The aim of the presentation is not to give answers but to give reflections on the meaning of donor vigilance when looking to the future of the next generation of potential donors and the challenges to blood supply. This presentation is not the result of a study but based on the opinion of the presenter.

Results

The presentation will give an overview of donor vigilance and discuss other indicators to monitor in relation to donor vigilance.

Conclusion

Donor vigilance has until now focused on adverse reactions. Severe adverse reactions related to blood donation are rare. They do have a huge impact on the individual donor and the retention of that donor, but maybe less so on the total blood supply. The scope of donor vigilance could be expanded to include other indicators that can have a potential impact on the blood supply.

Recruitment and retention of blood donors

Nigar Ertuğrul Örüç[1]

[1] *University of Health Sciences Dışkapı Yıldırım Beyazıt Training and Research Hospital, Ankara, Türkiye*

Blood and blood component transfusion might be lifesavers for the patients, not only in emergency situations but also in certain medical treatments. The availability of safe blood is the cornerstone of any health service. Blood safety starts with the donor and volunteerism plays a major role in blood donation. Self-sufficiency in safe and sustainable blood supply provided from voluntary, non-remunerated blood donors (VNRBD) at national level is an essential component of every country's national health care policy and infrastructure. Countries have to obtain their safe and adequate blood supplies through VNRBD in accordance with World Health Assembly resolution 28.72[2].
Blood donation rate varies among countries, ranging from 0.6 to 53.0 per 1000 population. These donations are collected from all types of blood donors: voluntary non-remunerated, family or replacement, and paid. Countries with low blood donation rates are largely dependent on blood provided by replacement or even paid donors. They often do not have structured blood donor programmes and are unable to attract sufficient numbers of donors to meet the need[3].
Based on the 2012 Consensus Declaration of WHO12, there are 12 recommendations that national health authorities need to act on to ensure self-sufficiency of blood supply based on VNRBD[4]. Creating a sustainable system of safe blood donors requires a long-term approach. Development of a regulatory framework, such as national legislation with specific implementation, national policy, strategy and action plan, donor recruitment and retention programme, promotional and educational activities, financial support, and adequate donor database, is an important factor in achieving self-sufficiency in safe blood and blood components based on VNRBD[4,5]. Extra efforts should be put in to develop good recruitment strategies that are socially acceptable to the population concerned. Raising public awareness on the need for blood donation, the importance of voluntary donation and the importance of regular donation is crucial. Effective communication methods, use of media (social and scientific), educating potential donors, youth and social programmes and use of information technology is essential[6]. The younger generation are the most important resource and the ideal target in the blood donation programme. They are healthier and able to donate more regularly if dedicated.
To achieve safer blood, retention of donors is essential, which is not an easy task. They must be motivated as much as possible to become a regular donor. It is important to induct first-time blood donors and enable repeat donors to continue their behaviour for donation. Adequate and qualified staff with good organisation, marketing and communication skills must be appointed to manage blood donation. The first experience of donation plays a big role in donor retention. Positive attitudes are key to creating a safe and relaxed environment, diminishing anxiety and fear during blood collection. Optimal emotional attitudes of the staff towards the donor are the ones which express patience, affection, attention, sympathy and good mood. First-time donors should be followed up with appreciation and reminder messages to stimulate their willingness to donate again. The longer the time that has elapsed from the last donation, the more likely this group of donors will not come back for donation. Invitation or reminder messages can facilitate the donors' return. It is important to give them spiritual satisfaction to retain them in the donor pool and ensure they continue to donate[5,6,7]. Regular donors should be followed up with the same approach to continue their positive feelings about being able to help someone in need with donation.

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[7] Thomas Watkins DO. Recruitment of Blood Donors. Transfusion Medicine, Fifth Edition. Edited by Jeffrey McCullough. John Wiley & Sons Ltd Press 2021, pp. 25-36.

Mapping of AI initiatives and challenges in Europe

Mart Janssen[1], Rodica Popa[2], Mikko Arvas[3], Ólafur Eysteinn Sigurjónsson[4]

[1] *Sanquin Blood Supply Foundation, Amsterdam, the Netherlands*
[2] *European Blood Alliance, Brussels, Belgium*
[3] *Finnish Red Cross Blood Service, Helsinki, Finland*
[4] *Iceland Blood Bank, Landspitali, Reykjavík, Iceland*

Background/Introduction
The application of artificial intelligence (AI) is undergoing rapid development. Applications are being developed in many areas that create new insights and possibilities and achieve great efficiency. However, there are many barriers that prevent the endorsement of this technology in practice. To promote collaboration amongst European Blood Alliance (EBA) members, the EBA initiated a new special interest group on AI in transfusion medicine and blood banking, the "Blood Byte Circle". At the second meeting of this group, it was decided to send out a survey among EBA members to map the current landscape of AI initiatives. The aim of this survey was to not only acquire insight into current AI developments within the EBA community, but also to identify potential areas for collaboration and support among members and inform strategic planning and possible development of EBA-wide AI initiatives.

Methods/Study Design
In March 2024 a survey was sent out to all EBA members containing questions about current and planned AI initiatives, specific areas of application, implementation phases, observed or expected benefits, challenges encountered, and the type of support required.

Results
The survey was conducted among 28 member organisations from 24 countries involved in transfusion medicine and blood banking within EBA member countries. There was a response rate of 75% (21 organisations from 19 countries) indicating the importance of this topic perceived by the members. The survey revealed varied levels of AI engagement: 19% of organisations indicated they have ongoing initiatives, 5% are planning such activities, but most organisations indicated they are considering (52%) AI initiatives. AI is being applied across diverse areas, the most frequently mentioned are related to donor recruitment (31%), demand forecasting (19%) and data analytics (13%). Of the applications reported, 17% are currently in operation, but most initiatives are in the scientific research (42%) or exploration/trial phase (25%).
A significant concern reported was regulatory compliance, where organisations seek guidance on navigating complex laws such as the GDPR and the new European AI Act. One respondent specifically asked for "regulation guidelines," while another suggested that the EBA could advocate a harmonised regulatory approach which may consist of providing a "regulatory toolbox" for members starting with AI.

Conclusions
There is a great diversity in the level of adoption of AI technology among European blood banks. Where some have embraced this new technology and have implanted this in specific operational areas, others are in the phase of considering and/or planning. These differences indicate a high potential for collaboration and sharing technology and experiences. The survey responses indicate a strong desire for a broader collaboration and underline advocacy of efforts to address issues related to data protection, confidentiality and liability.

Adding virtual badges to the incentive strategy of blood donation

Norbert Niklas[1], Christian Mühleder[1], Stephan Federsel[1], Claudia Loimayr[1], Susanne Süßner[1]

[1] *Red Cross Transfusion Service for Upper Austria, Linz, Austria*

Background / Introduction

Multiple strategies exist that keep blood donors motivated beyond pure altruism. Incentives have proven to be most effective, although there is an ongoing discussion whether those shall be monetary or nonmonetary (Graf *et al*. *Transfus Med Rev* 2024;38:150809). Voluntary and unpaid blood donation is a fundamental principle in Austria. We introduced a gamification concept in our blood donor app that awards donors with virtual badges when completing activities associated with blood donation. We analysed the effects on donation behaviour and evaluated the effectiveness of such virtual incentive.

Methods/Study Design

The virtual badges can only be achieved when using our blood donation app. Donors can earn regular badges multiple times: donate twice a year, save paper by exclusively switching to the digital medical report, share blood drive invitations with friends and connect with other donors. Collecting enough regular badges elevates the donor to the next level. Additionally, donors can gain special badges for donating on special dates (e.g. summer or winter holidays, when donation numbers are usually low) or healthy activity.

Our study includes data from 18 months after the introduction of these virtual incentives. We identified three groups of donors: the first uses gamification in an active manner, the second group uses our blood donation app and the third donates in the conventional way without the app. For the first group we only count badges that require a user action.

Results

In the analysed period, there were 85 432 whole blood donations and 9 880 deferrals from 58 826 individual persons at our institute.

11.5 % of these donors collect badges actively, they account for 15 431 donations. On average, there are 144 days between two donations of this group. They donate more regularly than the two other groups (175 app donors, 197 non-app). With an average age of 34.9 years, they are usually younger compared to 38.4 and 44.2; the percentage of first-time donors is higher in both groups that use the app (16.9 % and 18.1 % compared to 12.3 % first-time donors in the group without the app). The most frequently obtained badges were the hero-badge that is awarded for a minimum of two donations per year and the eco-badge for waiving of the postal report.

The group of gamification and app users had similar deferral rates (5.4 % and 7.7 %), whereas users with the conventional paper questionnaire had a higher rate of 22.4 %.

Conclusions

The virtual badges have proven to be a good addition to other incentives (give-aways, award ceremonies) that particularly attract young donors. The proportion of first-time donors and repeat donors is promising for maintaining the donor pool.

Since the digital feature operates autonomously, it is cost-effective and easy to integrate into the workflow. It can motivate donors to engage in blood donation-related activities even between donations. Currently, incentives are not actively promoted at our institute; moderate communication about them might yield additional benefits.

Session A2: Blood collection & apheresis

Blood collection and apheresis

Johanna Castrén[1]

[1] *Finnish Red Cross Blood Service, Helsinki, Finland*

Collecting blood through whole blood donations and apheresis is essential for blood transfusion therapies and in the manufacture of plasma-derived medicinal products. One of the key figures of blood supply is the number of blood donors per population. In Europe this varies significantly, but even at its highest, the proportion of blood donors in the population is less than 5.5%. Regarding the criteria for donation suitability, it is estimated that more than half of the individuals who are of suitable age to donate blood could do so.

The legal framework (big picture) related to blood donation does not depend on whether a person donates whole blood or its components (where the non-essential parts are returned to them). It involves the donation of a substance of human origin (SoHO) material for the treatment of a recipient, and the rights and safety of individuals at both ends of this chain must be safeguarded. Ethically, the rights or safety of individuals at either end of the chain cannot be prioritised over the other. The cornerstones of this balance are voluntary and unpaid donation, comprehensive testing requirements, and the principle that blood donation is not a human right, but patients have the right to receive treatment and the safest possible products.

The focus areas of blood collection, blood products and apheresis activities evolve over time. We have already witnessed several periods and phases: for example, the replacement of whole blood transfusions with component therapies and now the renewed need for whole blood products in modern emergency treatment schemes. It is possible to envision the future by considering two perspectives: the growth of individuality and the benefits of generic approaches. Individuality is represented by new and more precise laboratory tests of the biological characteristics (for example genetic testing) of donors and recipients. Generic approaches, on the other hand, focus on blood supply that is as resilient as possible and meets the most essential transfusion therapy needs even in exceptional circumstances and crises.

The presentation examines trends in blood collection in Europe based on the latest statistics from the Council of Europe's Annual Reports. It reviews current observations related to different types of donations (whole blood donation, plasmapheresis, platelet apheresis and other types of donations) and delves into the current challenges of blood collection and apheresis. Future scenarios are discussed from the perspectives of the "individual and general" approaches.

Hypothesis-generating analysis of active donors using a new personalised nomogram for source plasma collection

Eva Hellmann[1], Jan Hartmann[1], Andrew Sette[2]

[1] *Haemonetics Corporation, Boston, United States*
[2] *Haemonetics S.A., Signy, Switzerland*

Background

Life-sustaining and life-saving plasma-derived medicinal products require human plasma for their manufacture. Four European countries, including Germany, and the US currently provide the majority of the EU's source plasma. A three-tiered weight-based approach sets donation volume limits in Germany, and the US has historically implemented a similar method. Nomograms with further personalisation have been studied. For example, a continuous nomogram personalised to a donor's total plasma volume calculated using height, weight and haematocrit was studied in a randomised, controlled trial (IMPACT trial, NCT04320823) and cleared by US FDA for use in US plasma collection centres. Compared to the US standard nomogram, collection volumes increase for donors with higher total plasma volumes and decrease for those with low volumes. This exploratory research studies the personalised nomogram's hypotensive adverse event (AE) rate and theoretical average volume gain compared to the German nomogram for active US donors and the subgroup with a modelled German donation schedule.

Methods

Real-world plasmapheresis data for active donors using the personalised nomogram at US centres from May 2021-2022 were analysed. Two groups of active donors, defined as those donating at least once per quarter, were reviewed: the full US active group (USG) and the subgroup adhering to a modified German donation schedule (GMG). Compared to Germany, the US allows more donations per year (104 vs. 60) and a shorter gap between donations (twice weekly and one donation-free day between donations vs. two donation-free days between donations). In the absence of Germany-specific data, the GMG subgroup was modelled by identifying donors with a 60-donation maximum and at least two donation-free days between a majority (defined as ≥75%) of donations. For the two groups, the real-world significant hypotensive AE rate (1.2+ according to the International Quality Plasma Program Standard for Recording Donor AEs, as defined in the IMPACT trial) was determined. In addition, the target volumes and percent change for the standard German nomogram compared to the personalised nomogram were calculated.

Results

The active donor dataset contained 455 100 donations by 8 510 donors (USG) and 208 353 donations by 4 649 donors (GMG). The significant hypotensive AE rates using the personalised nomogram were 0.00026 (USG) and 0.00031 (GMG). The average target plasma volume increased from the standard German nomogram to the personalised nomogram for both groups (USG: 759 to 855 ml; GMG: 756 to 845 ml), corresponding to increases of 12.6% (USG) and 11.8% (GMG) (Table 1).

Conclusions

This analysis suggests, based on US data modelled to the German framework of donor plasmapheresis, a personalised nomogram could have a low significant hypotensive AE rate and an average increase in target plasma volume for active donors. As this research was limited to US donations, additional research is required to assess the definitive impacts of a personalised nomogram on the German donor population, considering donor demographics and donation schedules. A similar personalised nomogram may be one option to consider for improving European self-sufficiency of source plasma.

Table 1 Active Donor Results

		USG	GMG
N Donations		455 100	208 353
N Donors		8 510	4 649
Nomogram Target	German	759 +/- 38	756 +/- 41
Plasma Volume	Personalised	855 +/- 109	845 +/- 109
(ml)	% Change	12.6%	11.8%
Sig. Hyp. AE Rate		0.00026	0.00031

Emergency collection of whole blood in preparedness – an implementation guide and report from the Norwegian Civilian Walking Blood Bank Project

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Introduction

A walking blood bank (WBB) is a structured system for emergency collection of whole blood from a preselected donor pool, used in military and civilian settings for treatment of patients with life-threatening bleeding when banked blood is unavailable. Scenarios include 1) long transport times or delayed patient transport as in remote areas, 2) large scale events like disasters or war or 3) reduced availability of blood in hospital caused by destroyed infrastructure, pandemics or impaired resupply.

The Norwegian Center for Blood Preparedness has been working together with the Northern Norway Regional Health Authority to develop a programme for emergency collection of whole blood in smaller rural communities and local hospitals in the northern part of Norway.

In this study, we aimed to evaluate our programme against the new European Regulation for substances of human origin (EU SoHO (https://data.consilium.europa.eu/doc/document/PE-8-2024-REV-1/en/pdf)).

Methods

The Norwegian Civilian Walking Blood Bank programme was evaluated according to the criteria given in EU SoHO Article 65, which states that derogation in authorisations of SoHO preparations can be permitted in health emergency situations provided that the use is: a) in the interest of public health, b) the product has a level of quality and safety that is acceptable and c) the recipients of the product have no therapeutic alternatives, the treatment cannot be postponed and the prognosis is life-threatening so that the expected benefit outweighs the risk.

Results

The programme developed and tested systems needed to establish emergency collection of whole blood in smaller rural communities and local hospitals and included recruitment of emergency donors according to national donor selection criteria, training of personnel, and external review and certification of the system.

Four Civilian WBBs were established during the study period (2021-2024). They have approval and undergo inspections by regulatory authorities as for ordinary blood services in Norway. All are under the supervision of a local blood service, referred to as the "Mother Blood Bank".

Roles and responsibilities are defined and include the municipal health leadership and the medical director of the Mother Blood Bank. Local WBB co-ordinator(s) are responsible for maintenance of the emergency donor pool and training sessions for personnel. Standard operating procedure templates have been developed for all aspects of the programme and adapted locally. These include donor selection criteria, algorithms for activation of WBB, procedures for collection and transfusion, systems for traceability and haemovigilance, educational material and equipment.

The main risk identified is transfusion-transmitted disease (TTD). Mitigation strategies are post-transfusion TTD testing, strict donor selection criteria, regular testing and detailed interviews of donors every 6th month, and donor information.

Emergency collected whole blood is for immediate use for a defined patient population with life-threatening bleeding who have no other therapeutic alternative and where the treatment cannot be postponed. Based on this we find that the expected benefit outweighs the risk.

Conclusions

We conclude that emergency collection and transfusion can be performed in a structured and sustainable way in a civilian WBB, and that it can be done in accordance with the requirements described in the new EU SoHO Article 65.

Table 1 Key numbers: The Norwegian Civilian Walking Blood Bank programme* (**Numbers given per July 2024*)

Civilian Walking Blood Banks established	4
Number of activations	7
Mean time from activation to blood bag ready for transfusion	30 minutes
Personnel completed trained (total)	>60
Emergency whole blood donors included (total)	>100

Information video:

Session A3: Donor protection

How would we decide on a good plasmapheresis frequency? Results and recommendations from the SUPPLY project

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Background & Aim

Most plasma used for manufacturing plasma-derived medicinal products (PDMPs) such as albumin, immunoglobulins (Ig) and clotting factors is obtained from source plasma collected via plasmapheresis, the majority of which is contributed by the United States where donors can donate plasma up to twice per week and up to 100 times per year. SUPPLY is a project co-funded by the European Union that aims to strengthen voluntary non-remunerated plasma collection capacity in Europe, to enable a stable and adequate supply of PDMPs).

The aim of this study was to facilitate evidence-based plasma donor protection practices.

Methods

The following tasks were executed in one of the SUPPLY work packages (WP5):

- Collection of information on current plasma donor protection practices
- Evaluation of the best available evidence of plasmapheresis and donor health by conducting:
  - A scoping review and evidence gap analysis
  - A systematic review to identify, analyse and critically appraise available studies that assessed the impact of plasmapheresis frequency on donor health
- Develop a support tool on standardised donor vigilance data to be collected

Results

Based on 18 complete survey responses from 17 countries:

Annual donation limits vary from 12 donations per year (Luxembourg) to 26 (the Netherlands) to 60 (Germany) to 104 (USA). The minimum donation interval ranged from 2 to 28 days.

Donation procedures (equipment, volume limit, flow rates, citrate-based anticoagulants) varied across organisations.

Hydration advice (12 organisations), trained staff (7 organisations) and special attention to new donors (5 organisations) were the most common preventive measures.

All organisations assessed total proteins (with varying limits).

The scoping review identified 94 research articles and 5 registrations of ongoing studies, of which 90% were observational studies. Different evidence gaps were identified. The systematic review included 4 cohort studies, 1 non-randomised, controlled trial (non-RCT) and 2 RCTs (of which one is ongoing):

The 4 included cohort studies were graded as providing very low-certainty evidence (due to methodological limitations and imprecise results because of limited sample sizes)

The non-RCT showed no statistically significant or clinically meaningful differences in total protein or immunoglobulins (IgG, IgA, IgM) after weekly compared to bi-weekly plasmapheresis during 6 months (low-certainty evidence).

The completed RCT found that very high frequency plasmapheresis (2x/week) may result in a large reduction in ferritin and IgG levels (low-certainty evidence).

Requirements were described for a support tool on standardised vigilance data to be collected (recording and analysing plasma donor protection practices, standardised adverse event classification).

Conclusions – recommendations

- A maximum of two plasma donations per month, pending sufficient evidence confirming the safety of higher donation frequencies. This recommendation is based on expert opinion and reflects the view of most WP5 members.
- IgG levels should be monitored. Evidence of optimal IgG algorithms and test intervals is lacking.
- Urgent initiation of prospective studies to examine the health consequences of plasma donation at varying frequencies.
- Implementation of a register for standardised haemovigilance data on a mandatory basis.

These recommendations are based on the precautionary principle, placing donor safety, first while awaiting further evidence.

Whole blood donor iron management across Europe: experiences and challenges in four blood establishments

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Background
Whole blood donors lose iron while donating and frequent blood donation is therefore known to induce a risk of iron deficiency and/or anaemia. We present, compare and discuss the pros and cons of four distinctive donor iron management strategies in England, Finland, the Netherlands, and Denmark.

Methods
Donor iron management policies in the countries concerned are described for the year 2021, and data on donor and donation numbers, low haemoglobin (Hb) deferral rates and Hb levels are presented.

Results
In England Hb levels were only measured in donors failing a copper sulphate test, while in the other three countries Hb is measured at every donation (Table). In Finland, donors considered at risk of iron deficiency receive iron supplements, while in the Netherlands, ferritin-guided donation intervals without iron supplementation are in place. In Denmark, iron supplementation is provided to donors with low ferritin levels. Hb deferral rates in repeat donors were 10.0%, 2.4%, 3.9% and 4.2% for women and 4.7%, 1.0%, 1.3% and 1.4% for men in England, Finland, the Netherlands and Denmark, respectively. In Finland, the Netherlands and Denmark, mean Hb levels for repeat donors were 8.7, 8.5 and 8.5 mmol/L for women and 9.6, 9.5 and 9.4 mmol/L for men, respectively.

Conclusion
Despite significant diversity in donor iron management approaches, low Hb deferral rates and average Hb levels are similar among the included countries except for England, where higher deferral rates were observed that are likely attributed to the absence of iron supplementation or ferritin-guided deferral. Achieving an optimal, more tailored iron management strategy requires further research and a nuanced understanding of both donor demographics and physiological responses to optimise the effectiveness and safety of blood donation practices.

Table 1 Iron management methods used in 2021

Blood establishment	Hb measurement	Hb measurement timing	Ferritin measurement	Iron supplementation
NHSBT (England)	Capillary Copper sulphate, followed by capillary HemoCue if low	Pre-donation, only if copper sulphate test fails	None	None
FRCBS (Finland)	Capillary CompoLab, followed by venous CompoLab if low/high	Pre-donation, always	None	Iron supplementation for risk groups (females 18-25 yrs and high-frequency donations)
Sanquin (the Netherlands)	Capillary HemoCue	Pre-donation, always	Venous EDTA, post every fifth donation	None (except for RCT)
Central Denmark Region (Denmark)	Venous Sysmex Venous HemoCue	Pre-donation sample analysed post donation (Sysmex) Pre-donation sample analysed before donation if donor was deferred for low Hb at previous donation	Venous EDTA, female first-time donors and in all donors when Hb is low	Ferritin-guided iron supplementation

Minimising iron loss in plateletpheresis is an important component of Lifeblood's donor iron health strategy

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Background and objectives
Lifeblood has recently introduced ferritin testing in whole blood donors and are exploring options to retain donors identified with non-anaemic iron deficiency. Because apheresis returns most of the red cells, our policy allows these donors to continue apheresis whilst they have a period of deferral from whole blood. Conversely, we may invite apheresis donors to contribute to the whole blood pool as a strategy to offset losses associated with deferrals for iron deficiency. Our inline red cell losses for plasma and platelet apheresis are equivalent to approximately 8 mL and 75 mL of whole blood, respectively. Our plateletpheresis procedure does not include a plasma rinseback. We collect platelets almost exclusively from males and have a 2-week minimum donation interval. Our iron health strategy together with the recent literature that has highlighted the plasma rinseback process as a strategy to mitigate frequent plateletpheresis-associated lymphopenia has prompted Lifeblood to review donation patterns and iron status in platelet donors. Whilst Lifeblood does not perform routine ferritin screening of platelet donors, ferritin testing is performed if abnormalities in the full blood count (taken with every donation) are suggestive of iron deficiency, or there is a greater than 20 g/L drop in haemoglobin from their previous donation.

Materials and Methods
Donation data were extracted for all plateletpheresis donors who donated in 2023 and 2023/2024 financial year. Donation patterns were evaluated both within the platelet panel and across panels. Ferritin results from 2018 were analysed for donors with the 100 highest cumulative lifetime donations. Inline red cell loss was compared with and without rinseback.

Results
There were 26 369 plateletpheresis donations in the 2023/24 financial year from 8 069 unique donors. Mean donation frequency was 3.27, but 71% of donors only donated 1-3 times. Donors donating more than 13 times a year only made up 2.8% of platelet donors yet contributed 14% of all donations. There was significant cross over of the platelet panel with whole blood, with approximately 10-20% of the panel donating 9-19 platelets a year also donating whole blood. Of the top 100 donors who donated in 2023, 69 had one or more ferritin tests ordered by Lifeblood since 2018. The period prevalence of iron deficiency (ferritin <30 µg/L) in this highly motivated cohort was 53/69, 77%. The supplier of our plateletpheresis platform notes that the current 30 mL red cell (inline) loss can be reduced to 10 mL if plasma rinseback is instituted. With a haematocrit of 0.4, this reduces the current 75 mL of whole blood equivalent to 25 mL with rinseback, equating to a reduction in iron loss from approximately 37.5 mg to 12.5 mg. This calculation does not include losses from routine blood samples. The inline red cell loss alone associated with 20 platelet donations is the equivalent of 3 whole blood donations per year but would reduce to one if plasma rinseback was implemented.

Discussion/Conclusion
Plateletpheresis without plasma rinseback is associated with a significant iron loss compared to plasmapheresis and resulted in a very high detected prevalence of iron deficiency in frequent plasmapheresis donors. Rinseback may provide considerable benefits to the health and retention of a wide cohort of donors. Australia has undertaken to trial plasma rinseback, a process which has been successfully implemented in other countries. Limiting the number of whole blood donations in platelet donors may also be considered.

Change in haemoglobin to identify a novel threshold for iron deficiency: a study in blood donor populations

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Background & Aims
As whole blood donors are at risk of iron deficiency and anaemia, blood establishments use a haemoglobin (Hb) test to confirm a donor's eligibility for donation. However, Hb monitoring alone does not necessarily prevent donors from developing iron deficiency. An increasing number of blood establishments have therefore started to monitor serum ferritin in addition to Hb levels, to detect low iron stores in blood donors. According to WHO guidelines, healthy individuals with ferritin levels below 15 ng/mL are considered iron deficient, without clear evidence to support this threshold.
We aimed to define a functional threshold for ferritin based on a quantitative estimation of the association between change in Hb from baseline and ferritin levels in whole blood donors.
Methods
We used data from the Netherlands (Sanquin), the UK (INTERVAL), South Africa (SANBS), Finland (FinDonor) and the US (Vitalant). We selected donors for whom a baseline Hb was available (aiming to identify Hb levels not affected by prior donation). We then selected donations at which both serum ferritin and Hb were measured and analysed the association between log base 10 (log10) ferritin levels and the change in Hb from baseline (dHb). Where appropriate, we defined a two-segmented line with differing slopes and used maximum likelihood estimation to fit these and determine a changepoint. We generated confidence intervals by taking 1000 bootstrap samples for subsets containing either male or female donors.
Results
We observed a distinct change in the linear association between the dHb and log10 ferritin levels across all countries. Lower log10 ferritin levels were associated with larger declines in Hb levels, while above a specific log10 ferritin level donors on average recover to their pre-donation Hb level. Similar patterns were observed in the donor populations in each of the five countries, but the estimated ferritin threshold differs per country and donor subgroup (Table 1).
Discussion and Conclusion
The change observed in the association between log10 ferritin and dHb suggests that in healthy blood donors there is a specific ferritin level below which iron storage levels limit Hb production. Although this association is similar across settings, the ferritin threshold level is not. This discrepancy might result from differences in donor populations but is more likely due to the lack of a validated, commutable international reference material for ferritin. This underlines the need for the development and implementation of such a reference material to enable establishing uniform ferritin thresholds and allow the comparison of ferritin outcomes in different populations. The results indicate that ferritin levels may also be controlled by limiting the drop in Hb relative to the donor's baseline Hb level. Given the high (biological) variability in both ferritin and Hb, these biomarker values may potentially be combined to provide a more accurate predictor for the iron status of a donor.

Table 1 Estimated ferritin threshold per country and population subgroup.

Study population	Ferritin changepoint in ng/mL (95% CI)		
	Men	Premenopausal women	Postmenopausal women
The Netherlands	30.7 (30.1-31.7)	26.3 (24.4-27.5)	24.2 (23.1-25.3)
United Kingdom	41.2 (39.0-45.7)	34.4 (30.1-40.4)	27.0 (25.0-35.9)
South Africa	21.6 (20.7-22.7)	19.3 (18.1-20.2)	18.6 (17.1-20.3)
Finland	24.9 (22.4-33.1)	17.0 (14.1-45.0)	36.9 (30.0-68.1)
United States	29.6 (28.5-30.7)	25.1 (22.4-27.5)	30.6 (28.5-33.3)

Session A4: Recipient protection & blood safety

Development of high-throughput sequencing for detection of viruses in blood

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Introduction

Surveillance and early detection of viral pathogens causing human diseases are fundamental to reducing risk for transmission via substances of human origin used in medicine. Metagenomic next-generation sequencing (mNGS or HTS) is a promising technology for the detection of unknown or unexpected emerging viruses. Nevertheless, it is still expensive and requires careful standardisation, because each step of the workflow could introduce bias on the breadth of detection and impact sensitivity. We compared the breadth of detection and sensitivity of an adapted VirCapSeq-VERT system (a capture system) and a conventional non-targeted mNGS approach. We used seven well-characterised viruses, representing the different structures and genomes of viruses (WHO International Reference Panel for Adventitious Virus Detection in Biological Products by HTS).

Material and Methods

We spiked the WHO virus panel in serial dilutions from 10^6 to 10^1 GE/ml into plasma matrix and into a matrix containing Ad5 10^9 GE/ml. Plasma samples were analysed by the non-targeted and capture mNGS systems. The Ad5 samples were analysed only by the capture system. Sequencing workflow followed the standard steps: reverse transcription, nick translation based second strand synthesis step, fragmentation/end-repair, adaptor ligation, barcoding and amplification. Additionally, the capture workflow included different denaturation temperatures, and pooling of samples for hybridisation/capture with VirCapSeq-VERT probes followed by an additional amplification step.

Results

All viruses in the plasma background were detected by both systems. With the non-targeted system, we were able to detect all of them at 10^5 GE/ml and some up to 10^3 GE/ml, with the capture system we detected all of them at 10^3 GE/ml and some up to 10^1 GE/ml. In Ad5 background, all viruses were detected at 10^3 GE/ml and 5/7 viruses at 10^1GE/ml.

Conclusion

The use of a broad-spectrum capture system like VirCapSeq-VERT allows an increase of sensitivity between 100-1000-fold and reduces the cost of sequencing compared to traditional agnostic mNGS. These advantages could allow a wider use of this technology in the interest of public health, including surveillance of the blood donor population.

Risk factors for carrying *Trypanosoma cruzi* infection in non-endemic countries: a systematic review

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Background
Chagas disease (CD), caused by *Trypanosoma cruzi*, is endemic in Latin America, but is increasingly relevant in non-endemic areas due to migration and non-vector transmission routes. This systematic review aimed to identify factors associated with the carriage of *T. cruzi* infection in non-endemic countries to support the individual assessment of eligibility for donors of substances of human origin.

Methods
A comprehensive search of Medline and EMBASE (January 2000-June 2022) was conducted. Observational studies on characteristics (or risk factors) associated with *T. cruzi* infection in non-endemic countries were included. Two reviewers independently screened the studies and extracted the data. Risk of bias was assessed using JBI tools. Due to heterogeneity in estimates of associations between risk factors and *T. cruzi* infection, a vote-counting synthesis based on direction of effect was performed.

Results
Of 23 961 articles screened, 79 studies were included, with 51 in the final synthesis. Key characteristics consistently associated with *T. cruzi* infection were: 1) being born in an endemic country (19 studies), particularly Bolivia (16 studies); stay in an endemic country (1 study); history of living in rural areas (13 studies) or poor housing conditions (12 studies); contact with the vector (7 studies); history of blood transfusion in endemic countries (9 studies); being older age (15 studies); having a family history of CD (13 studies) or having prior knowledge of CD (8 studies); being female (17 studies). There was limited published evidence on the association of *T. cruzi* infection and maternal origin from endemic countries (1 study). See Table 1. Findings were consistent across EU/EEA and other non-endemic countries, and among blood donors.

Conclusions
This review provides a comprehensive overview of factors associated with carrying *T. cruzi* infection in non-endemic settings. The most frequent association identified was being born in an endemic country, in particular in Bolivia. No studies in this review reported measures of the association between travelling to an endemic country and *T. cruzi* infection. However, positive cases born in non-endemic countries who had travelled or lived in endemic countries were reported. The strength of this review is its adherence to PRISMA standards and representing the largest synthesis of data on factors associated with carrying *T. cruzi* infection in non-endemic countries. The following limitations are noted: the review excluded grey literature, a meta-analysis could not be conducted due to heterogeneity, and inclusion of underpowered studies, potentially affecting the detection and interpretation of certain risk factors. Results from this systematic review could be considered when implementing prevention measures supporting identification of donors at risk to reduce SoHO-transmission of *T. cruzi* in non-endemic countries.

Table 1 Summary of key factors associated with *T. cruzi* infection in non-endemic countries

Risk factor for *T. cruzi* infections	Number of studies
Being born in an endemic country (of which Bolivia)	19 (16)
Stay in endemic country	1
History of living in rural areas	13
History of living in poor housing conditions	12
Contact with the vector	7
History of blood transfusion in endemic countries	9
Being older age	15
Mother or grandmother born in endemic country	1
Having a family history of CD	13
Prior generic knowledge of CD	8
Being female	17

Assessment of travel related donor eligibility in Switzerland using the online digital tool "Travelcheck"

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Introduction

Blood product safety related to transfusion-transmitted diseases (TTD) is a key concern for blood transfusion services. Risk behaviour and travel to countries endemic to transfusion-transmittable pathogens can potentially lead to TTD. Transmission is possible in the event of a donation during the window period when antibody, antigen or virus load levels are too low to be detected by current screening methods. Adding questions about travel history to regions endemic to various pathogens and deferring donors is a risk mitigation measure adopted in Switzerland and many other European countries. Deferral duration depends on the incubation time, taking into account test window periods. Swiss transfusion SRC has implemented an online digital tool named "Travelcheck" to assist our personnel in assessing travel-related donor eligibility and applying the needed deferral periods.

Method

The tool is used nationally by staff and donors, taking into account endemicity, prevalence and deferral periods of the following infectious agents: arboviruses (chikungunya, West Nile virus, dengue virus, Zika virus), malaria, chagas, hepatitis B and C and HIV. Available recent epidemiological data are used to regularly update the tool. Arboviruses in Europe are monitored weekly using ECDC (European Centre for Disease Prevention and Control) reports during the active season from June to November, specific NUT 3 risk regions are added depending on the detection of confirmed human cases and a 30-day deferral is introduced. Malaria regions are updated once a year, with a deferral period of 6 months or 4 months if malaria serology is performed. Country-related epidemiological data for chagas, HIV, HBV and HCV are monitored at longer intervals (2-5 years) using different data sources, with deferral periods ranging from permanent if born in an endemic country to 4-month deferrals. Search requires entry of visited country or city as well as the start and end dates of travel. The tool reveals donor eligibility, displays the first possible donation date, risk-dependent coloured country map (red, orange, green) and the corresponding TTD risk information. The Travelcheck tool is available in three Swiss national languages (German, French and Italian).

Results

Travelcheck is used by both blood establishment staff and donors and has resulted in accurate, simplified and harmonised travel-related deferrals. Donors can check their donor eligibility themselves before donating blood, thus giving them the possibility to avoid on-site deferral. Ten out of the existing eleven regional Swiss blood transfusion services responded to a survey one year after its implementation. The Travelcheck tool was perceived as simple, understandable and efficient. It is appreciated, because it can quickly and reliably help find countries and unknown regions.

Conclusion

The introduction of the Travelcheck tool was an important step towards safety, national harmonisation and digitalisation. Tools for simple queries which are available for donors and collection centres should be further promoted (for example: medication, donor eligibility criteria) to assist both staff and donors and enhance blood product safety.

Is antibody testing enough to protect the blood supply from transfusion-transmitted malaria?

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Background

Transfusion-transmitted malaria (TTM) occurs in both malaria-endemic areas (EA) and non-EA. The main risk for non-EA TTM stems from persons who donate blood after travel to or residence in EA. Past EA residents may be chronically infected but asymptomatic. To mitigate TTM risk, the EDQM (EDQM Blood Guide, 21st ed. 2023) requires deferrals for donors with a history of malaria, malaria-like illness, or recent travel to or residence in EA. The deferral period may be shortened if a donor has a negative antibody test 4 months or later after the deferral event; however, the EDQM does not recognise nucleic acid testing (NAT) for this donor re-entry. No *Plasmodium* antibody tests have earned IVDR Class D certification; 1 NAT test has been Class D certified for donor screening under the IVDR. Most of the enzyme-linked immunosorbent assays (ELISAs) do not detect all 5 species that cause human infection.

These antibody tests may be under new pressure because of increasing travel to/from EA, increasing immigration from EA, and demand for a more diverse donor pool to supply phenotypically matched blood for patients from EA. Climate change, which is broadening the geographic habitat of *Anopheles* mosquitoes (*Plasmodium* vector), may soon increase risk of local transmission.

High-throughput NAT able to detect the 5 *Plasmodium* species responsible for most human malaria infections could serve as effective new tools to detect malaria and to better prevent TTM. Current DNA-based molecular tests are not high-throughput and are ~1000-fold less sensitive than new tests developed to detect both DNA and ribosomal RNA (rRNA) that drive sensitivity down to ~3 parasites/mL.

Methods

Literature and publicly reported evaluations regarding the ability of commercial antibody ELISAs to detect *Plasmodium* infections were reviewed.

Results

Three summaries of ELISA evaluations were identified: commercial ELISA sensitivity ranged from 50% to 84.2%. Mangano *et al*. (*Malar J* 2019) showed sensitivity for 5 commercial ELISAs ranged from 53.6% to 64.2% in samples that were positive by immunofluorescence antibody testing. Le Cam (presentation TU1-06, AABB Annual Meeting 2019) demonstrated 50% to 84.2% sensitivity using 5 ELISAs. Jimenez-Klingberg *et al*. (*Transfus Med Hemother* 2023) reported 70% sensitivity of the ELISA they evaluated. Pichl *et al*. (*Transfus Med Hemother* 2024) showed that a different ELISA detected only 1 of 2 DNA-positive donors. In addition, a review of laboratory detection of donors causing TTM reported that 4 of 7 (57%) were negative by ELISA. (Galel, *Vox Sang* 2024;119 (Supp. 1)). In contrast, 10 of 12 donors causing TTM were detectable by DNA-based PCR assays. The 2 PCR-negative cases were tested only on samples likely to have deteriorated from prolonged refrigerated storage.

Conclusions

Several reports suggest that serologic tests may lack sufficient sensitivity and specificity to reliably detect malaria-infected donors. Current serology tests for screening donors for malaria infection have gaps in performance that result in TTM in non-EA. Climate change and increased travel to and immigration from areas where malaria is endemic will increase TTM risk in Europe. High-throughput high-sensitivity *Plasmodium* rRNA NAT can close serologic tests' performance gaps and enable improved blood safety. Thus, rRNA NAT offer an effective complement to existing serologic tests.

Highly sensitive nucleic acid test for detection of *Plasmodium* RNA: a potential tool to increase blood safety and availability

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Background/Introduction

Malaria is caused by protozoa of the genus *Plasmodium* and transmitted by *Anopheles* mosquitos. *Plasmodium* can also be transmitted from mother to fetus and from blood products from infected donors. In non-endemic areas, transfusion-transmitted malaria (TTM) is a growing concern due to increased travel from, and former residents of, endemic areas. To reduce TTM risk many countries defer at-risk individuals, negatively impacting blood availability. Alternatively, selective or universal donation screening with a sensitive *Plasmodium* nucleic acid test (NAT) would reduce the number of such deferrals. The Procleix Plasmodium Assay on the Procleix Panther System is a CE-marked, qualitative transcription-mediated amplification (TMA) assay that detects 5 *Plasmodium* species: *P. falciparum, P. ovale, P. vivax, P. malariae* and *P. knowlesi*. Enhanced sensitivity is the result of targeting 18S ribosomal RNA, present in thousands of copies (c) per parasite. The published 95% limit of detection is 8.47–11.89 RNA copies/mL and 2.10–6.82 infected red cells/mL. Clinical specificity reported was 99.99% in individual donations (N=12 800) and 100% in pools of 16 (N=283); clinical sensitivity was 100% in both individual donations and pools (N=50) (Tonnetti *et al*. *Transfusion* 2024;64:94-103). To further demonstrate the assay's performance, we evaluated the assay reproducibility and tested asymptomatic blood donors from Cameroon and Madagascar.

Methods

Reproducibility of the Procleix Plasmodium Assay on the Panther System was assessed by testing *P. falciparum in vitro* transcript panel members of 100 c/mL, 30 c/mL, and negative, along with positive and negative whole blood (WB) samples. Percent agreement and mean signal-to-cutoff (S/CO) ratios for panel members were evaluated including percent coefficient of variation (%CV) for 5 variance factors (inter-operator, inter-instrument, inter-day, inter-lot, and intra-run). WB samples collected from asymptomatic blood donors from Cameroon (N=223) and Madagascar (N=249) were tested in the US on the Panther System. A subset of the donations from Cameroon (N=131) and Madagascar (N=248) were tested with the Captia™ Malaria Total Antibody EIA (Trinity Biotech; Wicklow, Ireland).

Results

Percent agreement was 100% for positive reproducibility panel members and 99.8%-100% for negative members. Intra-run (random error) was the largest contributor to total variance in the signal variability for analyte S/CO results in positive members. High *Plasmodium* prevalence was seen in donors from Cameroon, with 41% (91/223) WB samples testing TMA repeat reactive (RR) versus 1% (3/248) in donations from Madagascar. Matching plasma samples corresponding to a subset of WB samples yielded 86% (113/131) EIA positivity from Cameroon and 27% (68/248) from Madagascar. Antibody detection was not seen in 10% (5/49) of matching TMA RR samples from Cameroon, indicating a possible limitation of antibody testing.

Conclusions

The Procleix Plasmodium Assay has high sensitivity and results here demonstrated high reproducibility. The assay also detected *Plasmodium* RNA in asymptomatic blood donors from Cameroon and Madagascar showing a range of RNA prevalence in endemic regions. A potential limitation of antibody detection was observed, as 10% of TMA RR samples from Cameroon were not detected by antibody testing. These results suggest that this fully automated NAT may be useful to address malaria risk in blood donors.

Oral presentations – topic B: blood components

Session B1: Innovative & novel blood components

Dried plasma: current considerations in Europe

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Background

An increasing interest in dried plasma (also referred to as freeze-dried plasma and/or lyophilised plasma) was identified by many European Blood Alliance (EBA) members who are facing queries about and/or requests for the product. These increases in demand are being driven by both civilian and military situations, for a number of reasons including:

- Shift in policy when it comes to treatment of patients with severe bleeding from a clear fluid-based to a blood-based resuscitation strategy
- Civilian and military guidelines recommend early blood transfusion for treatment of patients with life-threatening bleeding to improve survival

Study Design and Method

The EBA Working Group on Innovation and New Blood Products' subgroup on Dried Plasma performed a survey among the EBA member states.

Results

The response rate was 60% (15 responses from the 25 EBA member states).

Of these, dried plasma is currently in use in 8 (53%) countries, exclusively via a commercially available product. All countries (9) who have received a request for dried plasma received it from a pre-hospital setting, with 2 also receiving requests from an in-hospital setting. The requests are originating from both civilian and military sources. In 6 (40%) countries, there is a request or an initiative to have a national stockpile of dried plasma.

Countries which are either not currently producing or not considering producing dried plasma in the future cite source limitations (insufficient plasma or plasma prioritised for other uses – fractionation, FFP, etc.) and the lack of availability of technology for local production as the main reasons. Lack of demand, being too expensive to produce and regulatory concerns were also cited. The 4 (27%) countries which are either currently producing or considering producing dried plasma in the future are all performing research into dried plasma.

From a regulatory perspective, in 8 (53%) countries the classification of dried plasma as either a blood product or a pharmaceutical depends on how it is produced. Two countries classify it as a blood product and one as a pharmaceutical.

Conclusions

This survey contributes to a better understanding of the dried plasma-related challenges and demands faced by Blood Establishments. In addition to studies in Canada, Australia and the USA[14], our survey confirms that dried plasma projects are underway in several European nations.

Considering the well-publicised current demands for donated plasma (including, inter alia, for fractionation into plasma medicines, for transfusion, for reagents)[15] it seems appropriate that stakeholders involved in the development and management of national and international plasma strategies take account of all current and anticipated plasma requirements, including potential dried plasma stockpiles. Consideration should be given to the inclusion of both civilian and military stakeholders in the development of these strategies to ensure that sensitive data on possible and anticipated demand, for dried plasma and other blood products, is both included and appropriately treated. Comprehensive risk-based return-on-investment considerations should also be included to ensure appropriate resourcing.

To facilitate and optimise decentralised production of dried plasma, clear technical guidelines for the production of dried plasma with a regulatory classification as a blood product should be provided against the context of the new SoHO Regulation and the new pharmaceutical legislation in revision. This would be assisted by the inclusion of a monograph on dried plasma in the EDQM Blood Guide.

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Establishing spray-dried plasma as a blood component in the UK: regulatory and scientific aspects

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Background

Most military deaths occur within 60 minutes due to catastrophic injury, head injury or major haemorrhage (MH). Early administration of plasma in addition to red cells reduces mortality from MH. For plasma, this is a logistical challenge due to freeze-thawing/cold chain requirements in austere environments. Dried plasma provides a potential solution; however, commercially available dried plasma products have limitations: primarily glass bottle storage containers and concerns regarding global sufficiency of supply. Velico Medical have developed the FrontlineODP™ drying system, to allow blood establishments to produce a dried plasma component in a blood bag from a single unit of plasma.

Aims

NHS Blood and Transplant (NHSBT), in collaboration with Velico Medical and the UK Ministry of Defence (MoD), aim to assess the suitability of the system for production of a UK-derived dried plasma component for clinical use. This includes laboratory validation, a suitable clinical trial and gaining all the necessary regulatory approvals to manufacture dried plasma in the UK.

Methods

A custom-developed facility in Cambridge, UK, will house the Velico FrontlineODP™ drying system, and allow the manufacture of spray-dried plasma in a blood bag in a GMP/GPG-compliant laboratory. The process for gaining regulatory approvals was drafted and discussed with our regulator (MHRA).
In parallel, Velico will progress CE approval of their FrontlineODP™ drying system as a medical device. Regulatory approval will be sought to use the system to manufacture dried plasma for use in a clinical trial before CE marking is gained.
A total of 24 units of UK plasma have been dried by Velico Medical using the FrontlineODP™ system. These were then reconstituted and tested for plasma characteristics.

Results

Following discussion with the UK regulator, MHRA, NHSBT have established that dried plasma manufactured using the FrontlineODP™ drying system is considered a blood component, and that therefore its validation and manufacture falls under the Blood, Safety and Quality Regulations (BSQR). As such, validation and approval of the final specification for the product is the responsibility of the UK Joint Professional Advisory Committee (JPAC).
The requirements for a full laboratory/clinical evaluation of dried plasma necessary for clinical implementation, have been drafted, along with a draft provisional specification for the product, and agreed with JPAC, and will be performed by NHSBT. This group will review the output of the validations and trial to then approve a final specification for the component for routine manufacture.
In a small initial laboratory study using UK plasma, all dried plasma units (n=24) reconstituted within 5-8 minutes. All coagulation parameters decreased pre to post drying by <20% except APTT (24%), FVIII (31%) and vWF activity (40%). vWF antigen decreased by only 5.1%.

Conclusions

Initial data from UK dried plasma was comparable to previously published data generated with US plasma produced using the FrontlineODP™ system (Liu *et al*., *Transfusion* 2018). Further *in vitro* and *in vivo* evaluation of dried plasma is intended by NHSBT, and necessary to fully evaluate the suitability of the FrontlineODP™ system for clinical use. The regulatory classification and pathway for this product has been established in the UK, along with a proposed plan for validations and trial. This work and the specifications developed could feed into EU guidelines in due course.

Developing universal plasma and platelets - what challenges do we need to consider?

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Introduction

NHSBT, as well as other research groups, have initiated projects to develop universal plasma and platelets and to explore the challenges associated with implementing these novel blood components.
Clinical UK guidelines recommend transfusion of ABO-identical plasma and platelets where possible, as mismatches can lead to haemolytic transfusion reactions (HTRs) when transfusing across group (Estcourt *et al*. *Br J Haematol* 2017;176:365-94). However, due to stock availability (limited AB plasma and A negative platelets), and component shelf life (platelets - 5-7 day), mismatched plasma and platelet transfusions are frequent. To reduce the risk of an HTR, plasma and platelets that are low titre for anti-A/B are preferred. In some countries these are identified using a high titre (HT) screening method either on the donor or the final product. This risk could be further reduced by considering methods to selectively remove anti-A and/or anti-B antibodies from platelets and plasma.

Methods

Here we evaluate the current universal offerings for plasma and platelets and discuss important considerations for bringing a novel component to the market that will assist in the development of universal plasma and platelets and relevant specifications for these products.

Results

There are various methods that can reduce anti-A/B antibodies, including HT testing, dilution in platelet additive solution (PAS), pooling components, adsorption of antibodies using red blood cells (Raster *et al*. *Transfus Med Hemother* 2022;49(5):280-7) or a medical device. There is already a CE medical device currently on the market - Glycosorb® ABO column (Robbins *et al*. *Transfusion* 2023;63(S5):P-CB 22, 160A-161A) with others in development. Regardless of which method is chosen, when considering a safe universal component there are a number of important questions that we must answer. 1. How do we define universal plasma and platelets in terms of residual levels of anti-A and anti-B? 2. How do we ensure adequate antibody removal, in particular from HT donations? 3. Should the titration method of measuring anti-A and anti-B be standardised? 4. How do we balance supply and demand as we move to a new world of universal blood components? and 5. What else do we need to consider?

Conclusions

Although likely to bring huge benefits to both hospitals and the overall blood supply chain, the implementation of universal plasma and platelets into a blood manufacturing facility will bring many challenges, and the specification for these products needs to be defined.

Fetal haemoglobin-enriched red blood cell concentrates: an "investigational blood product" for preterm neonate transfusion

Luciana Teofili[1] and the BORN trial investigators (Stefano Ghirardello[2], Carlo Dani[3], Claudio Pellegrino[4], Genny Raffaeli[5], Francesco Cresi[6], Giulia Ansaldi[6], Giulia Remaschi[3], Maria Bianchi[4], Antonella Dragonetti[6], Carmen Giannantonio[4], Enrico Beccastrini[3], Stefania Villa[5], Paola Bergamaschi[2], Marco Fabbri[7], Tina Pasciuto[4], Giovanni Vento[4], Patrizia Papacci[4])

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Extremely low gestational age neonates (ELGANs) receive red blood cell (RBC) transfusions several weeks before the physiological switch from fetal (HbF) to adult haemoglobin (HbA) synthesis occurs. The substitution of HbF with HbA causes increased oxygen delivery and tissue extraction, thereby causing the hazardous condition of hyperoxia[8]. The pathophysiology of prematurity-related diseases derives from their susceptibility to oxidative stress: the immature antioxidant defences in ELGANs cannot effectively resist the pro-oxidant stimuli generated by infections, inflammatory diseases, oxygen therapy, surgery and anaemia. Non-physiological, high levels of HbA further contribute to this. Transfusing preterm neonates with cord blood-RBCs (CB-RBCs) raises haemoglobin levels without depleting physiological HbF[9].

The BORN study (NCT05100212) is a randomized, multicentre trial assessing the severity of retinopathy of prematurity (ROP) in ELGANs receiving either HbF-enriched or standard transfusions. ROP is one of the most frequent causes of blindness in infancy. An interim analysis of the first 58 patients, who received 153 transfusions (49 CB-RBCs and 104 adult-RBCs), confirmed the safety of this approach[10]. Indeed, the number of adverse events in patients receiving only CB-RBCs was lower than in patients receiving only adult-RBCs, with no adverse event likely due to CB-RBCs themselves. Adult-RBC transfusions significantly predicted severe ROP, even after adjusting for covariates with recognised effects on ROP. Specifically, every adult donor RBC transfusion had an odds ratio for severe ROP of 1.90 (95% CI 1.13-3.17), whereas CB-RBCs had no effect.

The BORN trial completed enrolment in October 2024 and conclusive results are expected shortly. Presently, CB is collected as the haematopoietic stem cell source for transplant use. Moving CB-RBC transfusion from the research setting to routine clinical practice would require extending CB use from the transplant to the transfusion setting, establishing specific criteria for donor selection and CB-RBC quality requirements, and improving storage conditions and product shelf life. In addition, the CB-RBC transfusion impact on the clinical outcomes of recipients should be monitored by establishing public registries in which recipients' data, along with data from donors and characteristics of CB-RBC products are gathered. This would help refine policies for CB-RBC concentrate utilisation and establish reference standards and quality criteria, from the collection up to the release, storage and distribution. Finally, by monitoring data on the production and consumption of CB-RBC units, it would be possible to quantify the additional costs and the economic impact of this new transfusion strategy in comparison with the standard approach.

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Implementation of a whole blood programme for treatment of patients with massive haemorrhage – a practical guideline for blood providers

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Introduction

Traumatic haemorrhage accounts for most preventable deaths from injury in both civilian and military healthcare. There has been a shift in resuscitation strategy for patients with severe bleeding, moving from a clear fluid-based to a blood-based resuscitation strategy. A growing number of civilian and military guidelines and publications recommend early balanced transfusion to patients with major haemorrhage, and whole blood (WB) has been reintroduced as a logistically feasible alternative to blood components as it includes red blood cells, plasma, and platelets in a physiological ratio. In a previous survey, the European Blood Alliance (EBA) Working Group on Innovation and New Blood Products identified an interest from the European Blood Services in implementation of WB programmes.

Methods

In this study, we aimed to provide a practical guideline for blood providers who wish to implement a WB programme. The study summarises recommendations and practical implications identified from published literature, regulatory requirements and current WB programmes in Europe.

Results

The following topics were identified: collection and production, storage and transport, regulatory requirements, validation, quality control, post-implementation follow-up, inventory management, and emergency preparedness.
WB donors are recruited based on national donor selection criteria. For patients with unknown ABO-type, low titre anti-A and anti-B group O WB (LTOWB) should be used. ABO-type like WB can be given. RhD positive and RhD negative donors are included depending on local criteria for emergency red cells. To reduce the risk of transfusion associated acute lung injury (TRALI), male donors or females tested negative for antibodies implicated in TRALI are preferred. CPD (citrate-phosphate-dextrose) and CPDA (citrate-phosphate-dextrose-adenine) are commonly used as anticoagulants. The former comes in a system which enables leukoreduction with a platelet-sparing filter. ISBT standards for labelling are recommended to favour interoperability between countries in emergencies. WB is stored between + 2 °C and + 6 °C. Depending on the anticoagulant used, WB is stored for up to 35 days; however, platelet function is reduced during storage.
Specifications for WB are described within the monographs of the EDQM Guide to the preparation, use and quality assurance of blood components ("the Blood Guide"). In these, minimum requirements for quality control are defined. Markers of red cells, platelet and plasma quality should be included in the validation of the product. Post-implementation follow-up of the programme includes haemovigilance and quality surveillance of the use and clinical effectiveness of the product. Users of the product should be involved in the development of the programme and training of clinical personnel must be performed.
Rotation of the stock between pre-hospital and in-hospital services and re-manufacturing of red cell concentrates from stored WB can minimise outdating. Establishing a structured system for emergency collection of WB will enable the blood services and hospitals to provide balanced transfusion to patients in remote areas, disasters and war.

Conclusions

We conclude that subject to successful validation, haemovigilance surveillance and authorisation by competent authorities, implementation of a whole blood programme for routine and emergency management of patients with severe bleeding can be performed in a structured and sustainable way.

Implementation and feedback of a new method for cryopreserved platelets with post-thaw minimal processing: the French experience

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Background/Case Studies
Cryopreserved platelets are a component mostly used in case of fresh platelet shortages on overseas islands due to supply issues. The former process to produce cryopreserved platelets involved a centrifugation after thawing to remove the cryopreservation additive solution. Those post-thaw steps last at least 2 hours. To reduce this duration, EFS implemented a new platelet concentrate freezing method.

Study Design/Methods
The process, which includes a centrifugation step before freezing the platelets and the addition of plasma, to resuspend the platelets and get a final volume suitable for transfusion, was assessed in 4 production sites for residual DMSO, platelet swirling, platelet content and recovery, mean platelet volume (MPV) and pH at different steps: before freezing (T0), immediately after thawing (T1) and 6 h after thawing (T2). Results and feedback after one year of routine use in overseas departments are described.

Results/Findings
Results during validation are described in Table 1. The method allows 77% recovery of platelets and shows no significant difference in MPV and pH 6 h after thawing. The pH is in accordance with French requirements. Mean residual DMSO is 0.8 ± 0.2 g per platelet concentrate (n=20); DMSO content is below the recommended limit of 10 g per platelet concentrate and below that of the former method: 3.5 g+/1.3 g (n=16). As with the previous method, platelet swirling index (SI) is weak in comparison with fresh platelets; however, SI is higher 6 h after thawing than immediately after. The post-thawing steps take less than 1 h per platelet concentrate.
During one year of routine use, 97 cryopreserved platelet units were thawed and 13 were discarded because of expiry but none were destroyed through handling. Among these platelet units, n=41 were controlled for recovery measurements. Results are described in Table 2. The mean platelet recovery was comparable to the validation process. The mean platelet contents were lower because of the selection of products with low platelet content for freezing. Visual aspects of the products were consistent and homogeneous, sometimes small platelet aggregates were seen and the swirling index was present, but weaker than fresh platelets. The benefits were confirmed: simplicity, quicker availability (between 45 to 75 min) and no centrifuge needed. The majority were used for haemorrhagic indication and, when platelet stocks were low, some for oncohaematology indications while waiting for fresh platelets.

Conclusions
The new freezing method has been successfully implemented in four production sites. After one year of routine use of cryopreserved platelets, their benefits are confirmed. This method allows an easier and quicker response to an emergency request for thawed platelets. This makes it possible to anticipate when the stock will become low in order to preserve fresh platelets for haematology prescriptions. Cryopreserved platelets seem to successfully fulfil their purpose.

Importance of research
This allows an easier and quicker way to issue platelets in case of fresh platelet shortages in France, notably on overseas islands.

Table 1 Results during validation

	Before freezing (T0)	Immediately after thawing (T1)	6 h after thawing (T2)
Platelet content per unit	6.08 ± 1.11x 10^{11} (n=56)	4.63 ± 1.10 x 10^{11} (n=56)	4.21 ± 1.12 (n=40)
Mean platelet volume (µm^3)	8.6 ± 1.4 (n=54)	8.8 ± 1.8 (n=56)	9.3 ± 2.2 (n=40)
pH	7.06 ± 0.23 (n=56)	7.22 ± 0.19 (n=56)	7.11 ± 0.19 (n=50)

Table 2 Results in routine use

	EFS site 1 (n=12)		EFS site 2 (n=29)	
	Before freezing (T0)	Immediately after thawing (T1)	Before freezing (T0)	Immediately after thawing (T1)
Platelet content per unit (x 10^{11})	5.4	3.6	4.6	3.6
Mean recovery (%)		68%		78%

Cold storage of amotosalen-UVA pathogen-reduced buffy coat platelet concentrates for up to 21 days: biochemical and functional characterisation, and identification of emerging platelet subpopulations

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Background

Current platelet transfusion requirements are evolving, with an increase in the need for therapeutic platelet transfusions compared with prophylactic transfusions. In this context, cold-stored platelets have gained interest owing to their specific potentially advantageous characteristics which, however, require thorough *in vitro* characterisation during storage. Our aim was to assess the effects of cold storage on the *in vitro* quality of buffy coat (BC) platelet concentrates (PCs) treated with amotosalen-UVA pathogen reduction and stored in PAS-E (SSP+) additive solution for up to 21 days.

Methods

A pool-and-split strategy was used to obtain BC-PCs produced from 8 whole blood donations, stored in PAS-E/plasma (55%/45%) and treated with amotosalen-UVA and stored i) at +22 ± 2°C with constant agitation or ii) at +4°C without agitation.

Results

Platelet counts declined similarly in both groups of PCs during storage without appearance of macroscopic aggregates, while platelet swirling was lost in PCs stored at +4°C, with platelets having a spherical shape as visualized by scanning electron microscopy. Storage at +4°C resulted in a significant reduction in glucose consumption and lactate generation as compared to storage at +22°C as of day 7, and a progressive decrease in pH, which, however, remained above 6.5 at day 21. Notably, sufficient glucose was still available on day 14 in PCs stored at +4°C, unlike in PCs stored at +22°C. Multicolour flow cytometry analysis for markers of platelet activation, apoptosis and mitochondrial membrane potential revealed emergence of several platelet subpopulations during storage. Among these, the resting, activated, aggregatory, procoagulant, apoptotic and senescent platelets are of prime interest for a better understanding of the functional properties of platelets. Spontaneous exposure of P-selectin, a marker of α-granule secretion, and of phosphatidylserine, a marker for platelet activation and apoptosis evaluated by annexin V binding, were significantly increased in PCs stored at +4°C as compared to +22°C during storage. Mitochondrial transmembrane potential, evaluated using the tetramethylrhodamine-methyl-ester fluorescent dye retained in functional intact mitochondria, decreased more rapidly in PCs stored at +4°C as compared to +22°C. The subpopulation of resting platelets remained predominant on day 7 at +22°C, while at +4°C this subpopulation was replaced by an equal proportion of procoagulant and apoptotic platelets, the latter becoming dominant on day 21. Finally, the ability of platelets to form thrombi on collagen in a microfluidic chamber was conserved until day 14 at +4°C but only until day 7 at +22°C.

Conclusions

Our results indicate for the first time that during storage of amotosalen-UVA pathogen-reduced BC-PCs stored at +4°C, healthy platelets are progressively replaced by procoagulant and apoptotic platelets. These platelets retain the ability to adhere and form thrombi on collagen under flow conditions for a prolonged duration (day 14). These new insights could lead to the development of new or improved platelet products to enhance inventories and access to platelet haemostatic support for bleeding patients.

Prolonged storage of purified granulocyte concentrates from pooled buffy coats

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Background
In the past years, the clinical applicability of granulocyte concentrates (GCs) has been broadened by a new purification method resulting in prolonged storability and the application in an extracorporeal therapy system to treat septic immune dysfunction[3, 4].
In Germany, granulocyte concentrates are typically produced by apheresis and require donor pretreatment with G-CSF and dexamethasone, often resulting in time delays and a bottleneck in the availability. It also exposes the donor to potential side effects.
In contrast, producing GCs from pooled buffy coats (BCs) of whole blood donations offers expanded availability and fewer donor risks. Recently, we published the production of purified GCs using BCs and hydroxyethyl starch[5]. Here, we present a manufacturing process involving the pooling of BCs and purification based on gelatine sedimentation to achieve the desired cell counts. Viability, functionality, and metabolism of the cells were investigated during prolonged storage.

Methods
Up to 20 ABO blood group-identical BCs were pooled. After adding gelatine (Gelafundin), the red blood cells sedimented. The remaining leukocyte-rich supernatant was washed three times with saline to reduce platelet content and was resuspended in ABO-identical donor plasma. The purified pooled GC (ppGC) was transferred to a platelet storage bag and stored at 20–24°C without agitation for up to 96 hours. Every day, cell count and viability, metabolic surrogate parameters and functionality were monitored.

Results
Pooling of 12 BCs resulted in ppGC with 8.5E9 granulocytes (N=12, range 5.3-12.2E9) corresponding to the EDQM specifications for pooled granulocyte concentrates (at least 5E9). Pooling of 20 BCs resulted in ppGC with 1.22E10 granulocytes (N=6, range 1.03-1.40E10) corresponding to the German Hemotherapy specifications for granulocyte concentrates (at least 1E10). During storage for 96h viability and phagocytosis rate were above 80%.

Conclusion
Granulocyte concentrates (GCs) from pooled buffy coats meet required granulocyte cell counts and demonstrate an extended storability. Both hydroxyethyl starch and gelatine can be used. This may allow the offering of granulocyte concentrates as an off-the-shelf product in the future for immediate use and broad applicability for transfusion and extracorporeal immune therapy.

[3] Altrichter J *et al*. *Crit Care* 2011:15(2):R82.
[4] Klinkmann G *et al*. *Transfusion (Paris)* 2022;62(1):194–204.
[5] Klinkmann G *et al*. *Transfus Med Hemother* 12. April 2024;1–10.

Session B2: Risk-based approach for implementing process changes

Toward a common approach to authorisation of a novel blood component: GAPP-PRO experience

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Background

One of the main reasons why the EU Blood, Tissues and Cells (BTC) directives have been repealed by the new Substances of Human Origin (SoHO) Regulation comes from the evidence that they were published around 20 years ago and that they no longer reflect the current scientific and technical developments in the SoHO field. In particular, they do not provide indications on how to deal with innovation in TC transplantation and transfusion medicine. The progress of scientific knowledge makes available new BTC components such as platelet-rich plasma (PRP) and serum eye drops, largely used in different clinical and surgical settings for reparative medicine, but differently regulated in the EU member states (MS). Innovative therapies based on SoHO, due to their biological nature, need to be homogeneously regulated to guarantee the same quality and safety standards as well as an equitable access to the novel therapies for all European citizens. In this regard, the new SoHO Regulation strengthens the role of the BTC establishments and the Competent Authority (CA) in submitting and assessing comprehensive preparation process dossiers, respectively, in the case of novel BTC preparations, which have to be authorised before their human application. In the BTC field, standard products are prepared in compliance with quality and safety specifications, mostly set in the monographs of the EDQM Blood and Tissues & Cells Guides. A novel BTC product or a product coming from an innovative preparation process, which is not yet included in the Guides, may often lack reference standard specifications. Thus, the evidence of safety and efficacy is mostly based on the available international literature. Furthermore, very new SoHO preparations challenge the CA in the assessment for the authorisation, requiring a deep knowledge of technical, scientific and clinical issues.

Methodology

The EU Commission, in preparation for the forthcoming regulation, launched and funded several initiatives aiming to reinforce a common approach among MS for assessing and authorising novel preparation processes in order to, among others, both provide MS with common risk-assessment tools for the evaluation of the risk of the novelty and to get a decision about the need to include or not include a clinical monitoring plan in the preparation process dossier according to the level of the risk. This methodology has been consolidated in the GAPP - FacilitatinG the Authorisation of Preparation Process for Blood, Tissues and Cells (https://www.gapp-ja.eu) Joint Action (JA) and was disseminated to the CAs while the regulation was being drafted and finalised. Most of the principles set out in the GAPP Overall Guideline for the authorisation of preparation process are reported in the regulation, so that the MS shall prepare themselves for their application until they become legally binding in 2027, when the regulation will come into force.

For this reason, a new JA was launched on February 2024, named GAPP-PRO (https://gapp-pro.eu/), with the primary goal to test the GAPP methodology and to verify its feasibility, including in MS where novel BTC preparations may sometimes be covered by a different regulatory framework.

The main challenge of the GAPP-PRO JA is verifying the capability to implement the GAPP model piloting the authorisation processes of some novel SoHO preparations, selected on the basis of results of a dedicated survey distributed among MS. Specifically, the survey will investigate existing types of preparation processes according to the identified product/s; critical quality attributes, critical process parameters, clinical indication as well as clinical follow-up included in the selected preparation process dossiers, where they exist. The results of the survey will be duly assessed in order to perform a gap analysis and to provide the technical work packages with the information for the pilot tests. The goal is to test the GAPP model in different MS with special reference to the assessment of the risk, and also with a view to multi-country assessment. Another new aspect of the GAPP-PRO is that in both the single country and the multi-country assessment, an active interaction among CAs, clinicians (final users of the SoHO therapies) and stakeholders from medical device and pharmaceutical fields, where involved, will be strongly encouraged.

Conclusions

The new regulation states that when SoHO are prepared with newly developed and validated collection, testing or processing methods, safety and effectiveness in SoHO recipients should be demonstrated by means of clinical outcome data collection and review. The extent of such required clinical outcome monitoring should correlate with the level of risk associated with the activities performed for that SoHO preparation and use. In case of high risk and of a positive benefit-risk assessment, as well as in cases where the risk or the benefit are not assessable due to a lack of scientific and clinical data or knowledge (novel preparations), a clinical monitoring plan should be included in the preparation process dossier. The SoHO CA should both approve the plan before its implementation and assess the outcome data as part of a SoHO preparation authorisation. Most aspects of the clinical monitoring of SoHO recipients are outside the scope of the regulation and fall under healthcare responsibilities. However, in this context, any reference to effectiveness should be considered to include an expected response in a SoHO recipient evaluated in accordance with a previously approved clinical outcome monitoring plan, when such a plan is required. The GAPP-PRO JA will support the MS to be prepared to follow these obligations. The multi-country approach will also facilitate the development of more efficient data collection from aggregated groups of SoHO recipients, applying standardised outcome measurements and reflecting outcomes in the 'real-world' setting. In this way, existing EU clinical registries could acquire added value as useful tools capable of ensuring that data quality and data management procedures are robust and allow for the data to be used for the purpose of SoHO preparation authorisation. SoHO CAs should share with each other information on newly authorised SoHO preparations, together with the evidence used for such authorisations through the EU SoHO Platform. Such sharing could allow SoHO CAs to accept previous authorisations granted to other SoHO entities, including in other MS, and thus significantly reduce the requirements to generate evidence.

Expanding the use of cord blood units for manufacturing platelet-derived products: assessment of clinical-grade products from small units or after expiration time

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Introduction

Umbilical cord blood (UCB)-derived platelet concentrates (PC) have been proposed as a novel medicinal product for several conditions, including skin ulcers (as a gel) and corneal lesions (as eye drops) (Samarkanova *et al.*, 2020; 2021). According to the initial acceptance criteria at our centre for the cryopreservation of haematopoietic cells and platelets, UCB collection bags must weigh at least 100 grams (equivalent to 50 mL net volume of blood) and be processed within 48 hours of collection. However, many collections do not meet these criteria (40% and 14%, respectively (2023)). Adopting less stringent criteria would increase availability and minimise waste.
We hypothesised that PC derivatives could be manufactured using UCB units processed beyond 48 hours after collection, as we expect that platelet viability and biological activity (reflected in the expression of growth factors) would not be affected by a longer expiry time. Additionally, we hypothesised that PC derivatives could be produced from UCB collection bags weighing at least 85 grams (equivalent to 35 mL of blood), given the small volumes required for the final products.

Methods

We therefore conducted a local validation study at Banc de Sang i Teixits (Barcelona, Spain) to assess the functionality and conformity of UCB-PC products manufactured using collections weighing at least 85 grams (small volume) versus 100 grams and processed from 48 h to 80 h versus within 48 hours after collection.
For validation, a total of 51 small-volume collections and 9 units were assessed after extending expiration time. Validations were performed from 10/51 small-volume and 9/9 longer expiry units.
Functional assessment of PC products was defined as a mesenchymal stem cell (MSC) duplication time of ≤2.1 days, a growth rate of ≥0.33 days, an exponential phase duration of ≥5 days, and growth factor levels (EGF, PDGF AA/BB, VEGF) within control sample ranges.

Results

Units with small volume resulted in a very inefficient procedure (<34% compliant final products), summarised in Table 1. Conversely, extending expiration time to 80 hours is feasible, summarised in Table 2.

Conclusion

This study found that small-volume units had poor platelet recovery, making them unsuitable for routine production (≥100g minimum recommended). Interestingly, extending storage time (48-80 hours) maintained platelet functionality. This suggests these units might be viable for topical use in regenerative medicine, but may require testing for haemolysis before processing.

Table 1 Comparison of initial UCB collection bag weights: minimum 85 vs. 100 grams

	Collections 85-100 grams (validation)	Collections ≥100 grams (standard)	Comparison 85-100g vs ≥100
Characteristics at initial collection (median, range)	(n=10)	(n=3)	
Weight collection bag, grams	93 (85-97)	122 (113-131)	ND*
Volume PRP, mL	6 (5-9)	10 (5-11)	ND
Platelet count, x10^9/L	853 (748-992)	887 (848-937)	ND
Functionality assay results	(1 pool, n=10)	(1 pool, n=3)	
Growth rate, x 1/days (≥0.33)	*ND* **	0.64	ND
Duplication time, days (≤2.1)	*Not determined**	1.08	ND
Exponential phase duration, days (≥5)	3	5	ND
Growth factor levels (mean ± SD), (pg/mL)	(n=10)	(n=3)	
Epithelial growth factor (EGF)	3 574 (2566-3851)	3 531±114	0.5
Platelet derived growth factor (PDGF)	12 242 (8236-14462)	11 955±1 603	0.8
Vascular endothelial growth factor (VEGF)	3 594 (2535-6586)	3 828±1 136	0.2
Basic fibroblast growth factor (bFGF)	1 542 (560-1956)	1 479±392	0.3
Interleukin-6 (IL-6)	1 582 (1133-1873)	1 525±204	0.9
Conformity for accomplishing required platelet count (800-1200x10^9/L)	(n=51)	(n=3)	
Accepted:	85-89 g (n=10) 1/10 (10%) 90-99 g (n=41) 14/51 (34%)	3/3 (100%)	ND

**ND – not determined*

***It is not possible to determine growth rate and duplication time if the exponential phase is less than 5 days.*

Table 2 Comparison of initial UCB collection expiry: minimum 48 vs. 80 hours

	Collections processed within 49-80 hours (validation)	Collections processed within <48 hours (standard)	Comparison 49-80 vs <48h
Characteristics at initial collection (median, range)	(n=9)	(n=3)	P=
Time since collection, hours	70 (55-80)	32 (16-32)	ND*
Volume PRP, mL	6 (4-10)	10 (5-11)	ND
Platelet count, x10^9/L	1074 (703-1173)	887 (848-937)	ND
Functionality assay results	(1 pool, n=8)*	(1 pool, n=3)	
Growth rate, x 1/days	0.49	0.64	ND
Duplication time, days	1.41	1.08	ND
Exponential phase duration, days	10	>5	ND
Growth factor levels (mean ± SD), (pg/mL)	(n=8)**	(n=3)	
Epithelial growth factor (EFG)	4 456±731	3 531±114	0.1
Platelet derived growth factor (PDGF)	11 862±1 809	11 677±1 084	1.0
Vascular endothelial growth factor (VEGF)	4 105±1 112	4 349±813	0.8
Basic fibroblast growth factor (bFGF)	1 304±2 176	1 700±115	0.6
Interleukin-6 (IL-6)	1 254±1 769	1 605±110	0.5
Conformity	(n=9)	(n=3)	
Accepted	8/9 (88.8%)	3/3 (100%)	ND

**ND – not determined*

***One validation unit (1/9, 11.1%) in the expiry comparison did not accomplish acceptance criteria due to low platelet count (of 703 x10^9/L).*

Stepwise process change implementation of a buffy coat pooling protocol to increase yields

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Background

Worldwide, many blood establishments use different methods for the production of pooled platelets (PPs). In Europe, the primary approach for producing PPs is the buffy coat (BC) method, pooling 4 to 8 BCs to produce a single or double unit of platelets in the end. Here, we present a stepwise process change implementation, where we aimed to increase the yield of blood products by optimising manufacturing steps, ranging from the whole blood unit to the pooling process itself.

Methods

We compared five different pooling approaches by measuring the volume and the yield of the platelet concentrates. First, we measured PP (n=107) from a pool concentrate containing 5 BCs, which was, until our process change implementation, the standard product from our blood bank. Second, we switched from pooling 5 BCs to 6 BCs to increase the yield (n=110). Third, we used a new haematology analyser (Sysmex XN-1000) equipped with a special blood bank mode to measure platelet concentrates (n=107). Fourth, we implemented an adjusted BC programme on our blood cell separators (Macopress Smarter, Macopharma) to produce a higher volume in the BCs and in the PP (n=107). Fifth, we adapted the soft spin of our centrifugation protocol (n=197) to further increase yields. The cutoff yield for dividing a concentrate is a yield of ≥ 4.4 per unit.

Results

First, we performed inter-day (n=9) and intraday (n=10) precision analyses for a control sample (PLT check), harbouring a coefficient of variation (%) of 4.3 (inter-day precision) and 2.8 (intraday precision) for the new Sysmex XN-1000 analyser. Optimising the manufacturing steps of our process significantly increased the yield of the products step-by-step after each single optimisation ($P<0.001$). The mean yield of the blood product was 2.83 (SD 0.39) for the first approach using 5 BCs, 3.12 (0.38) for the second approach using 6 BCs, 4.03 (0.49) for the third approach where the Sysmex XN-1000 was used, 4.30 (0.53) for the fourth approach where the protocol of the blood cell separators was adapted, and 4.81 (0.58) for the final approach after optimising the centrifugation procedure.

Conclusion

In addition to increasing the number of BCs, optimising BC volume, analyser selection, and improving protocols (blood cell separator and centrifuge) in the manufacturing process of PP shows that 6 BC are sufficient to produce double unit platelet concentrates with adequate yields, thereby reducing costs and minimising waste of blood.

Using a haematology analyser to count residual cells in blood components instead of flow cytometry

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Background

Flow cytometry is a validated and widely adopted method in laboratories for measuring residual cells as part of routine quality control measurements in blood components. The emergence of the so-called blood bank mode for the Sysmex XN-1000 automated analyser provides an alternative tool which is currently not broadly used. At the moment, there is still uncertainty regarding the comparability of results to flow cytometry, when counting residual cells in erythrocyte concentrates, plasma or platelet concentrates. It is unclear if haematology analysers can replace flow cytometry for the measurement of residual cells as a quality control parameter in blood banks in the future. Here, we present an example of a process change implementation as we switched from flow cytometry to Sysmex XN-1000 blood bank mode in some of our routine residual cell measurements.

Methods

We measured residual white blood cells (rWBC), residual red blood cells (rRBC), and residual platelets (rPLT) in erythrocyte concentrates, plasma, and platelet concentrates, respectively, using the BD FACS Lyric flow cytometer and the blood bank mode of the Sysmex XN-1000 haematology analyser in parallel. We further compared residual cell measurements in platelet concentrates obtained from pooling and apheresis procedures before and after pathogen inactivation. We used Bland-Altman analysis and Spearman correlation to quantify agreement of residual cells per µL between the two methods. Furthermore, we quantified pass rates according to cut-off values given by the EDQM Blood Guide.

Results

We performed intraday and inter-day precision analyses for two different levels of control samples, harbouring a coefficient of variation (%) of 5.6 (inter-day precision) and 4.0 (intraday precision) for level 1 and 2.8 (inter-day precision) and 1.5 (intraday precision) for level 2. In whole blood filtrated erythrocyte concentrates, a median of 0.4 (interquartile range (IQR): 0.2-0.7) rWBC/µL was detected using FACS compared to 0.4 (0.2-0.9) rWBC/µL when using XN-1000 (n=61). In inline-filtrated erythrocyte concentrates a median of 0.1 (0.0.-0.2) rWBC/µL was detected using FACS compared to 0.1 (0.1-0.3) rWBC/µL using XN-1000 (n=40). In plasma, rWBC/µL were also highly similar when using FACS compared to XN-1000 (n=60). However in pooled platelet concentrates (after pathogen inactivation) (n=34), 2.3 (1.4-3.0) rWBC/µL were detected when using XN-1000 compared to 1.1 (0.4-1.7) rWBC/µL when using FACS.

Conclusion

The blood bank mode of the Sysmex XN-1000 haematology analyser can serve as a reliable method to count residual cells (rWBC, rRBC, rPLT) in different blood components instead of using flow cytometry. It is especially valuable to discriminate correctly if a unit is below or above the cut-off value, defined by the EDQM. This is highly appreciable as costs and handling times by staff can be reduced. However, absolute rWBC values in pooled platelet concentrates after pathogen inactivation are significantly higher when using the XN-1000 blood bank mode, which would require further improvements of the methodology.

Session B3: Novel component development & clinical outcome monitoring

Hypoxic red blood cells: an innovative blood product

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Background

Storage of red blood cells (RBC) subjects them to oxidative damage resulting in decreased quality. Hypoxic storage, where the oxygen content of RBC units is reduced to <20% saturation of O_2 (SO_2) throughout storage, improves *in vitro* metrics of RBC quality, including oxidative lesions, oxygen delivery and cellular deformability (Rabcuka *et al*. *Blood Adv* 2022;6:5415-28). Hypoxic RBCs (HRBC) have an increased p50 and right shift in the oxygen-haemoglobin dissociation curve indicating reduced affinity for oxygen.

Process validations of the *in vitro* performance of the hypoxic storage system - CPD/PAGGSM Leukocytes-Reduced, O_2/CO_2 Reduced – were executed at blood banks in 4 countries, followed by a safety study.

Methods

Validations: Whole blood (WB) was collected and processed within 24 hours at ambient hold (20–24°C). Each unit generated 1 unit of HRBC that was stored for 42 days at 2–6 °C. Study acceptance criteria at 42 days were total haematocrit (HCT) >50% and haemolysis <0.8%. (Agostini *et al*. Poster (ISBT); June 2024)

Safety Study: The safety of HRBC was evaluated in transfusion-dependent cancer (CA) patients who had a haemoglobin (Hgb) transfusion trigger < 9 g/dL, received > 2 units RBCs in 1 transfusion event and diagnosis of MDS/haematologic malignancy, and acutely bleeding burn patients (AB) with total body surface area (TBSA%) burn ≥ 10% and ≤ 50% expected to require > 2 units of RBCs in 1 transfusion event. Adverse events (AEs) up to the subsequent transfusion or 28 days (± 1 day) post-transfusion and changes in Hgb were assessed. (Interim results: Reikvam *et al*. Poster (EHA); June 2023)

Results

Validations: HRBC units were evaluated after processing and after 21 and 42 days of storage (Table 1).

Safety Study

A single centre in Norway enrolled 10 CA and 10 AB patients after approval by the Ethics Committee. All CA and AB patients received one 2-hour transfusion of 2 units HRBC. Patient results are shown in Table 2.

In the anaemic CA cohort, Hgb levels increased 15% after HRBC administration; the AB group had a 2% Hgb increase, due to intra-operative blood loss replacement. One patient experienced 2 SAEs, wound infection and oliguria. No AE was deemed related to the blood product or device.

Conclusion: HRBC represent an innovation in the preparation of blood components. Validation studies demonstrate feasibility of manufacturing without altering the biological characteristics of the product as documented by the quality controls, and no safety issues were seen in a pilot study of CA and AB patients.

Table 1 Validation

	Baseline	Day 21	Day 42
HCT, mean (SD), %			
Germany	61 (2.4)	62 (2.8)*	63 (2.3)
Italy	61 (2.6)	66 (8.1)	63 (5.6)
Norway[a]	57 (1.7)	–	58 (2.6)
Switzerland	60 (2.2)	–	64 (3.4)
Haemolysis, mean (SD), %			
Germany	0.13 (0.02)	0.19 (0.04)*	0.25 (0.07)
Italy	0.10 (0.03)	0.20 (0.09)	0.25 (0.09)
Norway[a]	0.10 (0.03)	–	0.20 (0.05)
Switzerland	0.10 (0.02)	–	0.41 (0.19)[b]

Germany, N=26; Italy, N=30; Norway, N=33 (Bergen) and N=21 (Oslo); Switzerland, N=31.
*Day 23
[a] Average results from two blood banks: Oslo and Bergen
[b] One unit had haemolysis higher than 0.8% (0.81%) at end of storage, but this result remains within 90% acceptance criteria.

Table 2 Patient characteristics and adverse events

	CA (N=10)	AB (N=10)
Male	8	9
Female	2	1
Age, years	72 ± 16	46 ± 19
Pre-Transfusion Hgb, g/dL	8.0 ± 0.7	10.6 ± 2.3
Post-Transfusion Hgb (1 hour), g/dL	9.2 ± 0.8	10.9 ± 2.0
Adverse Events / Related to HRBC	9 / 0	13 / 0
Serious Adverse Events / Related to HRBC	0 / 0	2 / 0

Transfusion efficacy of amustaline/glutathione pathogen-reduced red blood cells: results of a randomised, controlled clinical trial

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Background/Introduction

Pathogen reduction (PR) technologies (PRT) for RBCs are not yet available for routine clinical use. The Red Cell Pathogen Inactivation (ReCePI) study was conducted as part of the clinical development programme for PR RBCs prepared with the amustaline/glutathione PRT (INTERCEPT™ Blood System for RBCs). The ReCePI study compared the safety and effectiveness of conventional and PR RBCs transfused in complex cardiac surgery patients using acute kidney injury (AKI) as an indicator of oxygenation of tissues (Karkouti *et al*. *Br J Anaesth* 2012;109 Suppl 1:i29-i38) and as a predictor of adverse postoperative outcomes, including mortality by day 30 post-surgery (Lassnig *et al*. *Am Soc Nephrol* 2004;1597-1605).

Methods/Study Design

ReCePI is a phase III, randomised, double-blind, non-inferiority study in complex cardiac or thoracic surgery patients. Subjects received conventional (Control) or PR RBCs (Test) during and for 7 days after surgery. The primary endpoint was the incidence of AKI for 48 hours from the start of surgery. The study had 80% power assuming an AKI incidence of 30% with conventional RBCs and a non-inferiority margin of half the conventional rate. Secondary endpoints included AKI occurring up to 7 days post-surgery (KDIGO Clinical Practice Guideline for AKI, *Kidney Int,* Suppl. 2012;2:1-138); death or the need for renal replacement therapy by 30 days post-surgery; PR RBC-specific antibodies; and death by day 75 post-surgery.

Results

Five-hundred and eighty-one subjects were randomised and 321 (55%) transfused in 18 US hospitals using restrictive blood management policies. In the modified intent-to-treat analysis, subjects receiving Test and Control RBCs had similar median [IQR] total blood loss (1 500 [940-2 475] mL Test, 1 733 [1 060-2 880] mL Control, p=0.310) and comparable median haemoglobin levels post-surgery (9.8 [8.9-10.9] g/dL Test, 9.6 [8.6-10.6] g/dL Control, p=0.157) and for 7 days after surgery. Test subjects utilised significantly less median transfused haemoglobin (169 [102-240] g Test, 188 [126-295] g Control, p=0.008). The incidence of AKI was 29.3% (46/157) for Test and 28.0% (45/161) for Control. The treatment difference was 0.74% (95% CI -8.9, 10.4%, non-inferiority margin 14.0%, p=0.001 for non-inferiority). Non-inferiority was also achieved by the per protocol analysis. Five of 159 (3.1%) RBC Test recipients developed antibodies specific to PR RBCs at low titres without clinical signs of haemolysis.

Conclusions

The incidence of AKI in patients transfused with PR RBCs was non-inferior to that observed with conventional RBCs and indicative of good tissue oxygenation in cardiac surgery patients. While treatment-related antibodies were observed in Test subjects, the antibodies were not clinically significant. Besides the known risk of antibodies to PR RBCs (Geisen *et al*. *Transfusion* 2020;60(10):2389-98), there was no increase in alloantibodies, auto-antibodies, adverse events (AEs), severe AEs or deaths. The ReCePI study did not identify any new safety signals associated with the amustaline/glutathione PRT.

Table: ReCePI study primary outcome results

	PR RBCs (Test)	Conventional RBCs (Control)	Treatment difference (95% C.I.) Non-inferiority Margin	p-value
	Subjects n/N (%)	Subjects n/N (%)		
AKI within 48 hrs: Modified Intent-to-Treat Analysis	46/157 (29.3)	45/161 (28.0)	0.74 (-8.94, 10.42) 13.98	0.001
AKI within 48 hrs: Per Protocol-Study RBC Only Analysis	31/129 (24.0)	33/123 (26.8)	-2.62 (-13.00, 7.77) 13.41	0.032

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Free amotosalen does not induce non-specific degranulation of basophils from healthy volunteers *in vitro*

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Introduction

Among labile blood products, platelet concentrates (PCs) are the leading cause of hypersensitivity transfusion reactions. Pathogen reduction technology with amotosalen and UV-A (INTERCEPT™ Blood System IBS) has been implemented for all PCs transfused in France since November 2017. The residual concentration of amotosalen is less than 7.5 µM per PC, resulting in a maximum circulating concentration of 0.4 µM per transfused PC. In order to evaluate whether amotosalen could lead to adverse immunologic responses, we assessed the *in vitro* effect of free amotosalen or neoantigens potentially generated in IBS-treated PCs, on basophil degranulation (BAT test) in the blood of healthy volunteers.

Methods

Free amotosalen (0.0003/0.003/0.03/0.3/3 and 30 µM) – within the range of concentrations potentially reached in the circulation after transfusion – was added to the blood of healthy volunteers (n=5) for 30 min at 37°C. Samples were analysed by flow cytometry to identify the basophil population (IgE^+ $CD203c^+$). Their activation status was assessed by measuring i) the percentage of CD63 positive cells, which correlates with histamine release, and ii) the stimulation index (SI) based on CD203c upregulation calculated as mean fluorescence intensities (MFI) of CD203c on stimulated basophils divided by the MFI of CD203c on resting basophils. Positive controls were obtained by stimulation of blood with a mouse anti-human IgE monoclonal antibody (clone G7-18) and FMLP (an IgE-independent activating peptide). Results were expressed as mean ± SD (n=5), with $p<0.050$ considered significant.

Results

In unstimulated blood, basal CD63 expression on basophils was low (2 ± 2%). Stimulation with the anti-IgE monoclonal antibody or with FMLP led to a significant increase in CD63 exposure on basophils reaching 47 ± 17% ($p=0.012$) and 49 ± 8% ($p=0.001$), respectively. In contrast, stimulation with increasing concentrations of amotosalen led to CD63 exposure levels between 4 ± 3% and 7 ± 4%, which were not statistically different from the resting state ($p>0.050$). The SI of CD203c on basophils reached 2.61 ± 0.46 ($p=0.006$) and 1.80 ± 0.27 ($p=0.012$) in response to the anti-IgE monoclonal antibody and FMLP, respectively. Conversely, the SI of CD203c remained between 1.05 ± 0.05 and 1.12 ± 0.08 in response to increasing concentrations of amotosalen, which was not statistically different compared with controls ($p>0.050$).

Conclusion

These results indicate that a wide range of concentrations of free amotosalen are unlikely to activate blood basophils from healthy volunteers *in vitro*. This study is currently being pursued by evaluating the ability of supernatants from IBS-treated PCs, stored for up to 7 days, to activate basophils *in vitro* in the blood of healthy volunteers.

Author index

All contributing authors are alphabetically listed according to their last name, the authors presenting an abstract at the conference are underlined.

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