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PROGRAM OF ABSTRACTS

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ORAL PRESENTATIONS

POSTER PRESENTATIONS

PresentationS from Sunday, October 2, 2022 to Monday October 3, 2022

Impact of 100% Pathogen Reduction and 7-Day Storage on Platelet Safety and Availability in France

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BACKGROUND/CASE STUDIES: In November 2017 the Établissement Français du Sang (EFS) and the French military converted the national platelet (PLT) supply to 100% pathogen reduced (PR) PLTs using the INTERCEPT® Blood System for Platelets. The shelf-life for PR PLTs in France was extended from 5 to 7 days in 2018-19. We compared the impact of these changes on transfusion reaction (TR) rates, including transfusion-transmitted bacterial infections (TTBI), and blood component use before and after the conversion to PR PLTs and 7-day storage as the national standard of care.

STUDY DESIGN/METHODS: Data on TRs and blood component use were extracted from annual hemovigilance reports published by the national health agency (ANSM). Data were stratified into two 3-year periods: 2015-17 (period 1 [P1]) and 2018-20 (P2). Chi-square, T-test, and Fisher's exact tests were used to describe year-on-year and 2-period trends, respectively. All severity and imputability grades were assessed.

RESULTS/FINDINGS: A total of 801,047 conventional PLTs were issued in France during P1 (79% of PLT supply). All PLTs in P1 had a 5-day lifespan; conventional PLTs were issued without bacterial screening. Fifteen (15) TTBI were associated with conventional PLTs in P1 (range: 2-9/year). One TTBI resulted in a fatality and 5 were life-threatening (severity grade 3). No TTBI were reported among PR PLTs in P1 or for 977,989 PR PLTs issued in P2 following the conversion to 100% PR PLTs and transition to 7-day PLTs. The difference in TTBI rates between P1 and P2 was significant ($p<0.001$). Mean overall TR rates per 100,000 PLTs issued fell from 425 (P1) to 367 (P2) (not significant [ns]), driven by decreases in mean rates for allergic reactions, febrile non-hemolytic transfusion reactions (FNHTR), alloimmunization and immunologic incompatibility. No cases of viral infections against which the INTERCEPT system is effective or TA-GVHD were reported with PR PLTs in either period. The mean rate of grade 3 TRs fell from 7.6 (P1) to 5.2 (P2) per 100,000 PLTs issued. Year-on-year growth in the number of PLTs issued annually increased from 0.4% to 1.6% per year, on average, in P1 and P2 (n.s.), due, in part, to lower dosing parameters and changes in pooling methods. Annual PLT growth stabilized in P2, declining from an increase of 3.8% per year in 2017-18 to an increase of 1.1% per year in 2019-20 after the transition to 7-day storage. The mean rate of ineffective PLT transfusions was unchanged between P1 (12.2) and P2 (12.3). RBC use declined by 5.5% from 2015-2020.

CONCLUSIONS: France has successfully converted from a largely conventional PLT supply without bacterial screening and a 5-day shelf-life to a 100% PR PLT supply with a 7-day shelf-life. The first 3 years of this conversion were marked by a significant reduction in TTBI incidence, improvements in common TR rates, and stable utilization patterns for PLTs and RBCs.

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US.

Psychrotrophic Bacteria Proliferate in Cold-Stored Platelet Components

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BACKGROUND: Platelet components (PC) are routinely stored at 20-24°C for up to 7 days to maintain platelet functionality. Unfortunately, these storage conditions allow contaminant bacteria to proliferate posing a safety risk to transfusion patients. PC stored in refrigeration are currently used by some blood centers to treat actively bleeding patients and it is assumed that cold storage limits bacterial growth. This is a study led by the ISBT Transfusion Transmitted Infectious Diseases Working Party-Bacteria Subgroup, with eight participant laboratories worldwide, that aimed to evaluate proliferation of bacteria, including psychotrophic species, in PC stored at 1-6°C.

STUDY DESIGN/METHODS: The study had a pool and split approach (N≥3) resulting in two PC units which were spiked at a target concentration of 25 colony forming units (CFU)/unit of five bacteria: *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Serratia liquefaciens*, *Pseudomonas fluorescens*, and *Listeria monocytogenes*. One split unit was stored under agitation at 20-24°C (control) for seven days while the second split unit was stored at 1-6°C with no agitation for 21 days. PC stored at 20-24°C were sampled on Days 1, 2, 3, 4 and 7, whereas cold-stored PC were sampled on Days 7, 10, 14, 17, and 21 of storage, to determine bacterial concentration.

RESULTS/FINDINGS: Data collected from 6 participant sites showed that initial inocula ranged from 0.03 to 0.63 CFU/mL. All species proliferated in PC stored at 20-24°C, reaching final concentrations of 10^6 to 10^9 CFU/mL by day 7. However, cold-stored PC only supported growth of psychrotrophic species with *S. liquefaciens* reaching a concentration of ~10^7 CFU/mL by day 10, followed by *P. fluorescens* which grew up to ~10^5 CFU/mL on day 14 of storage, and the slow grower *L. monocytogenes*, which only reached a concentration of ~10^2 CFU/ml on day 21. *S. aureus* and *K. pneumoniae* did not proliferate in cold-stored PC.

SUMMARY/CONCLUSIONS: Psychrotrophic bacteria proliferated during cold storage of PC, with *P. fluorescens* and *S. liquefaciens* reaching clinically significant levels (>10^5 CFU/ml) by days 10 and 14 of storage, respectively. Based on these results, it is recommended to limit cold storage of PC to minimize the potential of bacterial contamination safety risk in transfusion patients unless pathogen reduction is used, and the bacterial safety of cold-stored pathogen reduced PC is further confirmed.

Impact of Pathogen Reduction (PR) *vs*. LVDS Testing on Platelet Availability: A Study Based on Real-Life Experience

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BACKGROUND/CASE STUDIES: Blood shortages continue to raise interest in optimizing blood availability. Two bacterial risk mitigation strategies under the FDA are PR and large volume delayed sampling 48-hour (LVDS 48hr). These methods differentially impact platelet component (PC) availability for release, shelf-life, time to transfusion, and waste. An independent blood center (BC) that supplies >10,000 PC to more than 30 hospitals, assessed PC collection and distribution data to evaluate PC availability when comparing PR (INTERCEPT® Blood System) and LVDS 48hr. PC access also was evaluated at a level II trauma center hospital serviced by the BC. The BC and hospital requested to remain anonymous but reviewed the abstract and agreed with the results and conclusions.

STUDY DESIGN/METHODS: PC data from October 2021 through February 2022 were exported from the blood establishment computer software (BECS) including DIN, PC type, collection date/time, and shipment date/time. PC age at distribution and usable shelf-life were compared between LVDS 48hr and PR; usable shelf-life was calculated based on maximal shelf-life (7 and 5 days for LVDS 48hr and PR, respectively) and ship date/time. PC wastage at BC was also assessed. The hospital provided one month of data including the date/time of transfusion. Data was cross-referenced with the collection information from the BC; the PC age upon transfusion was determined and compared between LVDS 48hr and PR.

RESULTS/FINDINGS: The BC distributed 4,793 components during the study period; 90% were PR PC while the remainder were LVDS 48hr PC. Analysis of collection and distribution data demonstrated average PR PC release 64 hours (2.7 days) earlier with greater remaining usable shelf-life compared to LVDS 48hr PC. Earlier release translated to significantly fewer wasted PC with PR. At the hospital, most of the transfusions occurred between day 3-5 (82%) vs. LVDS 48hr between day 5 and 7 (76%).

CONCLUSIONS: In this study, earlier release of PR PC enabled earlier availability of PC and an extended usable shelf-life, particularly if BC production such as infectious disease testing turn-around time is optimized. Conversely, LVDS 48hr resulted in delayed sampling and a decreased usable shelf-life with increased waste. From a hospital and patient perspective, the comparison of PC age at transfusion demonstrated earlier availability and transfusion of fresher platelets with PR.

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Blood Center Distribution, Shelf Life, and Wastage

	PC Type		
	PR	LVDS 48Hr	p-value
Total # Units	4326	467	--
Average Age at Distribution (Hr)	47.7	112.4	<0.0001*
Usable Shelf-Life at Distribution (Hr)	96.3	79.6	<0.0001*
# Units Wasted (%)	341 (7.9)	120 (25.7)	<0.0001**

** T-Test; p<0.05 is statistically significant.*

***Chi-square test; p<0.05 is statistically significant.*

Monitoring Platelet Storage Age Distribution and Availability after Pathogen Reduction Implementation

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BACKGROUND/CASE STUDIES: Universal pathogen reduction (PR) of platelet concentrates (PC) was implemented in our transfusion service in March 2017. In June 2020, the Brazilian Regulatory Agency allowed for the extension of pathogen-reduced PC (PR-PC) shelf life to 7 days. We have evaluated the PR-PC age distribution, availability and wastage rate compared to the pre-PR implementation.

STUDY DESIGN/METHODS: Data were analysed in three consecutive periods: PC pre-PR (Nov13-Feb17), PR-PC 5-day storage (Mar17-May20) and PR-PC 7-day storage (Jun20-Feb22). Bacterial screening was performed in the pre-PR period on the day of collection, with a minimum of 24hr-hold before release. In the post-PR periods, PCs were treated using amotosalen/ultraviolet A (INTERCEPT®) in the night of the same day of collection and released to the inventory after 16 hrs, with no further bacterial culture. Additional management strategies were improved to avoid PCs wastages such as: a) PC collection control based on assessment of all PC transfusions in the previous 3-day period and projecting a similar demand over the next 3 days; b) PC transfusions issued on a “first in, first out” basis.

RESULTS/FINDINGS: There were 7,912, 7,263 and 3,741 platelet transfusion (PT) doses during the pre-PR, post-PR 5-day and post-PR 7-day storage periods, respectively. The PT dose distribution by storage day for all periods is shown in the table below and $p < 0.05$ was observed for all group comparisons (pre-PR vs. post-PR 5-day; pre-PR vs. post-PR 7-day; post-PR 5-day vs. 7-day).
The proportion of PCs released ≤ 3 days of storage for pre-PR, 5-day and 7-day post-PR were respectively 40.5%, 43.0% and 29.9% ($p<0.001$). The mean±sd storage days were respectively 3.81 ± 1.21, 3.71 ± 1.12 and 4.47 ± 1.54 ($p<0.001$). The wastage rate due to expiring decreased from 9.3% to 3.2% and finally to 0.7% in all 3 periods ($p<0.001$), whereas the dose availability increased by 27.7% in the 7-day period.

CONCLUSION: PR could be implemented as a routine to enhance platelet safety with PR-PC available for transfusion within ≤ 24 hours post-collection. Additionally, the extended PR-PC shelf-life allowed a more efficient inventory management, with significant wastage reduction and increase in platelet transfusion dose availability.

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Table: Platelet Storage Age Distribution in the pre-PR, post-PR 5-day and post-PR 7-day Shelf-life Periods

Number of PT doses by storage age (% of total):				
	pre-PR	**post-PR 5-day**	**post-PR 7-day**	**p***
Day 1	120 (1.5)	28 (0.4)	4 (0.1)	0.0101
Day 2	968 (12.2)	1,040 (14.3)	320 (8.6)	0.0000
Day 3	2,120 (26.8)	2,059 (28.3)	792 (21.2)	0.0000
Day 4	1,993 (25.2)	2,074 (28.6)	870 (23.3)	0.0236
Day 5	2,711 (34.3)	2,062 (28.4)	718 (19.2)	0.0000
Day 6	-	-	555 (14.8)	-
Day 7	-	-	482 (12.9)	-
PT total	7,912	7,263	3,741	-
Mean platelet storage age ± sd	3.81 ± 1.21	3.71 ± 1.12	4.47 ± 1.54	NS
Wastage	9.3%	3.2%	0.7%	NS

PT dose: 3.0 x 10^{11} platelets

p post-PR 7-day vs. pre-PR*

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US.

In Vitro Evaluation of Amicus Platelets in 100% Plasma Prepared with Pathogen Reduction

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BACKGROUND/CASE STUDIES: The pathogen reduction technology (PRT) INTERCEPT® Blood System for platelets, using amotosalen and UVA light, is FDA approved for the *ex vivo* preparation of pathogen-reduced Amicus apheresis platelet components (PCs) in PAS 3 to reduce the risk of transfusion-transmitted infection. This study evaluated the post-storage *in vitro* platelet function of PCs collected on the Amicus Separator, resuspended in 100% plasma, split, with a portion left untreated (Control) versus PRT treated (Test).

STUDY DESIGN/METHODS: This prospective, multi-center, open-label, pool-and-split, *in vitro* study used PCs from healthy volunteer donors. The study compared 65 Test PCs to 65 Control PCs stored through 5 days. PCs contained 3.0-7.2 × 10^{11} platelets in a volume of 290-410 mL. Test PCs were PRT treated using FDA-approved Small Volume, Large Volume, or Dual Storage INTERCEPT processing sets. Test and Control PCs were stored for 5 days at 22°C ± 2°C with continuous agitation. *In vitro* platelet physical and metabolic characteristics were evaluated at Day 5.

RESULTS/FINDINGS: Following PRT, dose recovery was 87 ± 3%, volume recovery was 95 ± 2%, and the mean platelet dose was 3.8 ± 0.9 × 10^{11} platelets. On Days 5 all units had pH22°C >6.2. *In vitro* PC quality at Day 5 was determined (**Table 1**). Test and Control PCs were statistically different for 14 indices. However, parameters indicative of platelet metabolism (pH, ATP, glucose, and lactate) and functional characteristics (MPV, morphology score) were well maintained which is consistent with *in vivo* functionality. Additionally, the level of platelet activation measured by P-selectin expression was not excessive.

CONCLUSIONS: While there were some differences between Test and Control components, PRT Amicus PCs in 100% plasma, using amotosalen/UVA, stored for 5 days retained *in vitro* metabolic and functional properties consistent with *in vivo* functionality.

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Table 1: Day 5 *In Vitro* Summary (Mean±SD) (n=65)

	Untreated	INTERCEPT
Component volume (mL)	288 ± 61	309 ± 51*
Platelet count ($\times 10^3$ cells/μL)	1335 ± 235	1178 ± 205*
Platelet Dose ($\times 10^{11}$ cells)	3.7 ± 0.6	3.7 ± 1.0
$pH_{22°C}$	7.4 ± 0.1	7.4 ± 0.1
pO_2 (μmol/hrs/10^{12} cells)	50.3 ± 13.7	61.9 ± 13.3*
pCO_2 (μmol/hrs/10^{12} cells)	9.3 ± 2.1	8.5 ± 1.9*
HCO_3^- (mmol/10^{12} cells)	9.7 ± 3.0	8.8 ± 2.5*
Supernatant glucose (mmol/10^{12} cells)	10.1 ± 2.4	10.4 ± 2.3*
Supernatant lactate (mmol/10^{12} cells)	3.7 ± 0.6	4.6 ± 0.7*
Total ATP (nmol/$\times 10^8$ cells)	3.9 ± 0.8	3.9 ± 0.8
Morphology	319 ± 12	316 ± 12*
Extent of Shape Change (%)	19.9 ± 4.2	17.5 ± 4.7*
Hypotonic Shock Response (%)	56.7 ± 16.6	52.9 ± 15.9*
Supernatant LDH (U/10^{12} cells)	175.5 ± 47.7	241.6 ± 84.0*
Total LDH (U/mL)	2.9 ± 0.7	2.6 ± 0.6*
Proportional LDH (%)	8.3 ± 2.0	11.0 ± 3.0*
P-selectin (%)	21.4 ± 8.9	27.0 ± 8.5*

** Statistically significant difference ($p<0.05$) between INTERCEPT and Untreated.*

Note: INTERCEPT process is not FDA approved for Amicus 100% plasma.

In Vivo Comparison of Recovery and Survival Methods with Pathogen Reduced Apheresis Platelet Components

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BACKGROUND/CASE STUDIES: *In vivo* recovery and survival studies are required by the FDA for evaluating platelet viability. Prior studies suggest that the Biomedical Excellence for Safer Transfusion Collaboration 4.2.1 (BEST) method for platelet component (PC) radiolabeling negatively biases stored apheresis PC recovery and quality. A variant (Variant 1) of the BEST method in which the steps involving anticoagulation/acidification and soft spin designed to reduce RBC contamination were eliminated was developed. This study compared the *in vivo* recovery and survival of PCs processed for radiolabeling using the BEST versus Variant 1 methods.

STUDY DESIGN/METHODS: This was a randomized, multi-center, two-period cross-over, *in vivo* study performed at two study sites. PCs were collected in 100% plasma on the Trima Separator, pathogen reduced (PR) using amotosalen/UVA (INTERCEPT Blood System for Platelets) and stored at 22 ± 2°C with agitation. *In vivo* post-transfusion recovery and survival of stored PR-PCs (Test) was compared to fresh autologous conventional PCs (Control). Test PCs prepared with either BEST or Variant 1 and Control PCs prepared with the BEST method were labeled according to randomization with either ^{51}Cr or ^{111}In. Autologous radiolabeled Test and Control PCs were then simultaneously infused to the subject. Blood samples through day 11 ± 1 post-infusion were analyzed and used to calculate *in vivo* recovery and survival. Subject procedures for each periods were identical, except for the radiolabeling method (BEST or Variant 1) for Test PCs. Each subject observed a minimum 4-week washout between each period.

RESULTS/FINDINGS: Variant 1 preparation resulted in improved *in vivo* and *in vitro* elution and *in vitro* platelet physical recovery. The mean post-transfusion survival and mean 24-hour post-transfusion recovery were similar for Variant 1 and BEST (**Table 1**). In addition, all Test PCs maintained a pH≥6.2, and active metabolism after storage.

CONCLUSIONS: Variant 1 avoided variable and uncontrolled processing loss of ~30% of the platelets inherent to the BEST method with no change in *in vivo* recovery or survival and avoided increased platelet damage or excessive RBC contamination. Variant 1 had improved in *in vitro* characteristics, notably P-selectin expression. Variant 1 was comparable to BEST in *in vivo* recovery and survival.

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Table 1: Recovery and Survival and Radiolabeling Metrics (Mean±SD) (n=12)

	Test Variant 1 Period		Test BEST Period	
	Test Variant 1	Control BEST	Test BEST	Control BEST
In Vivo Recovery (%)	39.5 ± 10.3	57.8 ± 11.6	39.1 ± 10.6	60.4 ± 10.5
In Vivo Survival (hrs)	150.1 ± 21.6	208.9 ± 15.8	143.2 ± 33.6	202.9 ± 24.4
In Vitro Elution (%)	8.3 ± 3.8	6.3 ± 3.5	12.3 ± 11.5	7.7 ± 5.6
In Vivo Elution (%)	6.9 ± 5.8	4.5 ± 4.0	11.6 ± 12.7	4.3 ± 2.9
RBC Contamination (%)	1.9 ± 3.1	2.6 ± 2.2	2.9 ± 7.7	3.5 ± 4.5
In Vitro Physical Recovery (%)	85.2 ± 6.8		67.7 ± 12.2*	
P-selectin (%)	54.2 ± 21.5		67.2 ± 17.7*	

**p<0.05*

Five Years with Pathogen Inactivation as a New Standard of Care for Blood Safety: The Honduras Experience

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BACKGROUND/CASE STUDIES: The National Blood Program (NBP) of the Honduran Red Cross (HRC) provides 80% of the platelets for Honduras with three distribution centers and two processing facilities. Considering the risk of transfusion-transmitted infections (TTIs) in Honduras with high prevalence of infectious disease in the population, the recurrence of emerging infectious disease outbreaks, and the awareness around bacterial contamination of platelets, HRC decided to implement pathogen reduction (PR). This study reports the positive impact of PR on platelet availability and inventory management.

STUDY DESIGN/METHODS: After balancing the benefits and cost of PR, the negative impact of bacterial screening on blood availability, HRC decided to implement the INTERCEPT Blood System for Platelets to treat 100% of the platelet components (PC). PC production methods were changed to random donor platelets (RDP) where whole blood-derived PRP platelets resuspended in 100% plasma are pooled by 6 before PR treatment by the end of collection day (Day 0). PR-PC, released on Day 1, are then stored for up to 7 days.

RESULTS/FINDINGS: Processing workflow was modified and now allows for early release of PR-PC on Day 1 post-collection as serology and NAT testing results are released with PR-PC meeting the local and AABB guidelines for adult platelet doses (≥3.0 x 10^{11}, $pH_{22°C}$ ≥6.2). PR implementation allowed for PC standardization with predictable platelet dose resulting in a change of transfusion practice going from one PRP/10kg patient weight to a transfusion of a well-defined platelet dose of ≥3.0 x 10^{11} platelets/adult product, which is well received by the physicians. Products are released on Day 1 at the same time as current production and have a shelf-life of up to 7 days. This means that PR-PC are available for two more days for distribution, accommodating hospital emergencies with available stock supply. Product discard using the previous workflow was >23% of collection and after PR implementation, the discard rate decreased to <0.06% of the units obtained over the last four years (**Table**). In addition, hospitals improved their inventory management so that PR-PC are transfused more efficiently.

CONCLUSION: HRC was able to implement pathogen reduction to treat 100% of its platelet production making INTERCEPT platelets a new standard of care in Honduras. Since PR implementation in 2016, better management of inventories, resources, and personnel has contributed to reducing costs.

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Table:

Year	Produced	Wasted	Percentage
2016	19737	4442	22.5%
2017	17459	4132	23.6%
2018	20805	1026	0.04%
2019	28070	0	0.0%
2020	11437	15	0.001%
2021	17008	3077	0.18%

The INTERCEPT Blood System for 7 day storage of platelets is not approved in the US.

Comparing Usable Shelf-Life of Pathogen Reduced Platelets vs LVDS Screened Platelets

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BACKGROUND/CASE STUDIES: Inventory management for platelet components (PC) can be challenging given the short shelf-life; PC availability is essential as shortages can adversely impact patients including delays in treatments and surgeries. Our blood center supplied over 150,000 PC to more than 250 hospitals in 2021; we evaluated the impact that different bacterial mitigation strategies per FDA guidance have on PC availability in terms of time to release, usable shelf-life, and time to transfusion, from blood center and hospital transfusion services perspectives. The strategies assessed were large volume delayed sampling at 36 and 48 hours (LVDS 36hr, LVDS 48hr) and pathogen reduction using the INTERCEPT Blood System (PR).

STUDY DESIGN/METHODS: PC data, including product description, collection, labeling, and shipment times and dates, were obtained and analyzed from collections spanning a two-and-a-half-month timeframe to determine PC age and usable shelf-life at release. Usable shelf-life was calculated based on absolute shelf-life (7 days for LVDS 48hr and 5 days for LVDS 36hr and PR) and distribution time. PC data, including time of receipt and time at transfusion, from January through February 2022, was also obtained from a large Central Florida hospital where we are the sole blood provider. Remaining shelf-life at the hospital and PC age at transfusion were determined and compared between LVDS 36hr, LVDS 48hr, and PR.

RESULTS/FINDINGS: We manufactured a total of 10,850 PC during the study period; 60%, 30%, and 10% were PR, LVDS 36hr, and LVDS 48hr PC, respectively. Approximately 980 units were received at the hospital; 63%, 33%and 4% were PR, LVDS 36hr and LVDS 48hr PC, respectively. Analysis of collection and distribution data demonstrated that PR PC were released 24 hours earlier than LVDS 36hr PC and 43 hours earlier than LVDS 48hr PC. Usable shelf-life at our blood center and at the hospital were least for LVDS 36hr PC and approximately equivalent between PR and LVDS 48hr PC. The difference in mean age was 2.2 days younger for PR PC (2.9 days) vs LVDS 48hr (5.1 days).

CONCLUSION: We demonstrated that earlier release of PR PC translates to sooner availability, equivalent shelf-life, and transfusion of fresher PC for patients vs LVDS 48hr. Conversely, LVDS 48hr PC delayed sampling and hold times may adversely impact product release and usable shelf-life.

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PC Age and Usable Shelf-Life at the Blood Center and Hospital

	Blood Center			Hospital		
PC Type	Total # PC Manufactured	Average Age at Distribution (Hr)	Usable Shelf-Life at Distribution (Hr)	Total # PC Received	Usable Shelf-Life at Hospital (Hr)	Average Age at Transfusion (Days)
PR	6469	44.2	99.8	618	89.9	2.9
LVDS 36HR	3237	68.6	75.4	321	64.2	3.6
LVDS 48HR	1144	87.2	104.8	43	87.8	5.1

Estimating the Impact of MSM Donor Inclusion on Platelet Donations

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BACKGROUND: Potential donors deferred as 'men-who-have-sex-with-men' (MSM) and their allies have broadcast their interest in donating blood, prompting the question of what the impact may be of deploying pathogen reduction (PR) technology as an alternative to the MSM deferral (currently the U.S. requires 3 months abstinence). Assuming blood center deferral data do not reflect the scope of available MSM donors due to self-deferral, this study estimates the number of MSM donors in one Florida county that could be recruited, and the resulting transfusable products, if MSM were allowed to donate for PR platelets.

METHODS: To obtain a conservative estimate of the number of new donors and products that might be accrued, data was gathered from one county in Florida. First the number of MSM residing in the county was estimated based on census and other survey data. CDC surveillance data were then used to estimate the number of men in the county living with HIV; although not all these men are MSM, this number was eliminated from the possible pool. HIV pre-exposure prophylaxis (PrEP) was likewise estimated from available data and excluded from the total number of possible donors. The percentage of men from the general population who donate blood, and their rate of deferral for other reasons, was assumed to be the same for this new group of donors. Donor statistics from a regional blood center on platelet donation frequency and the average number of products per donation were applied.

FINDINGS: Based on the demographics for this one county, an estimated 781 currently ineligible MSM donors could provide over 9,000 additional platelet products per year, more than doubling current collections.

CONCLUSION: Estimates not withstanding, every additional donor counts, and every donation is important. The estimates calculated here indicate that nearly 800 MSM in this one county might be eligible and willing to become platelet donors. While not guaranteeing a specific outcome, this donor population could have a significant impact on platelet availability.

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Table 1: Estimates of New Donors and Products

	Calculation	Result (#)
Men in County >18 years (y)		177,253
# Gay/bisexual men	(#Men >18 y) x (4.6% LGBTQ Adults in FL)	8,154
Potential new MSM donors who are ineligible because of PrEP use or living with HIV	(Men on PrEP) + (Men with HIV)	2,247
Potential new MSM donors	(# Gay/bisexual men) – (Ineligible donors)	5,907
Men who donate blood (15%)	(Potential new MSM donors) x15%	886
Men deferred for reasons other than MSM (11.8%)	(Men who donate blood) x11.8%	105
Corrected # of potential MSM donors	(Men who donate blood) – (# Men deferred for reasons other than MSM)	781
Average # donations annually		5.9
Average # of products per donation		2
Additional products estimated annually	(Corrected # of potential MSM donors) x (Avg donations annually) x (Avg products per donation)	9,215

The INTERCEPT Blood System for platelets and plasma is not approved for replacement of MSM deferral in the US.

Preparation of Pathogen Reduced Plasmas from Maxi-Pools Combined with Fast Thawing

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BACKGROUND/CASE STUDIES: The preparation of 12 frozen plasma units, pooled and pathogen reduced (PR) in "maxi-pools" with amotosalen and UVA light, and fast thawing in a radio-wave device was evaluated.

STUDY DESIGN/METHODS: 120 WB-derived leukocyte depleted plasma units were frozen within 24 hours at ≤25°C and stored for 7 days. After thawing in a dry Sahara (Sarstedt) plasma thawer, 10 maxi-pools of 10 A, B or AB, weight-selected, plasma units were constituted. After splitting each into 4 sub-pools of 650 mL, they were PR treated with A-UVA (INTERCEPT™ Blood System, Cerus Corp.). Further splitting into units of 3 results a total of 12 PR plasma units at 200 mL. The units were frozen at ≤25°C for 1 week, then thawed either in a CS201 (Conroy) fast plasma thawer for 5 min or in other control devices (Barkey Plasmatherm and Sahara, 17 to 23 min). Factor VIII, Fibrinogen, albumin, IgG, Protein S, and VWF were measured in plasma units, maxi-pools, and plasmas after PR treatment and thawing.

RESULTS/FINDINGS: Factor VIII and fibrinogen levels were not significantly reduced after freezing and thawing procedures. However, after pathogen reduction, there was a statistically significant ($p<0.05$) but still clinically acceptable reduction of these levels with 69% and 87% recovery for Factor VIII and fibrinogen, respectively. These concentrations are still over the recommended levels of ≥0.5 IU/mL and ≥2 g/L. Only Factor VIII was lower ($p<0.05$) using control devices versus the CS 201 fast thawer. Other studied proteins were not significantly affected in the processes. Relative decrease of protein S seen after final thawing may be due to analyzing method with CV ~10%.

CONCLUSION: Pooling 10 plasma units before the A-UVA PR treatment provides a standardization of volume and protein content of plasma units, besides the economic value of generating 12 products for transfusion. This procedure combined with a thawing time of plasmas of about 5 minutes is of value in emergency situations and may reduce plasma wastage.

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Table: Plasma Assays Before, After Pooling and In Split Units After PR and Thawing (Mean ± SD [min;max] n.t. = not tested

Parameter	Plasma units (N=100) Non-frozen	Plasma units (N=100) Frozen, thawed	Maxi-pools of 10 units (N=10) Frozen, thawed	Plasma units after A-UVA PR, 7-day ≤25°C storage, and thawing (N=20)	
				CS 201	Control thawers
Factor VIII:C (IU/mL)	n.t.	1.07 ± 0.3 [0.5;2.3]	1.08 ± 0.1 [0.91;1.32]	0.72 ± 0.06 [0.59;0.88]	0.68 ± 0.08 [0.52;0.88]
Fibrinogen (g/L)	2.7 ± 0.4 [1.7;4.0]	2.6 ± 0.4 [1.6;3.8]	2.6 ± 0.4 [2.4;2.8]	2.3 ± 0.1 [2.1;2.5]	2.3 ± 0.1 [2.1;2.6]
Albumin (g/L)	n.t.	33 ± 2 [27;39]	33 ± 2 [31;35]	33 ± 1 [32;33]	32 ± 1 [32;33]
IgG (g/L)	n.t.	8.66 ± 1.57 [4.6;13.3]	8.63 ± 0.52 [8;9.4]	8.55 ± 0.52 [7.7;9.3]	8.65 ± 0.05 [7.8;9.3]
Protein S (IU/mL)	n.t.	0.94 ± 0.17 [0.62;1.5]	0.94 ± 0.05 [0.84;1.02]	0.82 ± 0.08 [0.71;1.00]	0.84 ± 0.05 [0.74;0.93]
vWF (IU/mL)	n.t.	1.21 ± 0.37 [0.47;2.85]	1.19 ± 0.14 [0.99;1.5]	1.09 ± 0.13 [1.0;1.49]	1.10 ± 0.13 [0.94;1.43]

The INTERCEPT Blood System for plasma is not approved for post-thawed plasma pathogen reduction treatment in the US.

Pathogen Reduced Cryoprecipitated Fibrinogen Complex Restores Fibrinogen Levels, Clot Firmness and Thrombin Generation in a Hemodilution Model

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BACKGROUND/CASE STUDIES: Trauma induced coagulopathy (TIC) with coagulation activation, hyper-fibrin(ogen) lysis, and consumptive coagulopathy requires transfusions of plasma, platelets, and red blood cells (RBCs). Transfusion of large volumes of RBCs, platelets and plasma can result in dilution of fibrinogen (FIB) with poor clot formation. Transfusion of FIB enriched concentrates including Cryo-AHF (Cryo) and pathogen reduced cryoprecipitated fibrinogen complex (IFC) has the potential to increase FIB levels to improve fibrin clot formation. A dilutional coagulopathy (DC) model was used to evaluate the effects of Cryo, IFC, and FFP supplementation.

STUDY DESIGN/METHODS: Whole blood (WB,1.6 mL) was diluted 60% by the addition of Plasma-Lyte (Baxter) tomimic hemodilution with crystalloid. Washed RBCs were added to simulate RBC transfusion. FFP, IFC (Day 1 post-thaw) or Cryo were added back in 0.5–2.0 mL doses. The DC mixture was centrifuged to form platelet poor plasma (PPP). FIB and FVIII activity were measured by coagulation analyzer. Thrombin generation (TGA) was performed using a calibrated automated thrombogram (Diagnostica Stago). Thromboelastometry (FIBTEM) was used to assess fibrin clot formation.

RESULTS/FINDINGS: Cryo contained 1901 ± 83mg/dL of FIB, IFC contained 930 ± 21 mg/dL FIB and FFP contained 340 ± 25mg/dL FIB. WB mean baseline prior to dilution were: FVIII (79 ± 12IU/dL) and FIB (327 ± 20 mg/dL) and were FVIII (25 ± 5IU/dL) and FIB (97 ± 8 mg/dL) after dilution. Addition of 0.5 to 2.0 mL of Cryo and IFC without FIB dose adjustment decreased clotting time (CT) more than FFP (**Table**). Addition of Cryo, IFC, or FFP, resulted in dose-dependent increase in mean clot firmness (MCF). Addition of 0.5 to 2.0 mL of IFC, Cryo or FFP restored endogenous thrombin potential to comparable WB baseline levels.

CONCLUSIONS: In a model of DC, addition of IFC or Cryo corrected key coagulation parameters: FIB, CT, and TGA more than FFP. This suggests that early use of enriched sources of FIB including IFC stored thawed for 5 days offers the potential to improve TIC and may reduce the need for FFP or platelets transfusions.

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Table

FIB Source (n=6)	ǂFIB Level / FIB Dose			FIBTEM						TGA		
	CRYO	IFC	FFP	CRYO	IFC	FFP	CRYO	IFC	FFP	CRYO	IFC	FFP
Sample	ǂmg/dL			CT (sec)±SD			MCF (mm)±SD			ETP (nM• min)± SD		
WB Baseline	NA	NA	NA	60±23	68±7	74±3	18±5	16±2	15±4	1604±183	1764±239	1582±313
Diluted WB	NA	NA	NA	110±55	90±22	146±172	7±2	6±1	6±2	1847±236	1961±136	1697±168
0.5 FIB	0.15	0.15	0.10	52±4	56±6	71±12	20±2	13±1	8±2	2021±172	1930±139	1808±126
1.0 FIB	0.27	0.24	0.18	46±1	49±5	63±9	31±2	18±1	10±2	2143±147	2001± 152	1961±270
1.5 FIB	0.35	0.33	0.24	42±2	47±2	59±6	41±2	24±3	11±2	2073±160	1935±109	1879±121
2.0 FIB	0.41	0.38	0.25	39±1	45±1	59±4	45±2	26±1	12±2	2190±152	1877±100	1938±214

NA = not applicable

ǂmg/dL of FIB = [FIB sample] – [FIB diluted WB] /[Starting FIB in Cryo, IFC or Plasma]

In the United States, cryoprecipitated AHF manufactured from INTERCEPT® Plasma must be transfused within six hours of thaw. Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT® Fibrinogen Complex) manufactured using the INTERCEPT Blood System for Cryoprecipitation may be stored at room temperature for five days, post-thaw.

Survival and Growth of Bacteria during Manufacturing and Storage of Cryo-AHF Compared to Pathogen Reduced Cryoprecipitated Fibrinogen Complex

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BACKGROUND/CASE STUDIES: Cryoprecipitated-AHF, with a limited post-thaw shelf life of 4-6h at room temperature is used to treat major bleeding. Post thaw storage of CRYO-AHF and pooling of multiple units have raised safety concerns regarding donor exposure and transfusion transmitted infections including sepsis. The INTERCEPT® Blood System for Plasma inactivates a wide range of pathogens in plasma and in combination with the FIBRICEPT™ Processing Container allows for manufacturing of Pathogen Reduced Cryoprecipitated Fibrinogen Complex (INTERCEPT® Fibrinogen Complex, IFC) with an extended post-thaw shelf life of ≤ 5 days.

STUDY DESIGN/METHODS: To determine the growth of bacteria in plasma during hold conditions, 10-100 cfu of *Serratia marcescens* were inoculated into each plasma unit. One arm was held 18h at 25°C and the second arm was held 22h at 4°C. Bacterial titer was assessed after the hold time and post-INTERCEPT treatment.

To assess *S. marcescens* survival during the manufacturing and storage of cryo-AHF and IFC, pooled plasma was split into individual arms that were either INTERCEPT-treated or left untreated. *S. marcescens* (~1000 cfu) were inoculated into each test arm prior to processing. The arm for preparing IFC was treated with the INTERCEPT plasma kit and titer was assessed pre- and post-treatment and post-CAD. The INTERCEPT treated plasma was frozen at -80°C for 24h alongside the untreated arm for preparing cryo-AHF. Then all units were thawed and manufactured into cryo-AHF or IFC followed by another 24h freeze/thaw cycle. Bacterial titer was assessed pre- and post-thaw at 0h, 6h, 5d, and 14d.

RESULTS/FINDINGS: Significant bacterial growth in untreated contaminated plasma was observed after a hold at 25 °C (3.7 x 10 ± 2.7 x 10 cfu /unit) compared to 4°C (17 ± 13 cfu /unit). No bacteria were detected by the end of 14d storage for IFC manufactured with contaminated plasma. However, bacteria were observed in untreated cryo-AHF manufactured with contaminated plasma even after multiple freeze/thaw cycles (**Table**).

CONCLUSIONS: Plasma stored at 4°C slows proliferation of bacteria but does not kill bacteria. The INTERCEPT Blood System for Plasma successfully inactivated *S. marcescens* in IFC. The data indicate IFC remains sterile post-thaw for up to 14 days at 25°C for the tested organism.

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Table: Detection of *S. marcescens* During Cryo-AHF and IFC Manufacturing

Manufacturing Step		Titer (cfu/unit)	
		INTERCEPT	Cryo-AHF
Pre-Freeze		1261 ± 293	1273 ± 292
Post-illumination		0	-
Post-CAD		0	-
Post-Thaw		0	998 ± 436
Cryo Pre-Freeze		0	1224 ± 1026
Cryo Post-Thaw	0h	0	326 ± 55
	6h	0	131 ± 114
	5d	0	Too Numerous to Count
	14d	0	2.57 x 10 ± 4.95 x 10 cfu/mL

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Use of INTERCEPT Plasma, Platelets, and Pathogen Reduced Cryoprecipitated Fibrinogen Complex are contraindicated in patients with a history of allergic response to amotosalen or psoralens.
Consult instructions for use for indications, contraindications, warnings, and precautions.