New and Old Infectious Threats – Risks and Countermeasures

16.Střešovice Transfusion Day, November 15th, 2023

Dr. Marcus Picard-Maureau
Sr. Scientific Affairs Director EMEA

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Conflict of Interest

Marcus Picard-Maureau is employee and shareholder of Cerus Europe B.V., the manufacturer of the INTERCEPT Blood System

Agenda

1. Old Viral Risk – Still There?
2. Emerging (Arbo) Viruses
3. Preparedness – What Comes Next?
4. Bacterial Risk
5. Pathogen Inactivation for Platelets – All the Same?
6. New Applications for Safer Components
7. Closing

1. Old Viral Risk – Still There?

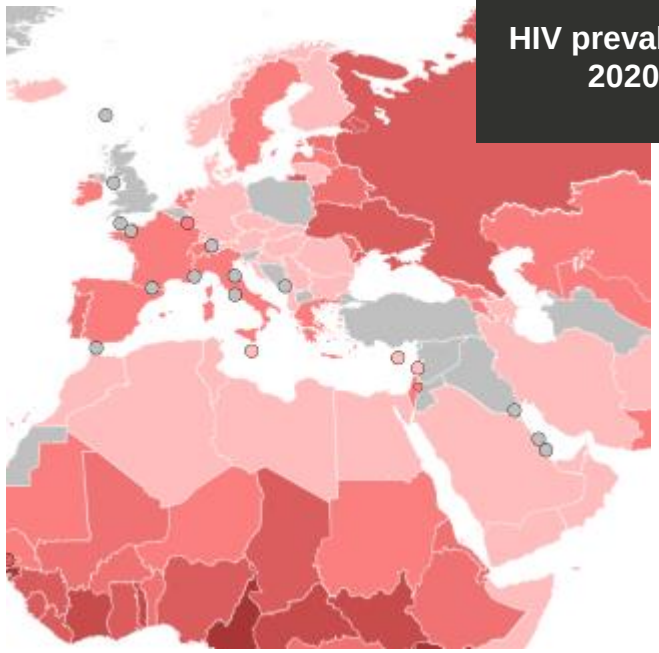
The 3 major pathogens: HIV, HBV, HCV

The Polaris Observatory HCV Collaborators. Global prevalence and genotype distribution of hepatitis C virus infection in 2015: a modelling study. *Lancet Gastroenterol Hepatol*. 2017;2:161–76.

Serology and NAT standard in almost all blood centers

Risk & Window Periods:

HIV: ~1: 2.9×10^6	11 d
HBV: ~1: 3×10^5	~34 d
HCV: ~1: 2.5×10^6	12 d



https://commons.wikimedia.org/wiki/File:World_map_of_countries_by_HIV-AIDS_adult_prevalence_rate_%282020%29.svg

Transfusion transmission by Serology and NAT negative donors regularly reported (low numbers)

Transfusion transmission possible in rare cases:

- Low viral load below LOD
- Window period
- New variants

Dwyre DM et al., 2011. Hepatitis B, hepatitis C and HIV transfusion-transmitted infections in the 21st century *Vox Sang* 100: 92-98

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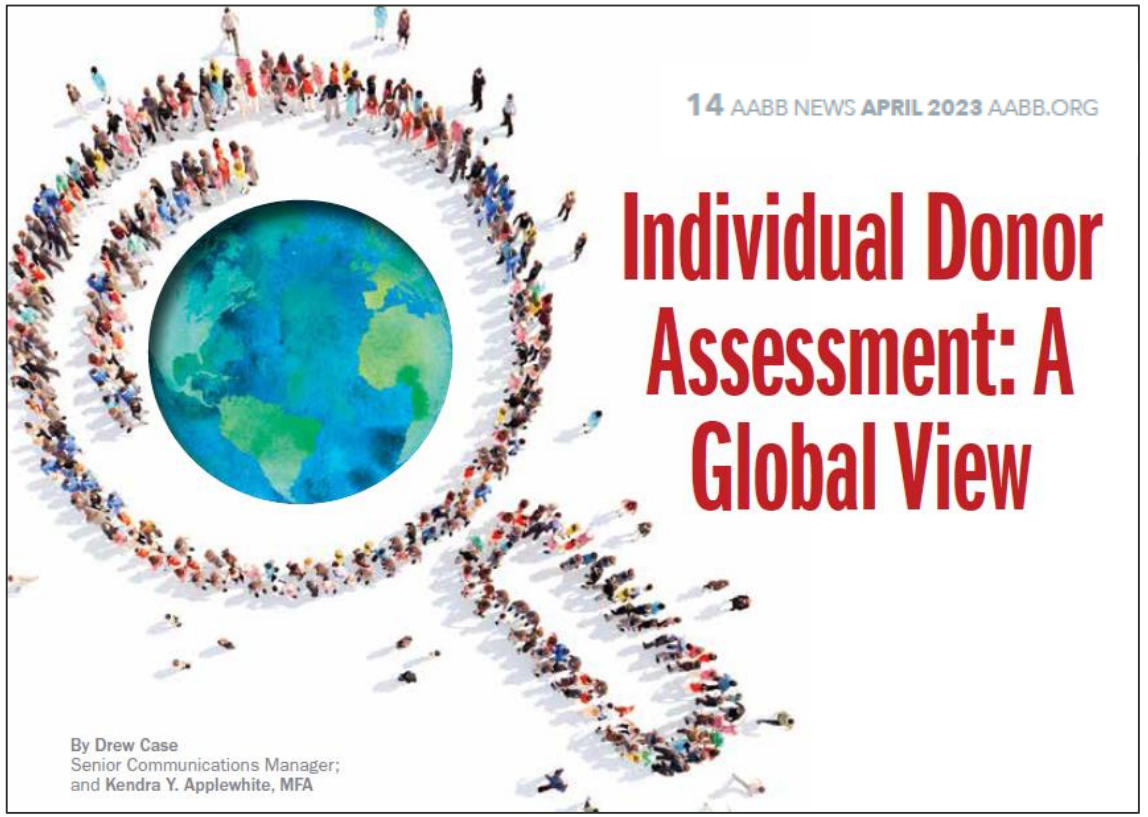
HIV – aren’t we testing?

Individual Donor Assessment

- MSM donors were in many countries **deferred indefinitely or for a certain period** of months/years after the last sexual contact.
- Such deferrals **were justified by an increased risk of MSM donors for transmission of STDs** (sexually transmitted diseases), especially HIV, HBV, HCV, Syphilis.
- **Assessing sexual risk behavior of donors individually** (w/o taking the sexual orientation into consideration) is becoming the standard in many countries.
- Are there any implications for **blood safety?**



Case D & Applewhite KY., 2023. Individual donor assessment: a global view. *AABB News* 25: 14-16

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Risk Profile of MSM donors

Received: 14 October 2022 | Revised: 21 March 2023 | Accepted: 26 May 2023
DOI: 10.1111/vox.13482

REVIEW

Vox Sanguinis ISBT International Society of Blood Transfusion

Men who have sex with men and risk for transfusion-transmissible infections in blood donors in Western countries: A systematic review update

Natalie Schroyens[1,2] | Vere Borra[1,2] | Veerle Compernolle[3,4] | Philippe Vandekerckhove[2,5,6] | Emmy De Buck[1,2]

Conclusion: There may be an increased risk of HIV in MSM blood donors. Shortening the deferral from permanent to 1 year may have little to no effect on TTI risk. However, there is limited, unclear evidence from observational studies concerning the impact of introducing 3-month or risk-based deferrals.

TABLE 4 Twelve Type III (case-control) studies.

Study	Donor population	Risk factor	Outcome				
			HIV	HBV (anti-HBC)	HBV (HBsAg)	HCV	HTLV-I/II
Allison, 2012, USA [47]	469 cases versus 217 false-positive controls	MSM	–	–	–	**RR: 8.79 [1.18; 65.25]**	–
Bruhn, 2021, USA [34, 38]	224 HIV cases, 11 male recent HBV cases, 18 male recent HCV cases, 553 false-positive controls (for HBsAg or anti-HIV)	MSM or sex with MSM during the past 12 months	**aOR: 16.7 [3.8; 74.4]**	–	–	OR: 1.50 [0.40; 5.60]	–
Busch, 1994, USA [35]	129 cases versus 131 age-matched controls (all males)	MSM	**OR: 45.0 [10.66; 189.84]**	–	–	–	–
Christensen, 2001, Denmark [39]	37 HBV cases versus 553 false-positive controls	Sex with homo/bisexual male	–	aOR: 5.44 [0.52; 50.20]	–	–	–
Custer, 2014/5, USA [36, 37]	149 HIV cases, 190 HBV cases, 45 HTLV-I/II cases versus 761 false-positive controls (all males)	MSM or sex with MSM	**aOR: 62.3 [27.6; 140.4]**	–	/ (HBV NAT)	–	RR: 2.60 [0.61; 11.18]

Schroyens M et al., 2023. Men who have sex with men and risk for transfusion-transmissible infections in blood donors in Western countries: A systematic review update. *Vox Sang* doi: 10.1111/vox.13482. Online ahead of print.

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Received: 10 March 2021 | Revised: 16 June 2021 | Accepted: 16 June 2021
DOI: 10.1111/vox.13176

ORIGINAL ARTICLE

Vox Sanguinis ISBT International Society of Blood Transfusion

HIV residual risk in Canada for apheresis source plasma donation without deferral for men who have sex with men

Eliana Aubé[1,2] | Antoine Lewin[2,3] | Sheila F. O'Brien[4] | Yves Grégoire[5] | Josiane Pillonel[6] | Whitney R. Steele[7] | Brian Custer[8,9] | Katy L. Davison[10] | Marc Germain[5] | Clive R. Seed[11] | Félix Camirand Lemyre[1,12] | the Surveillance, Risk Assessment and Policy Subgroup of the ISBT Transfusion Transmitted Infectious Diseases Working Party

Conclusion: Based on simulation results, there would be a negligible HIV residual risk associated with the removal of a time-based MSM deferral without quarantine for source plasma incorporating PI.

TABLE 4 Human immunodeficiency virus (HIV) risk estimate

	Deferral model	Most likely	Optimistic	Pessimistic i	Pessimistic ii	Worst-case
HIV positive donations per 1,000,000 donations	3-month deferral	2.79	2.71	5.10	5.68	–
	No deferral	3.01	2.86	5.96	6.32	57.4
Number of pools with a viral load (in 300,000 pools)	3-month deferral	1323	1259	2885	3136	–
	No deferral	1483	1335	3719	3994	8617
Mean viral concentration per pool after NAT and PI (RNA copies/ml)	3-month deferral	1.93×10^{-14}	1.82×10^{-14}	1.95×10^{-13}	1.97×10^{-14}	–
	No deferral	1.95×10^{-14}	1.66×10^{-14}	1.95×10^{-14}	2.01×10^{-14}	2.81×10^{-13}
Probability of getting a pool with a viral load	3-month deferral	0.00441	0.00420	0.00962	0.01045	–
	No deferral	0.00494	0.00445	0.01240	0.01331	0.02872
Mean copies per pool after NAT and PI (RNA copies/pool)	3-month deferral	9.76×10^{-8}	9.17×10^{-8}	9.75×10^{-8}	9.73×10^{-8}	–
	No deferral	9.79×10^{-8}	8.16×10^{-8}	9.70×10^{-8}	1.00×10^{-7}	1.63×10^{-6}
Median copies per pool after NAT and PI (RNA copies/pool)	3-month deferral	1.75×10^{-8}	1.55×10^{-8}	1.65×10^{-8}	1.72×10^{-8}	–
	No deferral	1.47×10^{-8}	1.49×10^{-8}	1.59×10^{-8}	1.64×10^{-8}	1.63×10^{-8}
Maximum copies per pool after NAT and PI (RNA copies/pool)	3-month deferral	1.77×10^{-6}	1.15×10^{-6}	2.05×10^{-6}	1.99×10^{-6}	–
	No deferral	2.20×10^{-6}	1.26×10^{-6}	2.00×10^{-6}	2.28×10^{-6}	0.01041

Abbreviations: NAT, nucleic acid testing; PI, pathogen inactivation.

Aube E et al., 2021. HIV residual risk in Canada for apheresis source plasma donation without deferral for men who have sex with men. *Vox Sang* 117: 201-2017

Aube E et al., 2022. HIV residual risk in Canada for apheresis source plasma donation without deferral for men who have sex with men. *Vox Sang* 117: 201-207

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U=U?

VoxSanguinis
The International Journal of Transfusion Medicine
ISBT International Society of Blood Transfusion
Vox Sanguinis (2019) 114, 628–630
© 2019 International Society of Blood Transfusion
DOI: 10.1111/vox.12790

COMMENTARY

Undetectable does not equal untransmittable for HIV and blood transfusion

Iain B. Gosbell,[1,2] Veronica C. Hoad,[3] Claire E. Styles,[3] June Lee[3] & Clive R. Seed[3]
[1] Clinical Services and Research, Australian Red Cross Blood Service, Sydney, NSW, Australia
[2] School of Medicine, Western Sydney University, Penrith, NSW, Australia
[3] Clinical Services and Research, Australian Red Cross Blood Service, Perth, WA, Australia

PARTNER and PARTNER2 study with 130.000 condom-less sex acts between an HIV-positive (under ART with a viral load <200 IU/mL) and HIV-negative partner

Rodger AJ et al., 2016. *JAMA* 316: 171-181; Rodger AJ et al., 2019. *Lancet* 393: 2428-2438

No transmission by sexual contact with viral serum load below 200 copies/mL

A minimum infectious dose of 291 copies in plasma PER UNIT was published (approx. 1.5 copies/mL)

With 10 copies/mL, 30 mL of plasma would be potentially infectious

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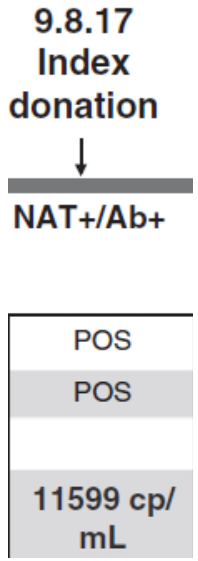
HIV Transfusion-Transmission in France 2017



Cappy P et al., 2019. Transfusion of HIV-infected blood products despite highly sensitive nucleic acid testing. *Transfusion* 59: 2046-2053

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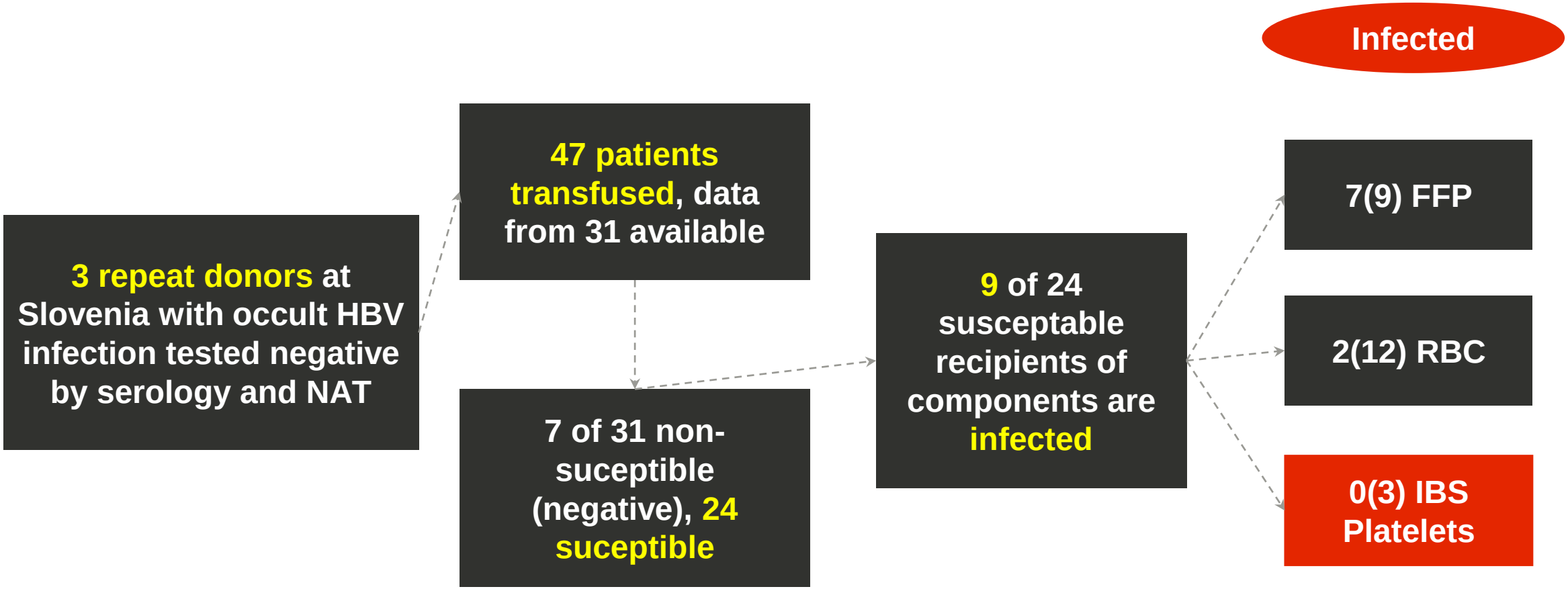
HBV and HCV – still there?

HBV-Transfsuion-Transmission in Slovenia, 2018



Candotti D et al., 2019. Multiple HBV transfusion transmissions from undetected occult infections: revising the minimal infectious dose. *Gut* 68: 313-321.

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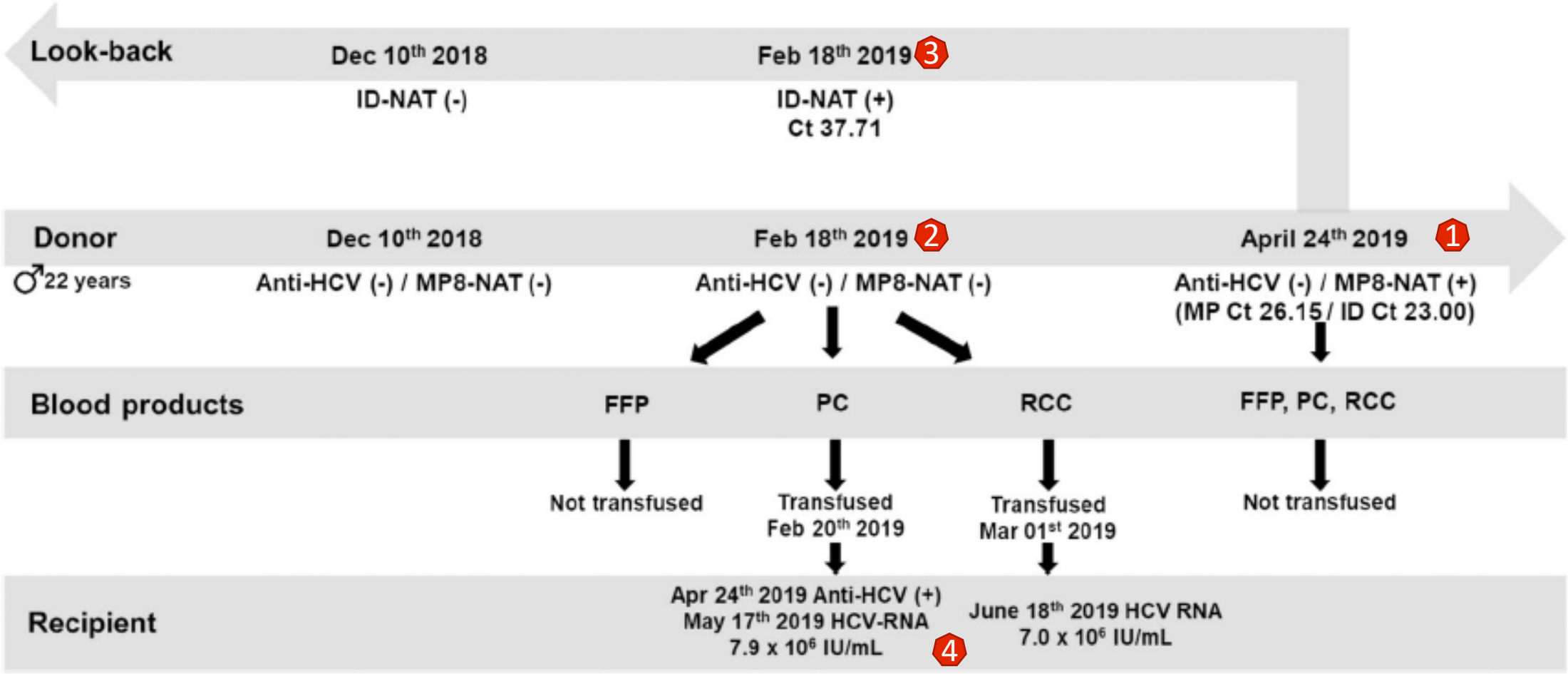
HCV Transfusion-Transmisison in Germany, 2019



Himmelsbach K et al., 2022. Second hepatitis C virus transmission by blood components since introduction of mandatory NAT screening in Germany. *Transfusion* Dec 14: doi: 10.1111/trf.17224. Online ahead of print.

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2. Emerging (Arbo) Viruses

Transfusion-Transmitted Arboviruses

PLOS NEGLECTED TROPICAL DISEASES

- The authors conducted a systematic literature search to assess (no start date, end date Nov 10, 2021) assessing **reported cases arbovirus transfusion transmission.**

- The data is used to assess the **risk for blood safety**.

RESEARCH ARTICLE

Transfusion-transmitted arboviruses: Update and systematic review

Ángel Giménez-Richarte[1]*, María Isabel Ortiz de Salazar[1], María-Paz Giménez-Richarte[2], Miriam Collado[1], Pedro Luís Fernández[1], Carlos Clavijo[1], Laura Navarro[1], Cristina Arbona[1], Pascual Marco[3,4], Jose-Manuel Ramos-Rincon[4]*

1 Valencian Community Blood Transfusion Center, Valencia, Spain, **2** Medicial student, Miguel Hernandez University of Elche, Alicante, Spain, **3** Service of Hematology, General- University Hospital of Alicante-ISABIAL. Alicante, Spain, **4** Clinical Medicine Department, Miguel Hernandez University of Elche, Alicante, Spain

* gimenez_ang@gva.es (AG-R); jose.ramosr@umh.es (J-MR-R)

- The majority of reported cases are **WNV (57%)** and **DENV** transfusion-transmissions **(24%).**

- **86%** of cases are viruses which are reported to be **effectively inactivated by INTERCEPT**

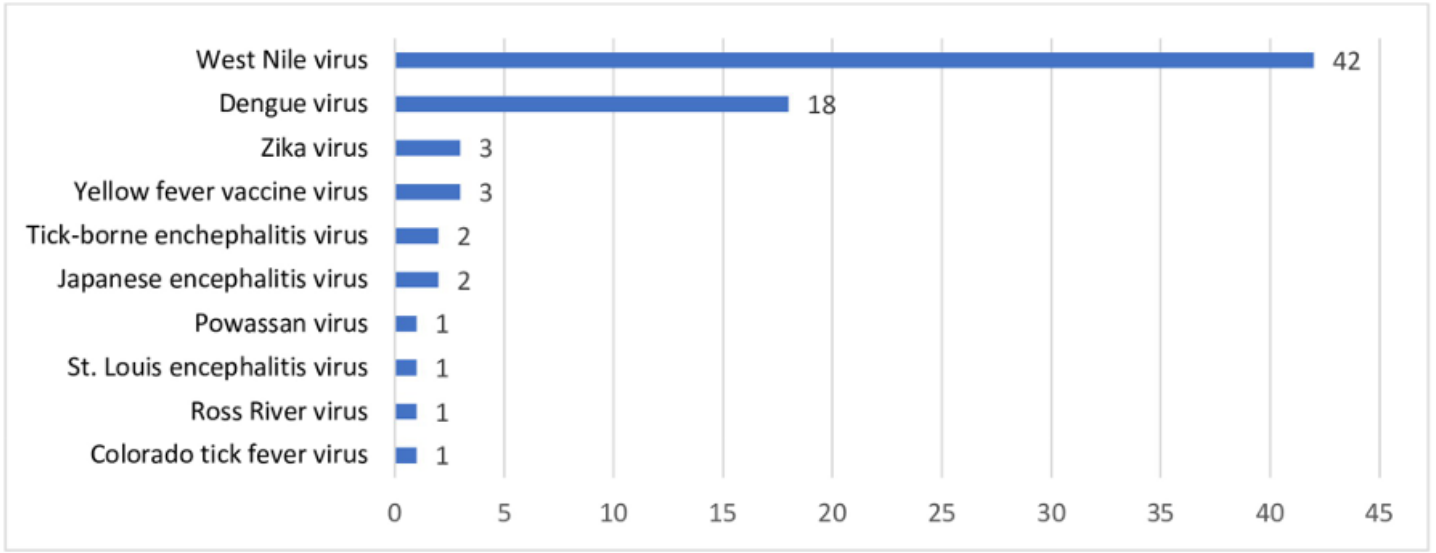

Fig 2. Reported transfusion-transmitted arbovirus cases.

https://doi.org/10.1371/journal.pntd.0010843.g002

Gimenez-Richarte A et al., 2022. Transfusion-transmitted arboviruses: Update and systematic review. *PLoS Negl Trop Dis* 16: e0010843

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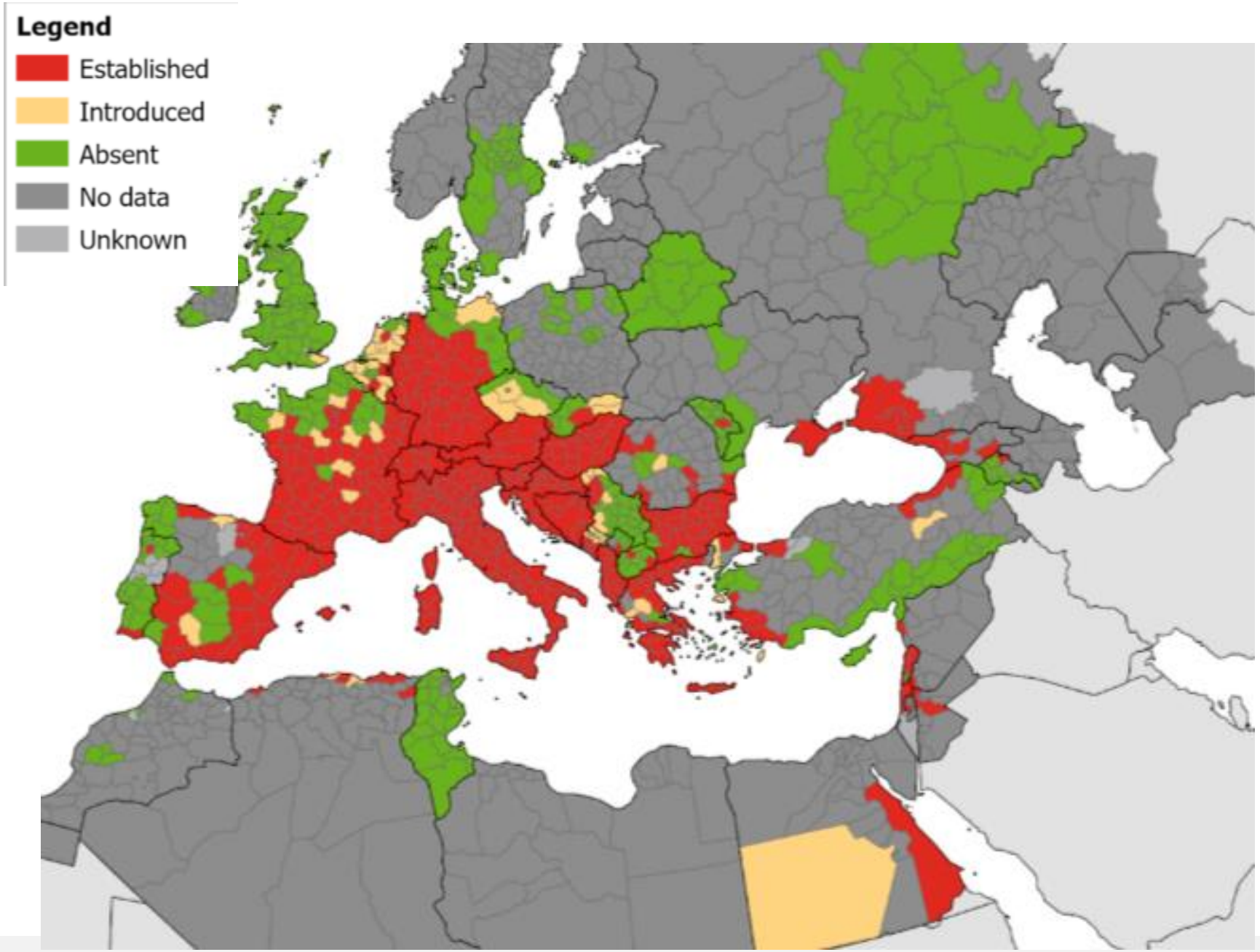
Distribution of invasive Aedes species (02/2023)

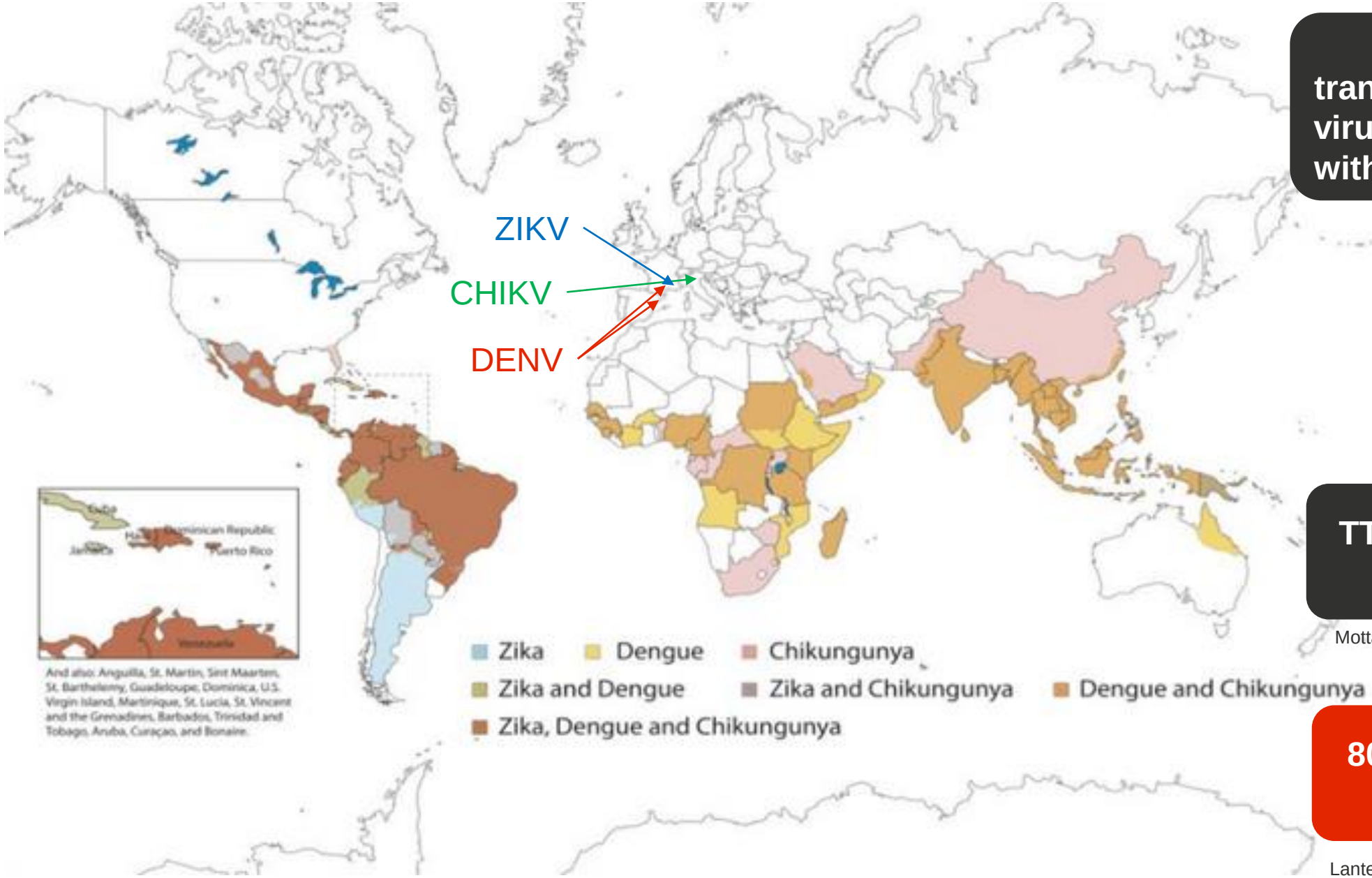


Potential carrier of Arboviruses:

DENV, ZIKV, CHIKV

https://www.ecdc.europa.eu/en/publications-data/aedes-invasive-mosquitoes-current-known-distribution-february-2023

Transfusion transmission of Dengue virus has been observed with RBC, FFP and PLTs



TTI with Zika Virus was reported for PLTs

Motta et al., 2016. *NEJM* 375: 1101-1103

80% of infected people are asymtomatic

Lanteri et al., 2016. *Transfusion* 56: 1907-1914

Patterson et al., 2016. Dengue, Zika and Chikungunya: Emerging Arboviruses in the New World. *Western J Emerg Med* 17: 671-679

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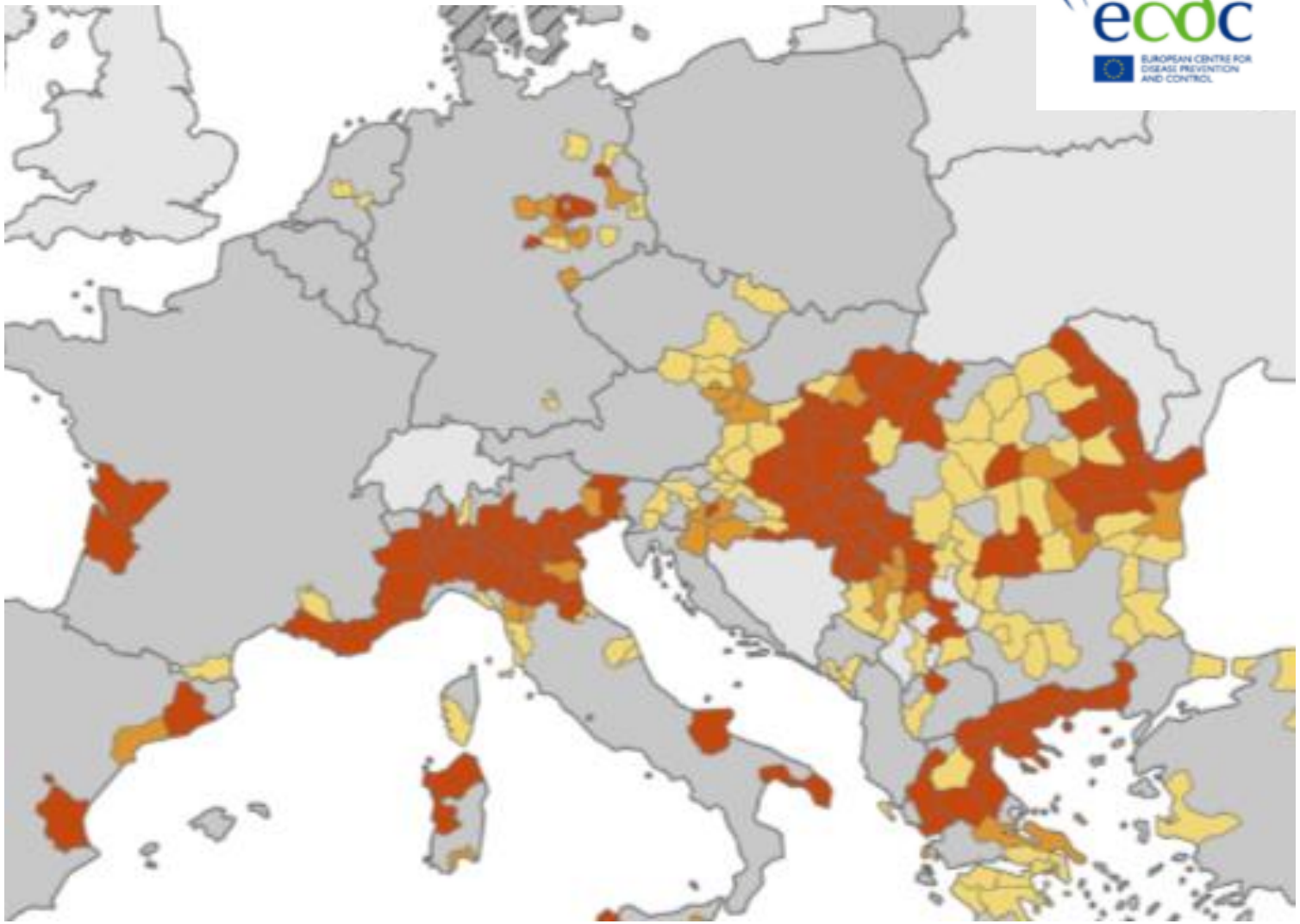


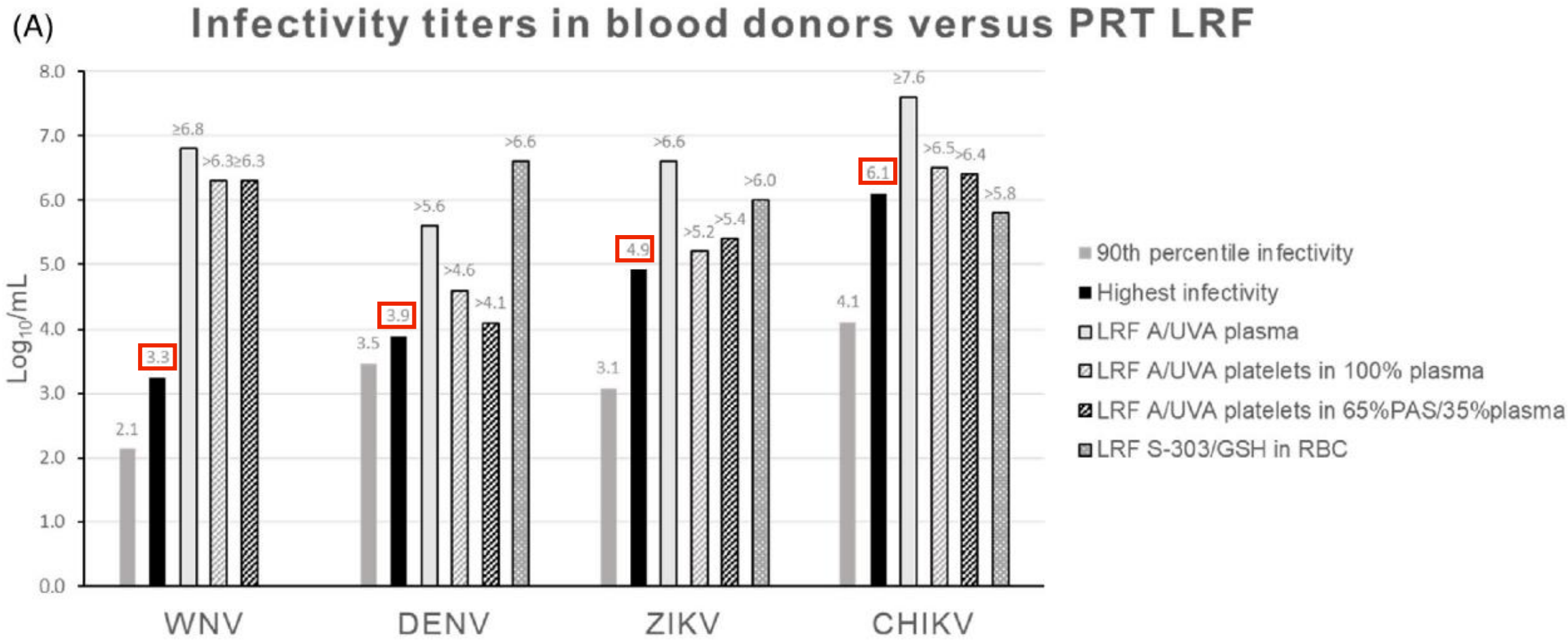
Distribution of human West Nile virus infections in NUTS 3 or GAUL 1 regions of the EU/EEA and neighbouring countries during 2013–2022, as of 27 of September 2023

- Human infections reported, current season (2023)
- Human infections reported, 2022
- Human infections reported, 2013–2021
- No data reported
- No infections reported
- Not included

WNV Cases 2023 compared to previous seasons

https://www.ecdc.europa.eu/en/publications-data/west-nile-virus-human-cases-compared-previous-seasons-27-september-2023

Highest projected infectious viral loads vs log reduction factors



Stramer SL et al., 2022. Mitigating the risk of transfusion-transmitted infections with vector-borne agents solely by means of pathogen Reduction. *Transfusion* 62: 1388-1398

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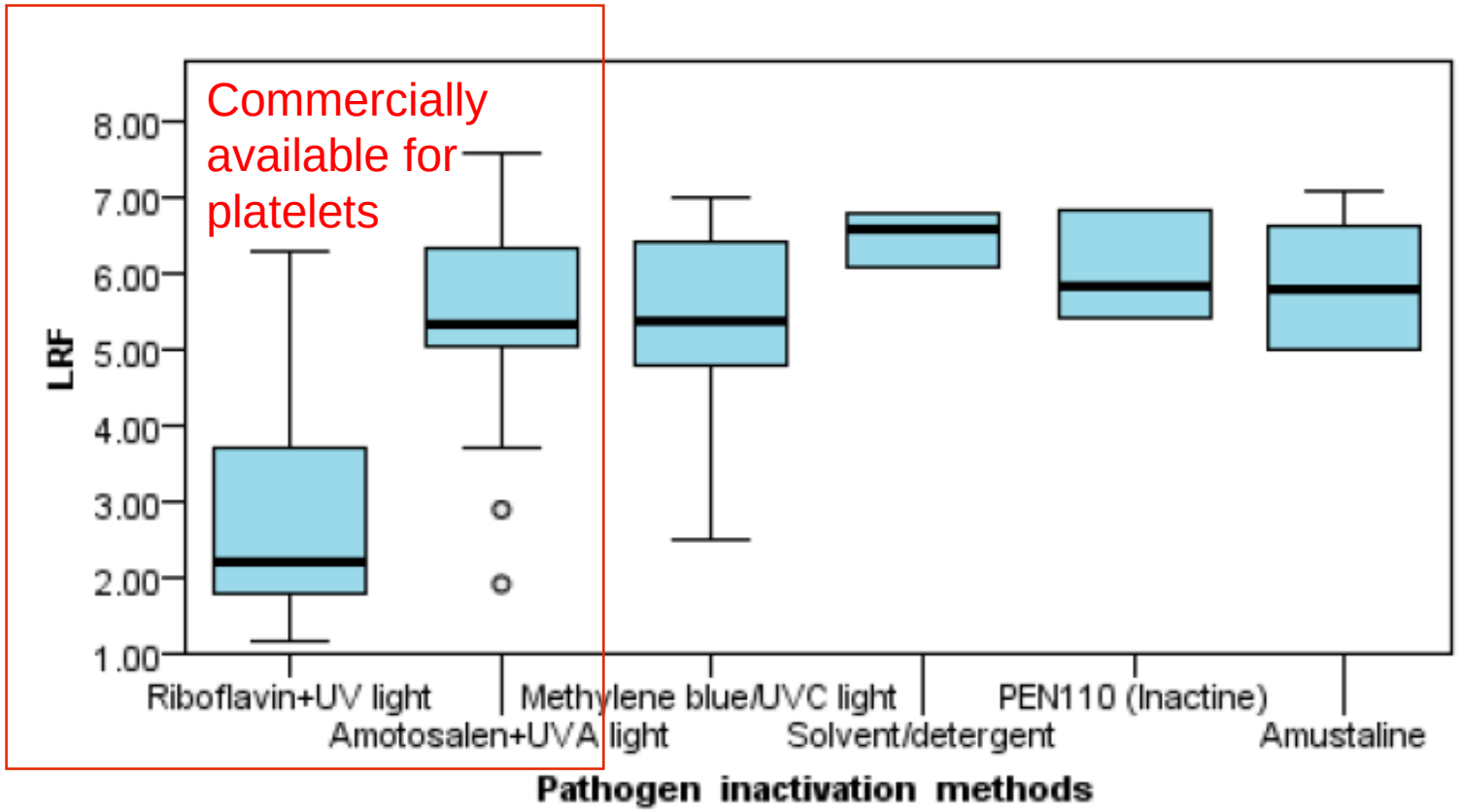
Arbovirus comparison - Summary



Bias risk: mixed abstracts & publications, mixed components, Theraflex MB and UV grouped

Figure 2. LRF achieved with each pathogen inactivation method. Box plots shows the distribution of the samples obtained with each PIM. The Kruskal-Wallis one-way ANOVA (independent samples) shows statistically significant differences ($p<0.001$).

Gimenez-Richarte et al., 2023. Pathogen inactivation methods to prevent transfusion-transmissible arboviruses. *Trop Med Int Health* doi: 10.1111/tmi.13863. Online ahead of print.

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Arbovirus Testing & PRT

Information for Blood Establishments Regarding FDA's Determination that Zika Virus is no Longer a Relevant Transfusion-Transmitted Infection, and Withdrawal of Guidance titled "Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components"

May 12, 2021

Bundesanzeiger
Herausgegeben vom Bundesministerium der Justiz und für Verbraucherschutz
www.bundesanzeiger.de

Bekanntmachung
Veröffentlicht am Donnerstag, 4. Juni 2020
BAnz AT 04.06.2020 B6
Seite 1 von 5

Paul-Ehrlich-Institut
Bundesinstitut für Impfstoffe und biomedizinische Arzneimittel

Bekanntmachung
über die Zulassung von Arzneimitteln
Anordnung von Maßnahmen, die das Risiko der Übertragung
einer in Deutschland erworbenen West-Nil-Virus (WNV)-Infektion
durch Blutkomponenten zur Transfusion
(zelluläre Blutzubereitungen und therapeutische Frischplasmen)
und durch Stammzellzubereitungen zur hämatopoetischen Rekonstitution
minimieren können

ZIKV Safety

- ZIKV NAT screening AND
- donor deferrals OR
- **pathogen inactivation (IBS)**

WNV Safety

- WNV NAT screening OR
- donor deferrals OR
- **appropriate pathogen inactivation**

3. Preparedness – What Comes Next?

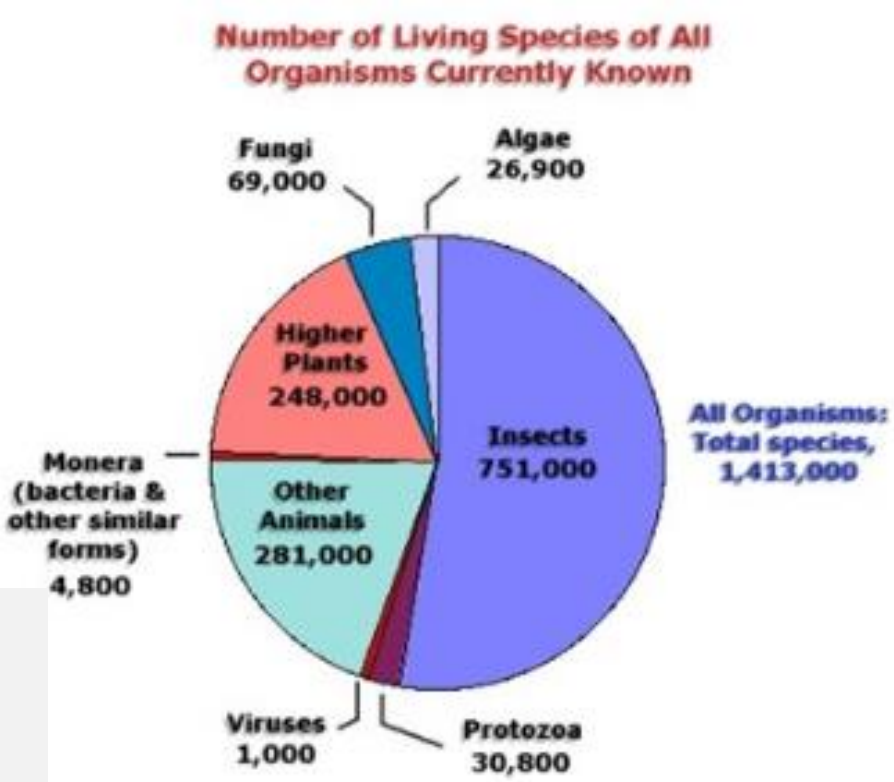
What will be next?

There are likely 1 Million vertebrate viruses, 99.8% are yet not discovered. That is a huge potential for future zoonotic Emergence!

We do not know:

- **What** will be next
- **When** will be next
- **How** and how fast it will be **transmitted**
- **How** and how fast disease will **progress**

1918 Spanish Flu
1957 Asian Flu
1968 Hong Kong Flu
1980 HIV
2002 SARS CoV
2004 Bird Flu (H5N1)
2009 Swine Flu (H1N1)
2012 MERS CoV
2015 Zika Virus
2019 SARS-CoV-2
2022 Monkeypox



Morse, S.S. 1995. *Emerg Infect Dis* 1: 7-15

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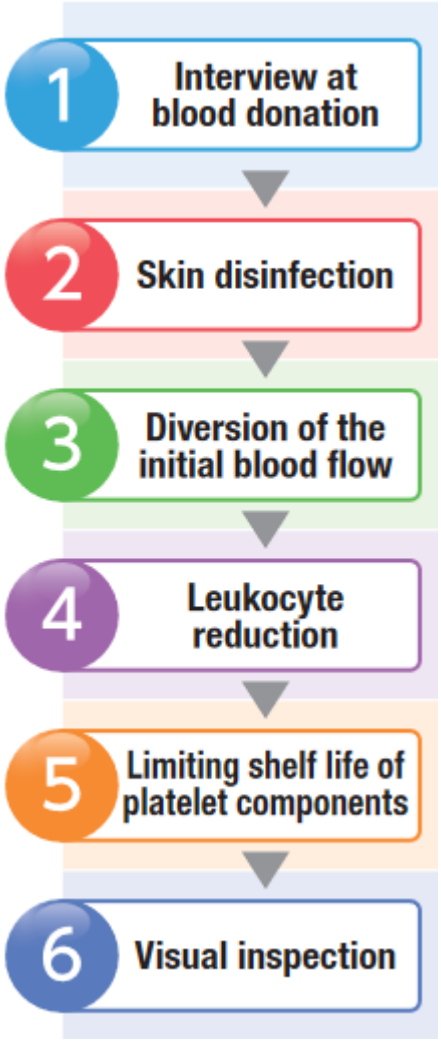
4. Bacterial Risk

Transmission of Bacteria by Transfusion (of platelets)

Such contamination is in the majority caused by **needle prick contaminations,** secondary by **donor bacteremia**. **The less well established safety measures are in place, the higher the contamination rate (human failure).**



Transfusion Information 1712-156 – The Japanese Red Cross

Primary Bacterial Culture:

Sensitivity 31%

Walker BS et al., 2020. Residual bacterial detection rates after primary culture as determined by secondary culture and rapid testing in platelet components: A systematic review and meta-analysis. *Transfusion* 60: 2029-2037

Wendel S et al., 2005. Double, double, toil and trouble. *Transfusion* 45: 1241

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FDA-guidance to enhanve the safety and availability of platelets

Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion

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Guidance for Industry

Additional copies of this guidance are available from the Office of Communication, Outreach and Development (OCOD), 10903 New Hampshire Ave., Bldg. 71, Rm. 3128, Silver Spring, MD 20993-0002, or by calling 1-800-835-4709 or 240-402-8010, or email ocod@fda.hhs.gov, or from the Internet at https://www.fda.gov/vaccines-blood-biologics/guidance-compliance-regulatory-information-biologics/biologics-guidances.

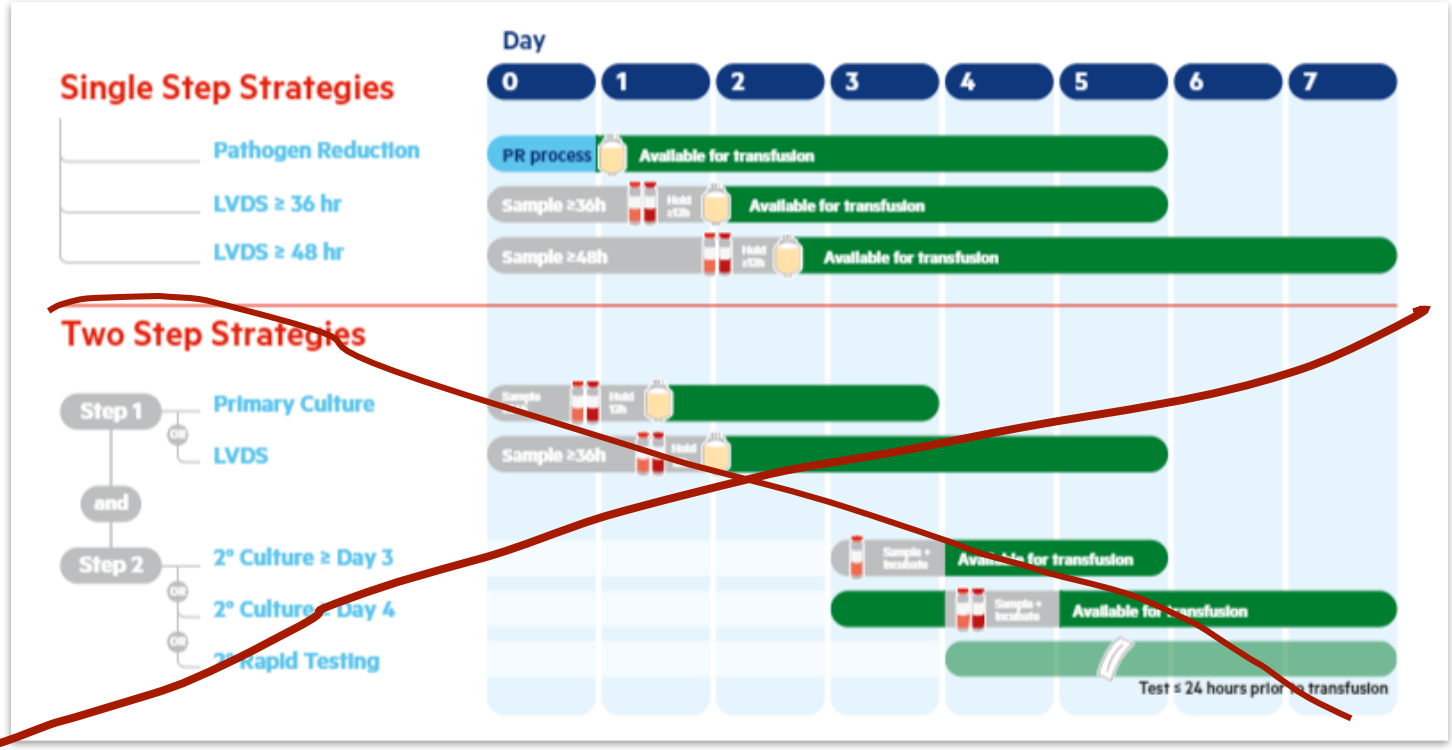
For questions on the content of this guidance, contact OCOD at the phone numbers or email address listed above.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
September 2019
Updated December 2020

https://www.fda.gov/media/123448/download

All PC have to undergo since 1-10-2021:

- Bacterial screening with enhanced protocol (LVDS) **OR**
- Bacterial screening in combination with 2e rapid test **OR**
- Pathogen Inactivation/Reduction



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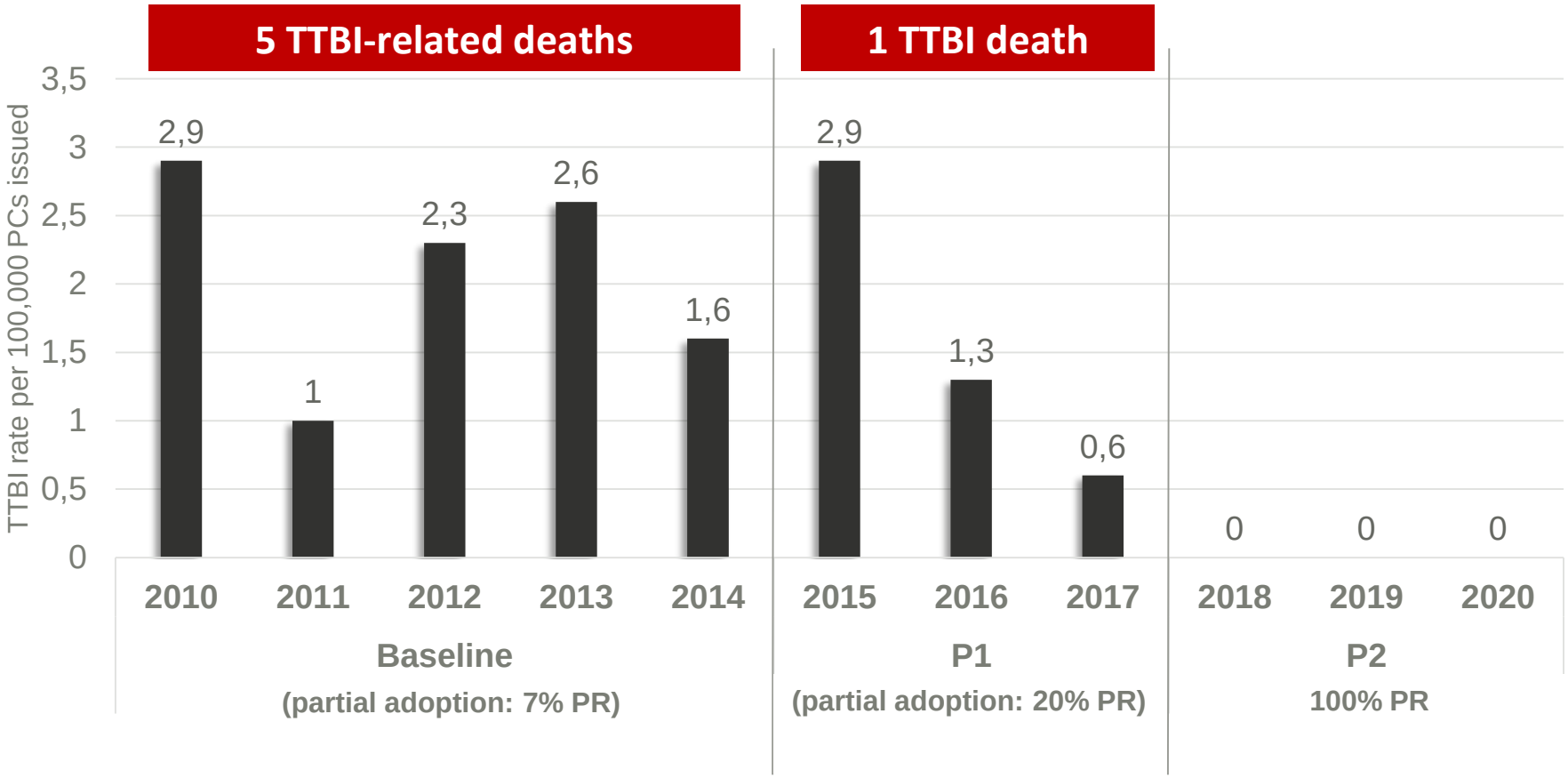
TTBI-related Cases and Deaths in France pre- and post PI



7% INTERCEPT 20% INTERCEPT 100% INTERCEPT

Pitman JP et al., 2023. Longitudinal analysis of annual national hemovigilance data to assess pathogen reduced platelet transfusion trends during conversion to routine universal clinical use and 7-day storage. *Transfusion* 63: 711-723

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TTBI-related Cases and Deaths in Switzerland

Year	Conventional platelet component transfusion-related sepsis (fatal)[b]	INTERCEPT platelet component transfusion-related sepsis (fatal)[c]
2005	6 (2)	
2006	2 (0)	
2007	2 (0)	
2008	2 (0)	
2009	3 (1)	
2010	1(0)	
2011	0 (0)	0 (0)
2012		0 (0)
2013		0 (0)
2014		0 (0)
2015		0 (0)
2016		0 (0)
Total	16 (3)	0 (0)

[a]Two-sided Fisher's exact test $p < 0.001$.
[b]Total units 158,502.
[c]Total units 205,574.

pathogen-reduced (INTERCEPT)
(80% of all PCs produced in 2011 → 100% since November 2011)

Platelet-additive solution
(~ 30% in 2010 → 100% in November 2011)

7-day storage
(from July 2013)

Jutzi M et al., 2018. Nationwide Implementation of Pathogen Inactivation for All Platelet Concentrates in Switzerland. *Transfus Med Hemother* 45: 151-156

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Significant Underreporting of TTI

- **TR/TTI are not recognized**
- **The confirmation/validation of TR/TTI is too complex**
- **TR/ TTI occur after a delay +24h post transfusion**
- **TR/TTI are not reported due other tasks / high work load**

TR: Transfusion Reactions
TTI: Transfusion-Transmitted Infections

How can we provide safe blood products?

Donor Management

Questionary

Deferrals

Risk: Donor could not tell the truth or not know

Diagnostic Testing

Bacterial culture

Serology, PCR

Risk: Only few known pathogens tested, false negative tests possible

Pathogen Inactivation

Plasma inactivation

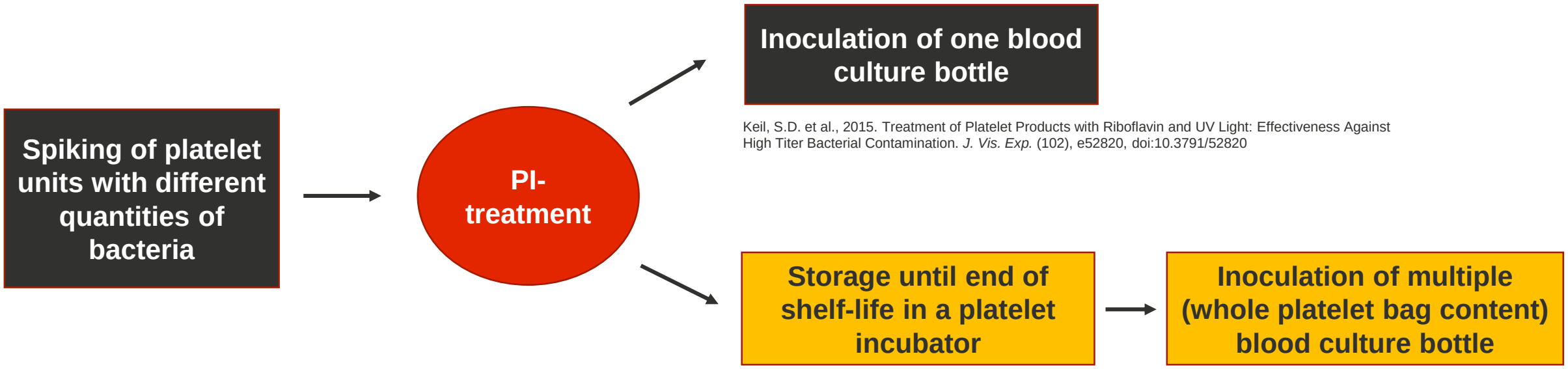
Platelet inactivation

(Whole Blood inactivation)

No inactivation for RBC yet

5. Pathogen Inactivation for Platelets – all the Same?

Assessment Pre- and Post PI-Treatment



Keil, S.D. et al., 2015. Treatment of Platelet Products with Riboflavin and UV Light: Effectiveness Against High Titer Bacterial Contamination. *J. Vis. Exp.* (102), e52820, doi:10.3791/52820

McDonald CP et al., 2021. Assessing the inactivation capabilities of two commercially available platelet component pathogen inactivation systems: effectiveness at end of shelf life. *Vox Sang* 116: 416-424

Assessment of the Inactivation Capacity: Bacterial Load Pre-inactivation Preventing Bacterial Detection until End of Shelf Life

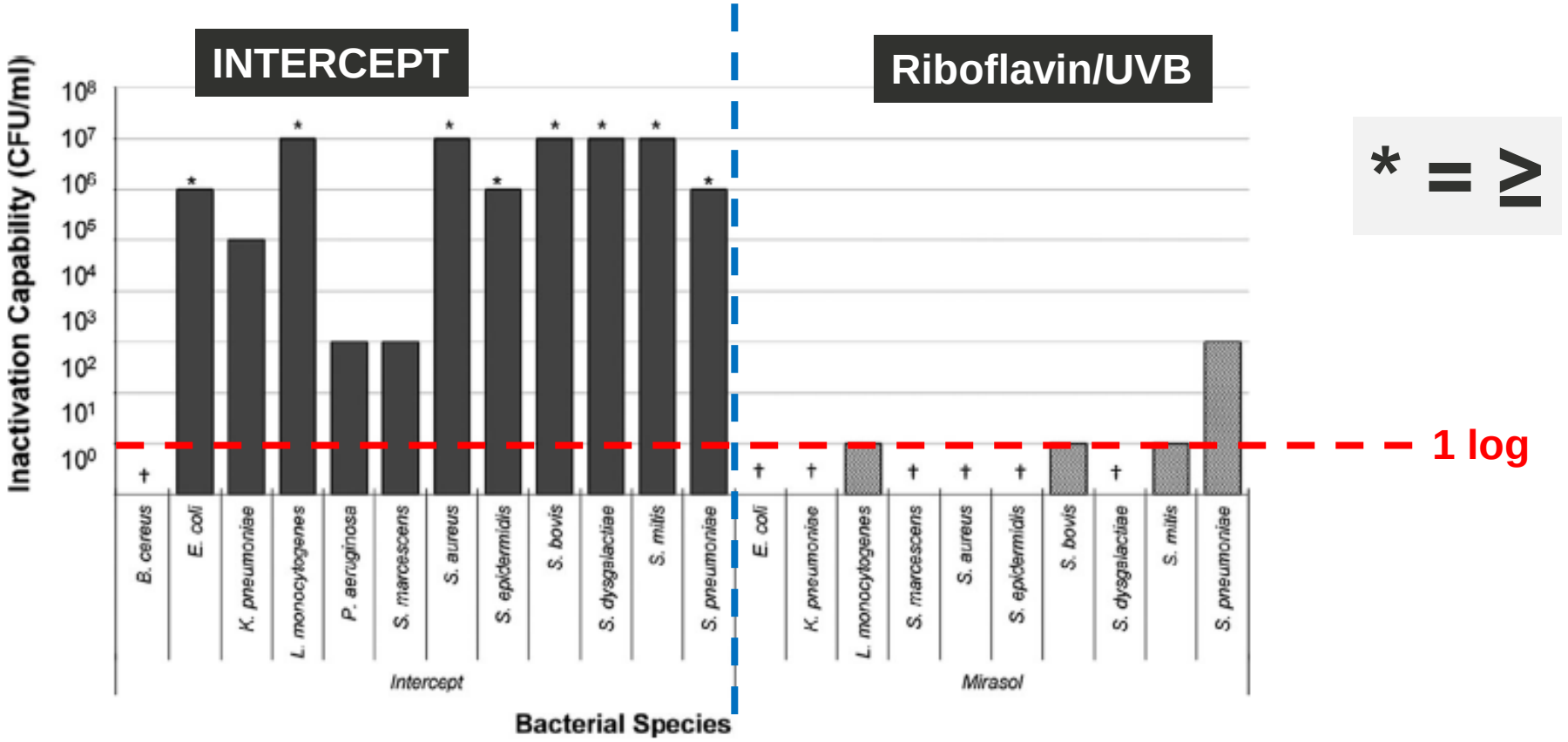


Fig. 2 Comparison of inactivation capability for intercept and mirasol. *Capability ≥ highest concentration assessed; †Capability ≤ lowest concentration assessed (<10^2 CFU/ml for *B. cereus* and *S. epidermidis*; <10^1 CFU/ml for other species).

McDonald CP et al., 2021. Assessing the inactivation capabilities of two commercially available platelet component pathogen inactivation systems: effectiveness at end of shelf life. *Vox Sang* 116: 416-424

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pathogens

MDPI

Article

In Vitro Comparative Study of Platelets Treated with Two Pathogen-Inactivation Methods to Extend Shelf Life to 7 Days

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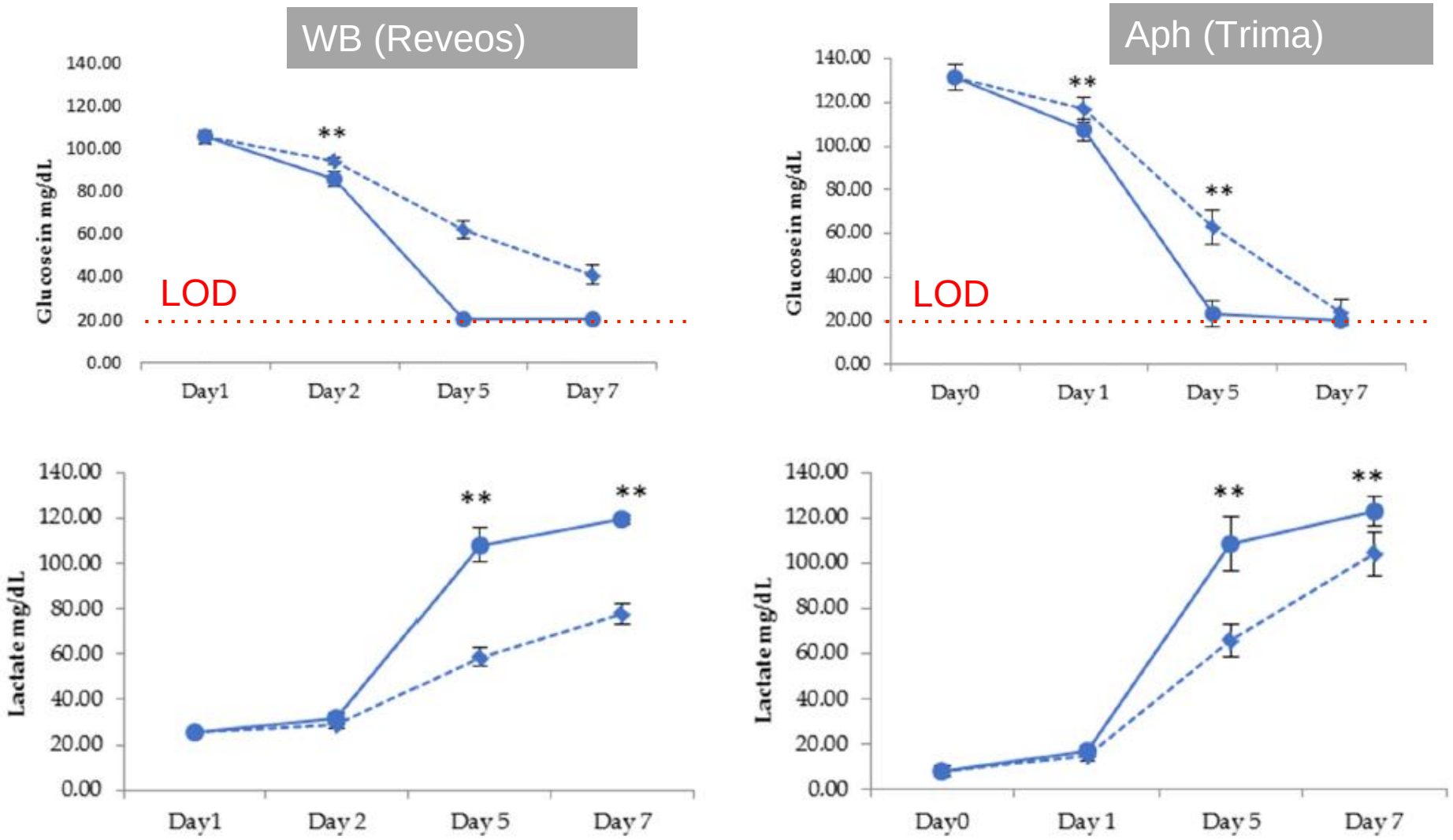

Pool- and split platelet units in 38% plasma and 62% T-PAS+

INTERCEPT

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Figure 1. Evolution of glucose and lactate concentration evolution of platelets treated with INTERCEPT (AM-PI—dotted line) and MIRASOL (RF-PI—solid line) upon 7-day storage for PPCs (Platelet Pool Concentrates) and APCs (Apheresis Platelet Concentrates); * $p < 0.05$, ** $p < 0.01$.

Malvaux N et al., 2022. In Vitro Comparative Study of Platelets Treated with Two Pathogen Inactivation Methods to Extend Shelf Life to 7 days. *Pathogens* 11: 343

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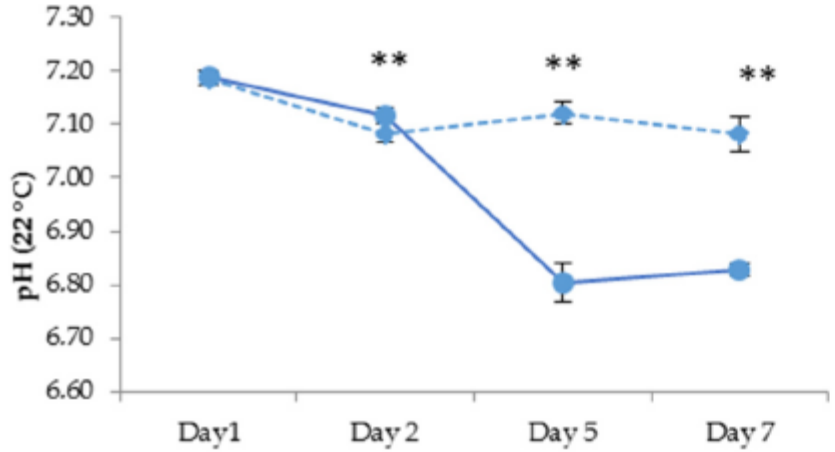
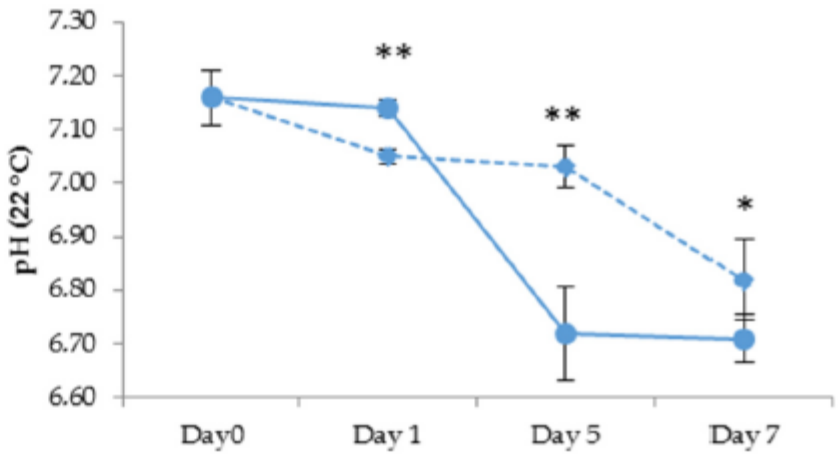
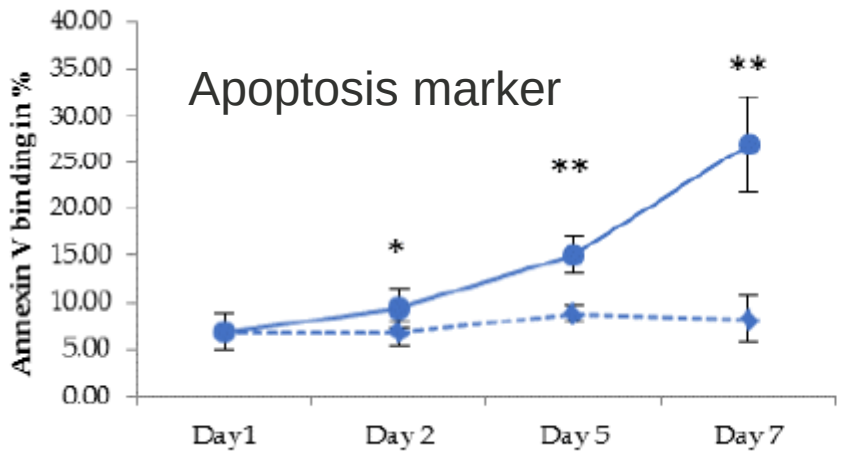
WB (Reveos)

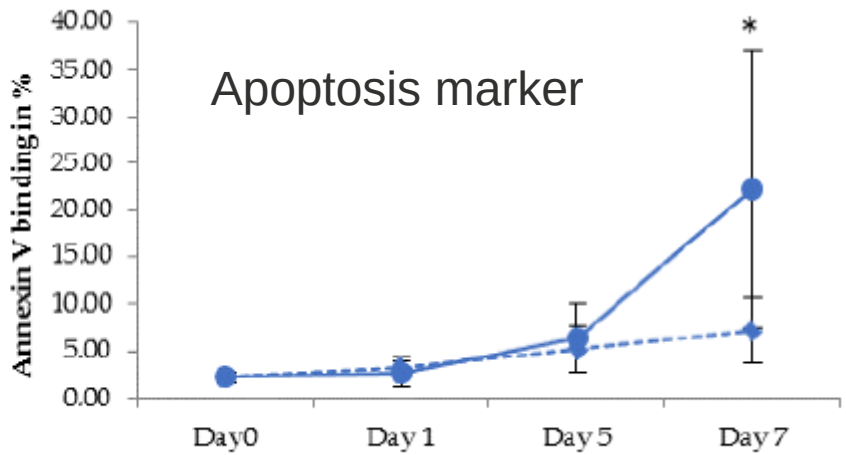
Aph (Trima)

Pool- and split platelet units in 38% plasma and 62% T-PAS+









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6. New Applications for Safer Components

Pathogen-Reduced Universal Plasma

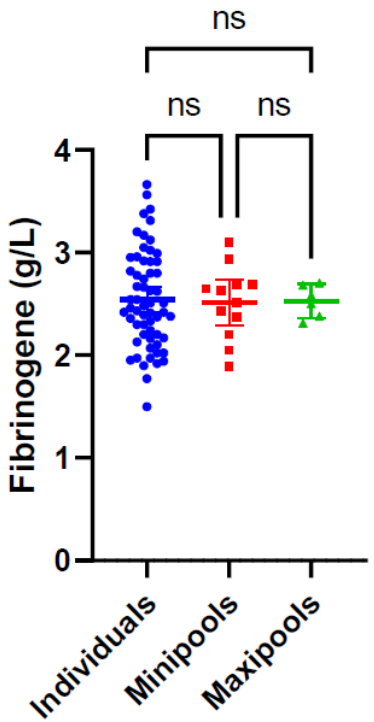
Pooled pathogen-reduced universal plasma

Pilot Study
Conference Poster

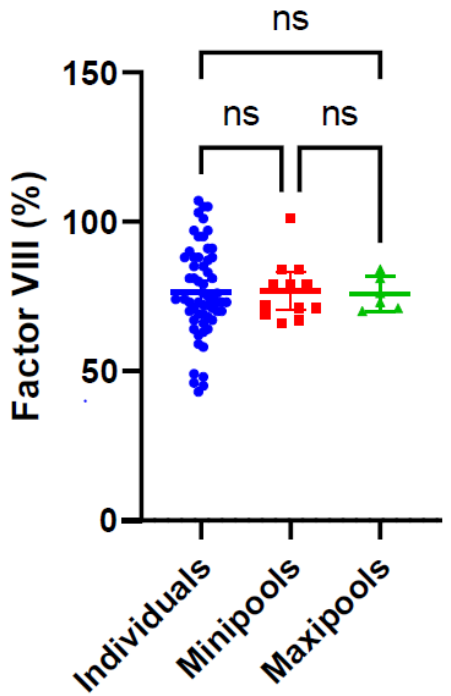
Comparison of:

Maxipools universal (10 units, 4 A, 4 B, 4 AB)
Minipools universal (5 units, 2 A, 2 B, 1 AB)
Maxipools single ABO (10 units)
Minipools single ABO (5 units)

PI-treatment post pooling (amotosalen/UVA)



Reduction of Variability with increasing pool size. Fib/FVIII content of universal plasma not comparable to individual



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FLyP – a French approach

- **Only donors with ≥90 IU/100 mL FVIII accepted (female donors anti HLA tested)**
- Apheresis donations, leukoreduced, pathogen reduced (amotosalen/UVA), frozen
- Thawed, pools of approx. 10 units (3 liters) mixed group A, B, AB
- Splitting, freeze-drying by sublimation (4 days)
- **Reconstitution in medical water**

2 years shelf-life at room temperature
ABO universal
>1400 units produced

Martinaud C et al., 2012. *In Vitro* Hemostatic Properties of French Lyophilized Plasma. *Anesthesiology* 117: 339-346

Pusateri AE et al., 2016. Dried plasma: state of the science and recent developments. *Transfusion* 56: S128-S139

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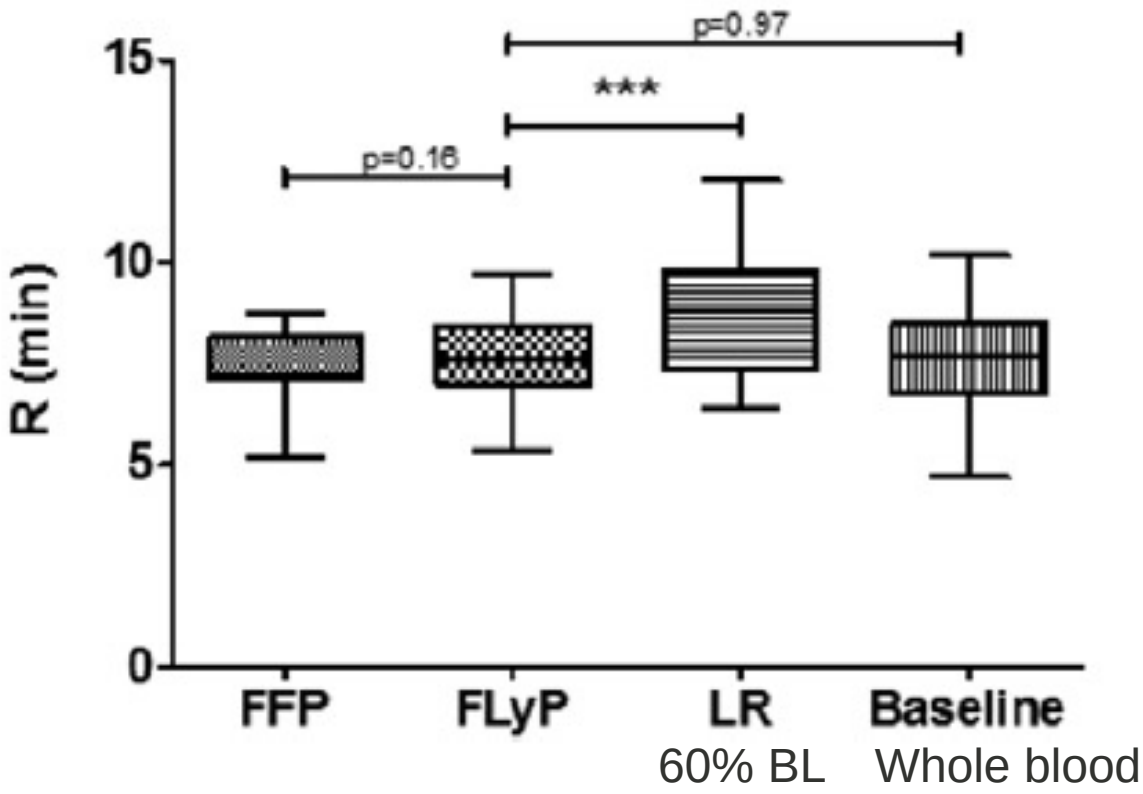
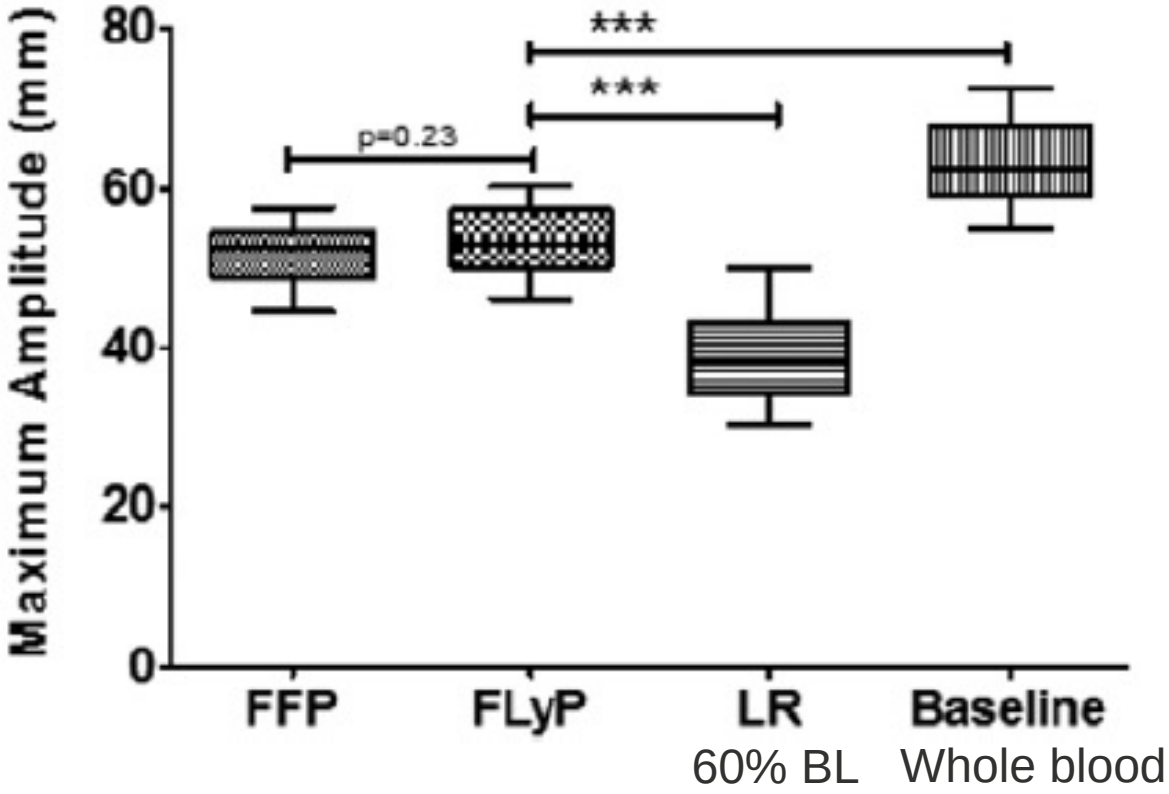
FLyP – a French approach

clotting time



maximum clot firmness



Sailliol A et al., 2013. The evolving role of lyophilized plasma in remote damage control resuscitation in the French Armed Forces Health Service. *Transfusion* 53: 65S-71S

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Tolerability & Clinical Efficacy – INTERCEPT® Plasma

The clinical safety profile of INTERCEPT plasma is comparable to conventional plasma/quarantine plasma*

*Bost V et al., 2015. Independent evaluation of tolerance of therapeutic plasma inactivated by amotosalen-HCl–UVA (Intercept™) over a 5-year period of extensive delivery. *Vox Sang* 109: 414-416
*Guignier C et al., 2018. Amotosalen-inactivated plasma is as equally well tolerated as quarantine plasma in patients undergoing large-volume therapeutic plasma exchange. *Transfus Clin Biol* 25: 73-77

The clinical efficacy of INTERCEPT plasma has been shown including the following indications:

- **Coagulopathy in liver disease[1]**
- **Liver transplant support[1,2]**
- **Therapeutic Plasma Exchange in Thrombotic Thrombocytopenic Purpura[3,4]**

[1]Mintz PD et al., 2006. Photochemically treated fresh frozen plasma for transfusion of patients with acquired coagulopathy of liver disease. *Blood* 107: 3753-3760
[2]Cinqalbre J et al., 2015. Comparative effectiveness of plasma prepared with amotosalen-UVA pathogen inactivation and conventional plasma for support of liver transplantation. *Transfusion* 55:1710-1720
[3]Garaud O et al., 2019. Amotosalen-inactivated fresh frozen plasma is comparable to solvent detergent inactivated plasma to treat thrombotic thrombocytopenic purpura. *Transfus Apheres Sci* 58: 102665
[4]Mintz PD et al., 2006. A randomized, controlled Phase III trial of therapeutic plasma exchange with fresh-frozen plasma (FFP) prepared with amotosalen and ultraviolet A light compared to untreated FFP in thrombotic thrombocytopenic purpura. *Transfusion* 46: 1693-1704

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Pathogen-Reduced Frozen Platelets

Pathogen-reduced, cryopreserved platelets to maintain individual platelet support

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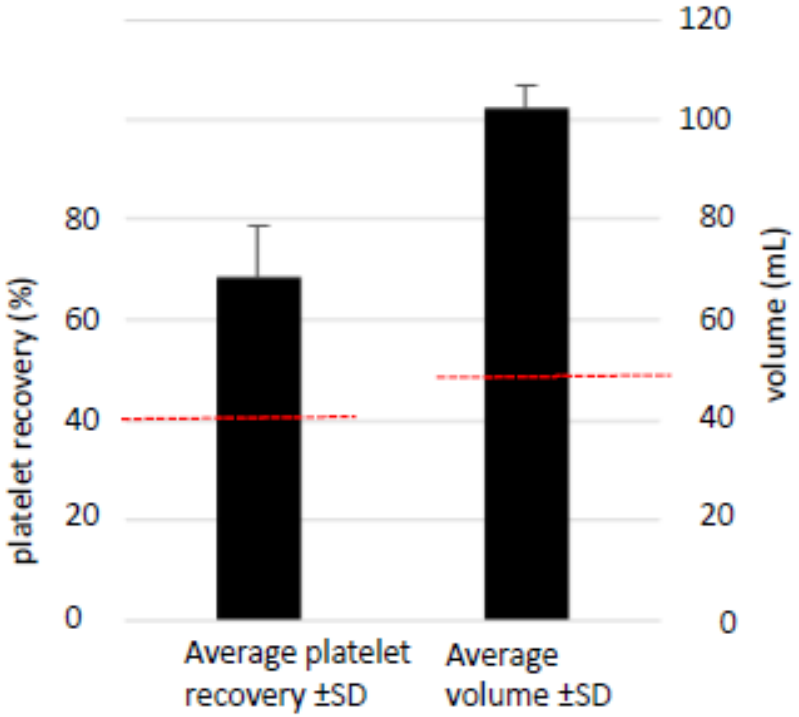

Fig. 2 platelet count and volume of CPRPs post freezing (n=156), the error bars represent the standard deviation. The dotted red lines represent the minimum quality requirements by Polish guidelines.

Summary:

- CPRPs are produced to mitigates shortages of HLA-typed platelets.
- Decreasing production and demand for CPRPs from 2020-2023, which may be explained by cessation of pandemic measures releasing donor restrictions.
- Polish quality requirements were fulfilled satisfactorily, the recovery rate (69.0 ± 10.5) was in line with previous data (70.6% in Sandgren et al., 2023. *Blood Transfus* 21: 127-143).
- No CPRP-transfusion related adverse events were reported.

7. Closing

Theoretical individual risk to receive a pathogen-contaminated platelet unit

TABLE 2. Comparison of infectious risk estimates for a transfusion recipient when calculated per unit or per patient exposure

Infection	Per-unit estimate (%)	Per-patient estimate (6 AP units) (%)
Bacterial contamination	0.067	0.4
Clinical sepsis	0.016	0.096
TT-CMV	0.1	0.3 (50% susceptible patients)*
Emerging acute agent	0.007-0.075 (0.025)†	0.042-0.45 (0.15)†
Emerging chronic agent	0.01-0.08 (0.045)†	0.06-0.48 (0.27)†
Aggregate infectious risk estimates	**Not calculated**	**0.4—Baseline** (bacterial transmission only) **0.1—Minimum** (clinical sepsis only) **1.18—Maximum** (bacteria, CMV, and highest EIA risk)‡§

* The per-patient CMV risk estimate that has been adjusted for recipient susceptibility based on only 50% of recipients being susceptible.
† The number in parentheses is the most likely value.
‡ The EIA risk used in this calculation is at the uppermost end of the estimated range for a chronic EIA (e.g., 0.48%).
§ The numbers can be tabulated to calculate a variety of other combinations of infectious risks; these might include an acute EIA rather than a chronic EIA, replacing bacterial contamination with clinical sepsis, and excluding CMV risk.

Kleinman S et al., 2013. A patient-oriented risk–benefit analysis of pathogen-inactivated blood components: application to apheresis platelets in the United States. *Transfusion* 53: 1603-1618

Blood Matters.

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