Bundesinstitut für Impfstoffe
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Microbial Safety of Platelet Concentrates: updates and outlook

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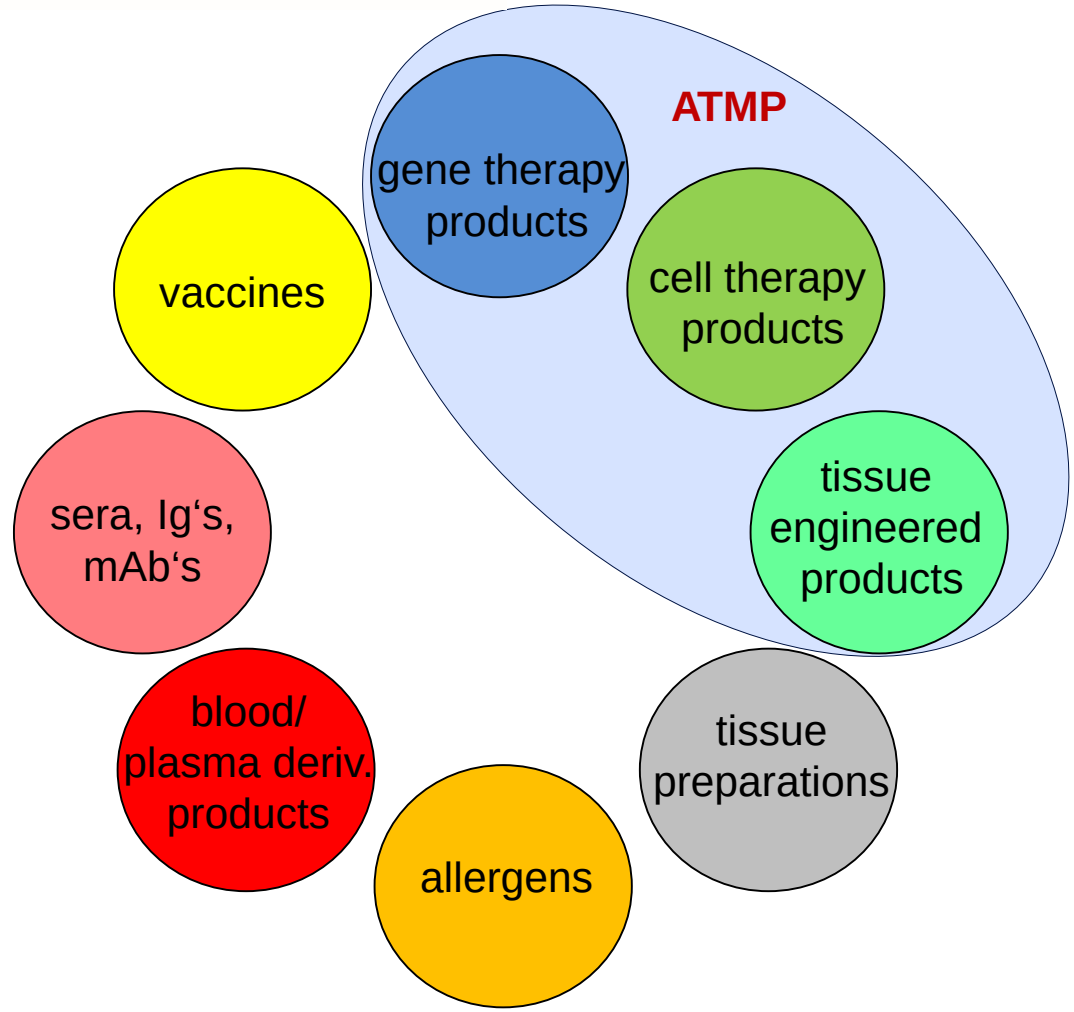
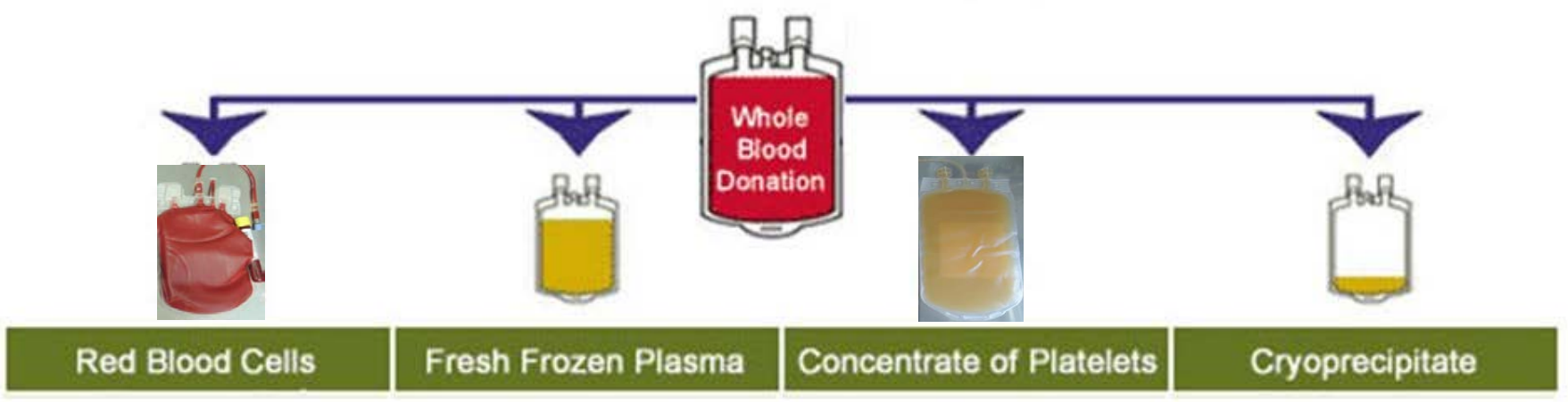


- Marketing authorisation
- Licensing of clinical trials
- OMCL batch release

Platelet concentrates are the most frequent source of the transfusion related septic reactions



Storage at: 4°C <-25°C 22°C

Permissive temperature!

Measures to prevent bacterial contamination

- donor deferral criteria of risk patients
- effective skin disinfection procedures
- aseptic blood collection and processing
- utilization of sterile equipment
- predonation sampling
- leukocyte depletion

How frequent are septic episodes after transfusion of PCs?

PEI hemovigilance report 2015

Transfusion-related bacterial infections (ppm)	2012	2013	2014	2015
RBCs	0,46	0,49	0,75	0,27
PCs	5,82	3,99	8,03	1,97
Plasma	0,00	0,00	0,00	0,00

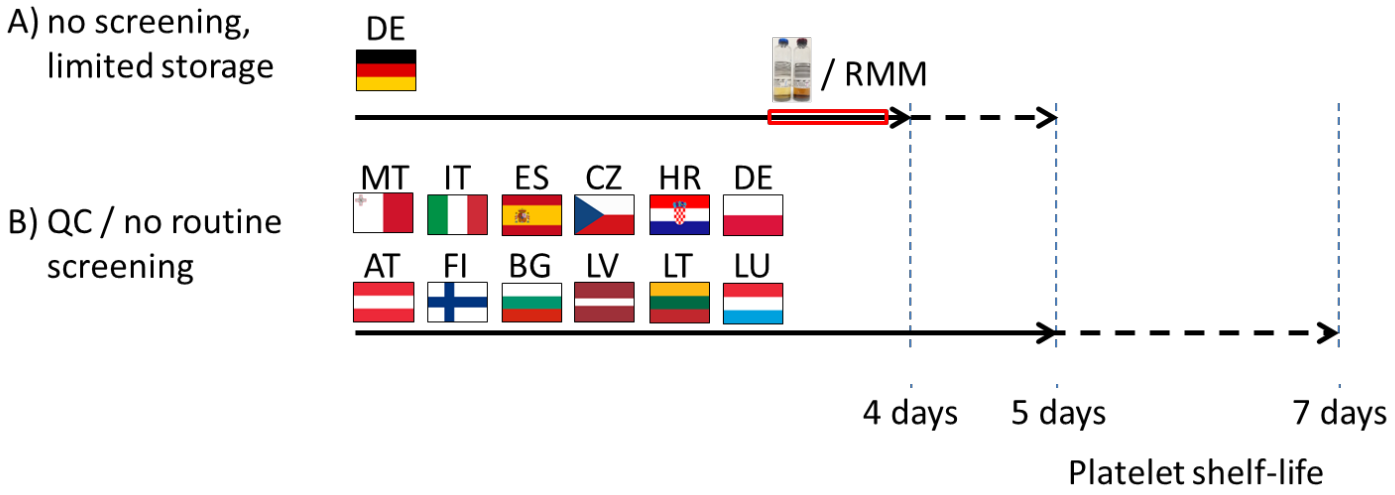
Microbiological control strategies for TCs are not harmonized among EU member states

EC Directives 2002/98/EC and 2004/33/EC

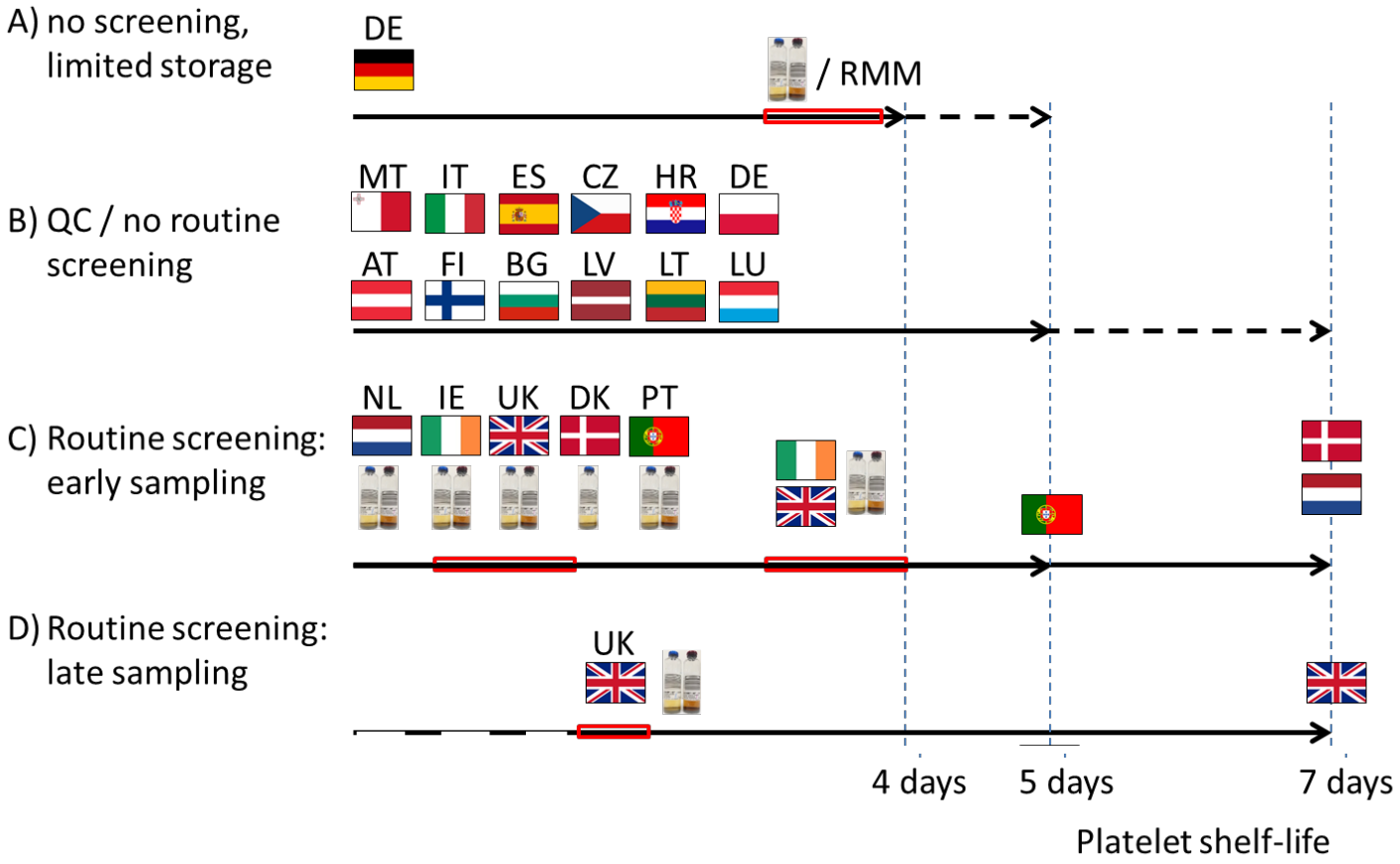
differently implemented at national level

PEI questionery / EDQM survey

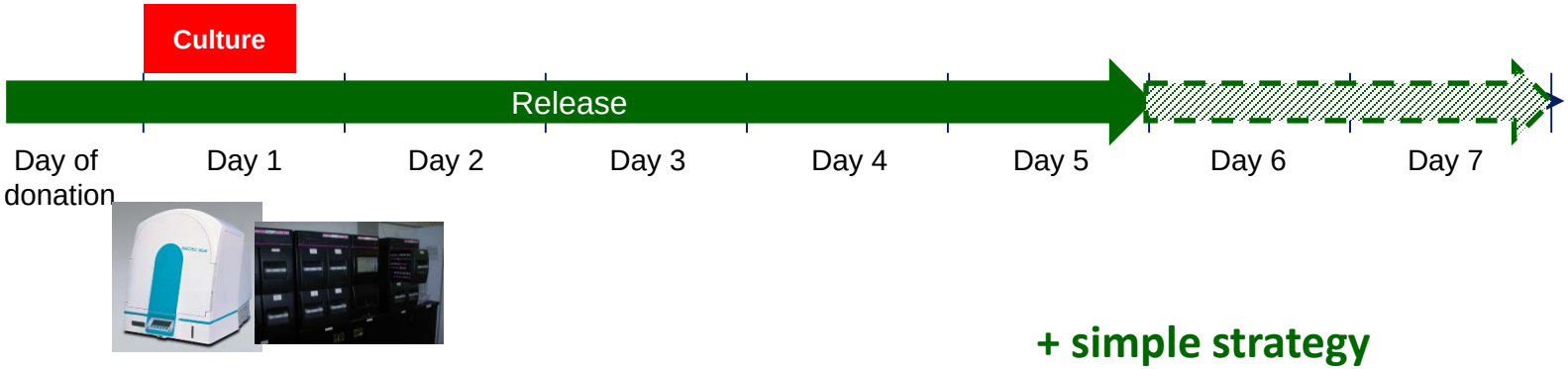
Risk mitigation strategies: overview



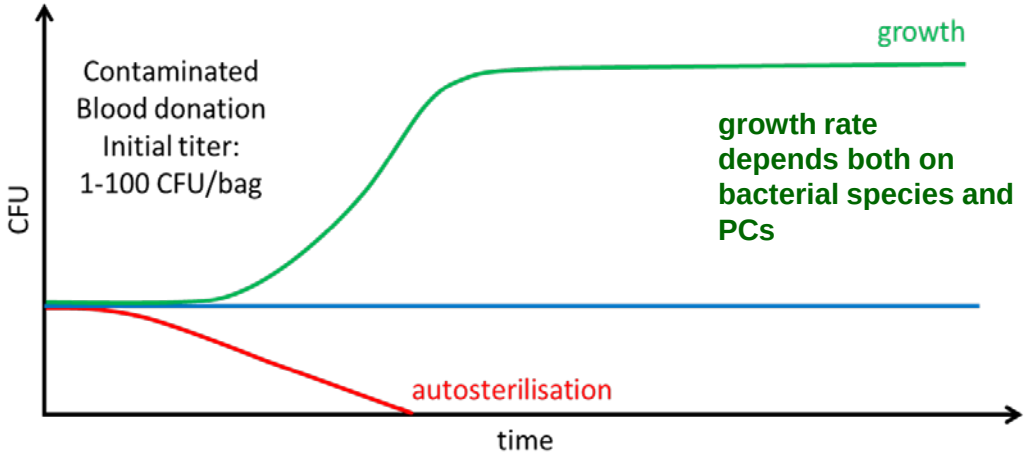
Risk mitigation strategies: overview



Early sampling sreening strategy is suboptimal for detection of microbial contaminants



+ simple strategy



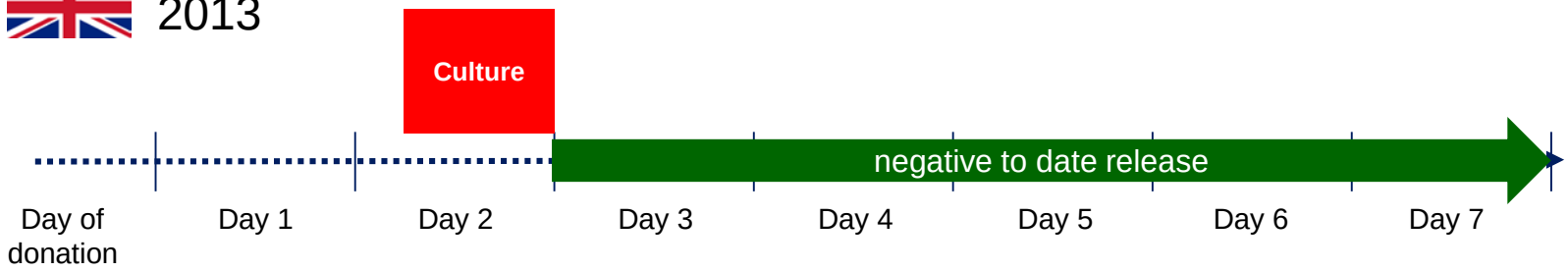
Antimicrobial peptides
Complement

- **inefficient due to sampling error: only 10-50% of true contaminants are detected**
  (Ramirez-Arcos 2017)
- **false positive rates due to auto-sterilization**

- **expenses**
  ca. $50000 for prevention of a single septic episode

State of the Art I: growth based Methods

JPAC
2013

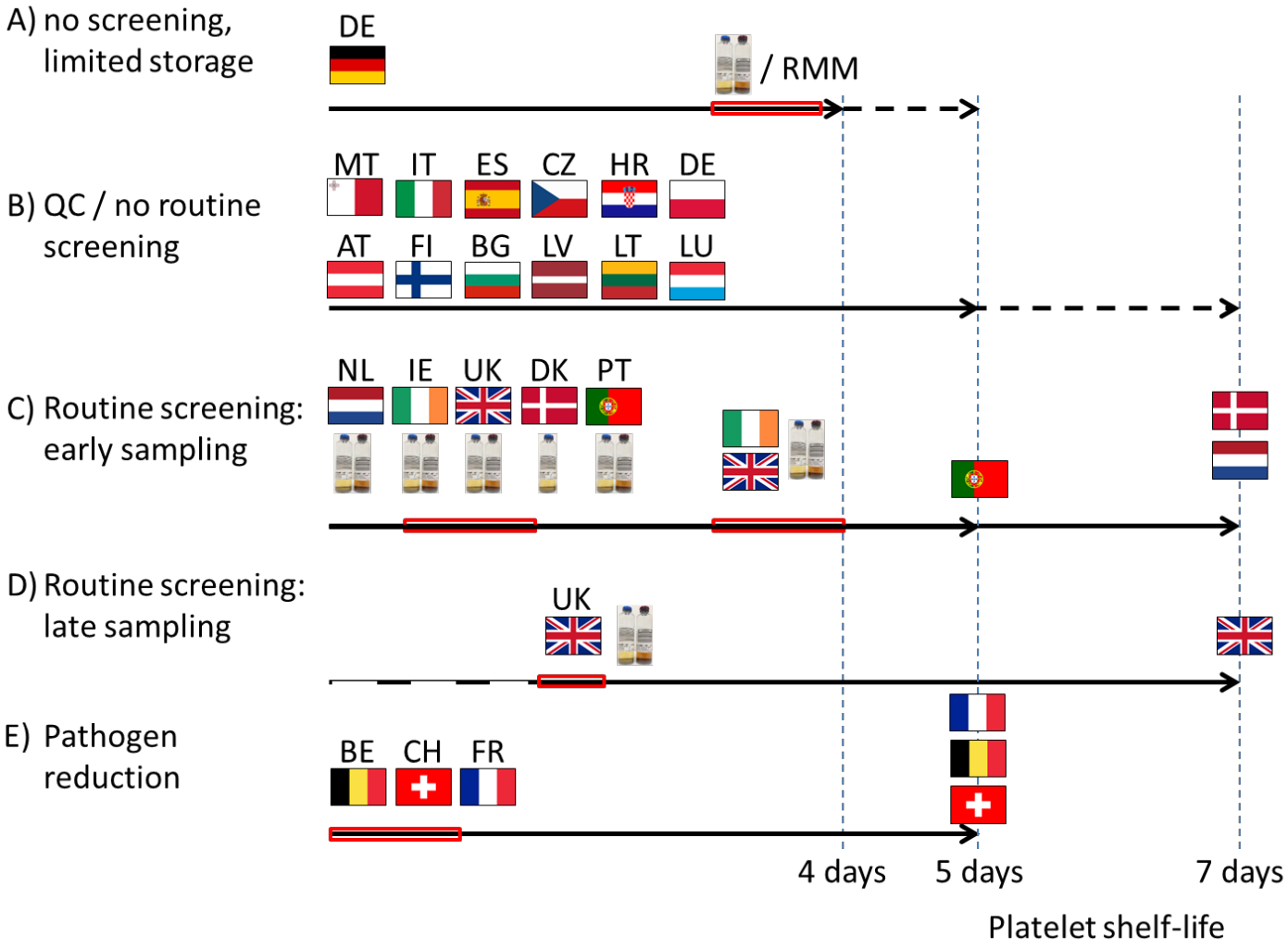


Late sampling (>30-48 h after donation)
Large Sample Volume > 8 ml / bottle
Both aerobic and anaerobic bottle
Quarantine before and during testing (6h)

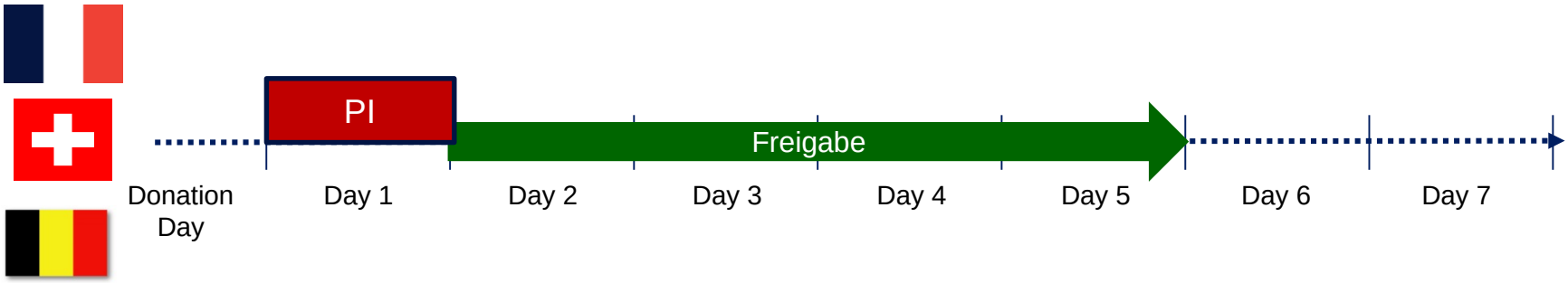
> 90% Reduction of septic reactions (McDonald 2017 NHSBT)

- **false positive rate (anaerobic)**
- **„negative to date“ concept**
- **expenses**

Risk mitigation strategies: overview



State of the art II: Pathogen reduction systems

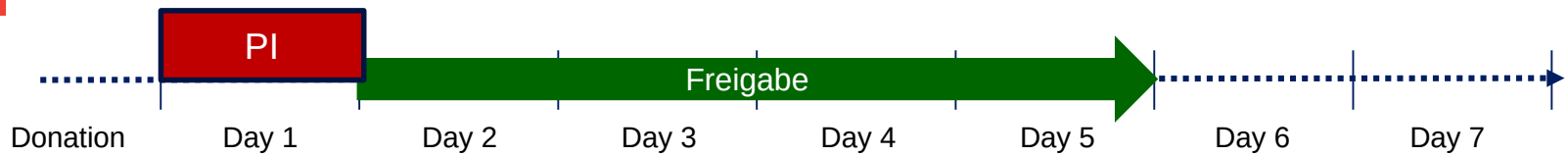


TC + Amotosalen + UV A
TC + Riboflavine + UV
TC + + UVC

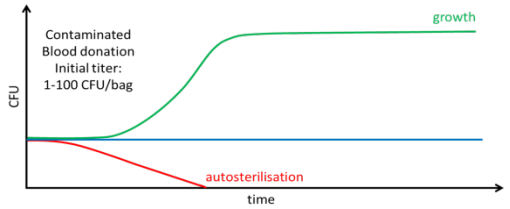
DNA crosslinking

⇒ Inactivation i.e. (several logs) reduction of viability for bacteria, fungi and viruses

State of the art II: Pathogen reduction systems



< 24h after donation



Septic reaction before and after the implementation of PR in Swiss

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.

Jutzi et al 2018

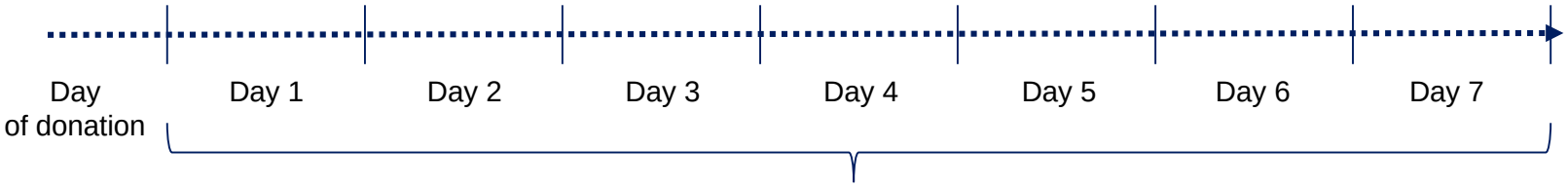
+ proactive strategy
+ efficient

- **additional step in the manufacturing**
- **quality of platelets?**
- **expenses**

Is it worth to implement microbial control strategy?

Reported incidence about 5 ppm = 0.0005%

What is the frequency of contaminated PC?



Culture of rapid method
at the time of transfusion or expire

(6 studies)

The frequency of contaminated TCs is 217-823 ppm
(0.02-0.08%; 1:1200-1:5000)

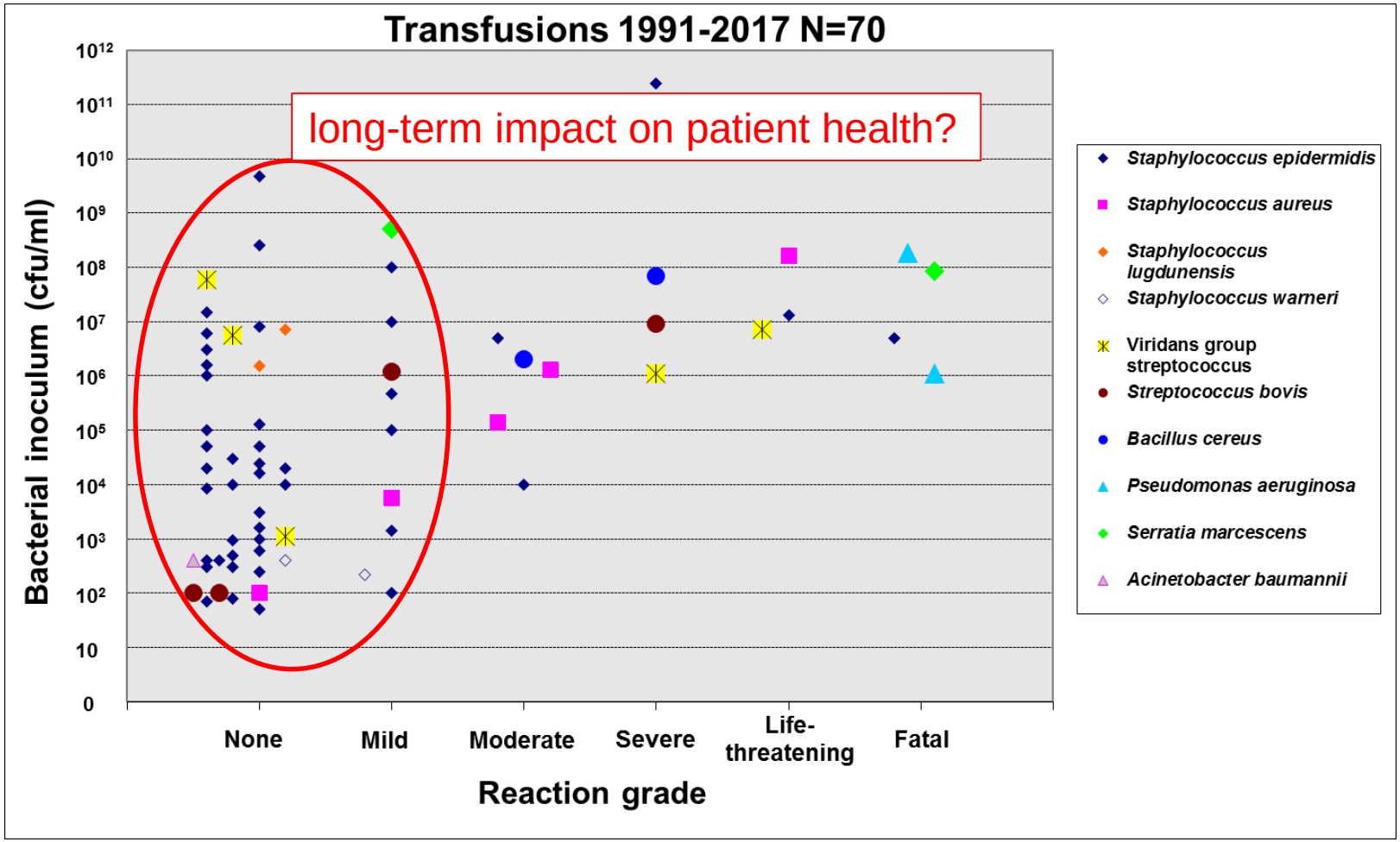
(that means for EU = ca. 600-2300 infected TCs units / year)

=> These figures are usually significantly higher than hemovigilance reports

Possible reasons for underreporting of septical episodes after PC transfusion

- passive vigilance report only 10-20% from total incidence (Jacobs et al)
- only 10% of reports have verified a root cause of infection (PEI Data)
- concomitant effective antibiotic treatment
- only acute septic (pyrogenic) reactions (till 4h after transfusion)

Transfusion of contaminated PCs is frequently asymptomatic



Hong et al 2016

Aubron et al. Critical Care (2017) 21:2
DOI 10.1186/s13054-016-1593-x

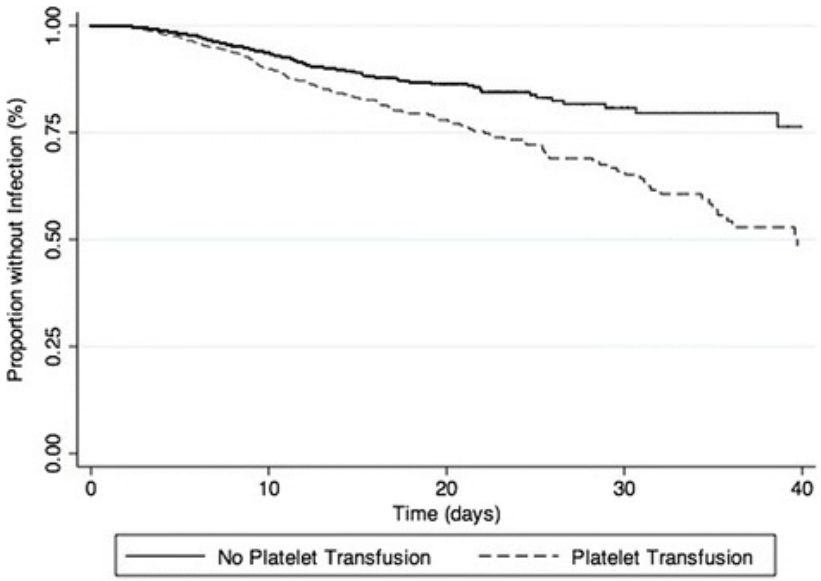
Critical Care

RESEARCH Open Access

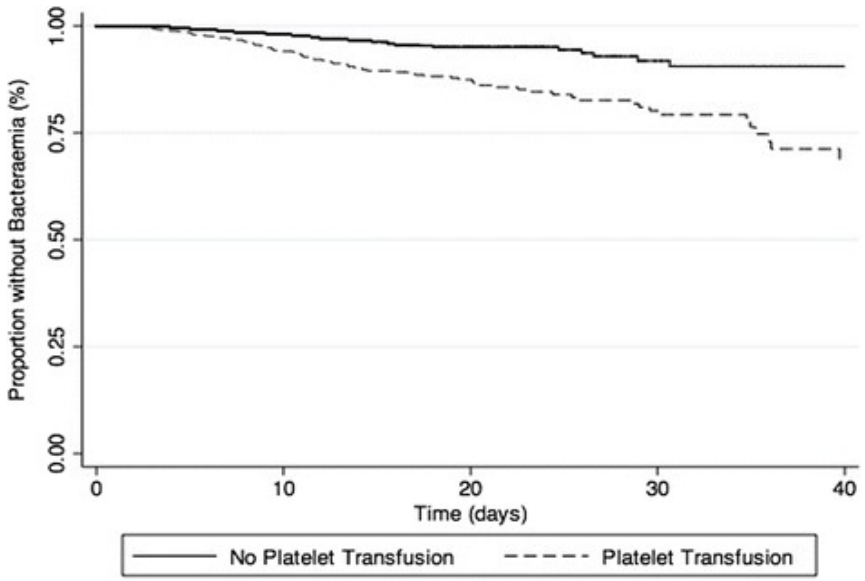
Is platelet transfusion associated with hospital-acquired infections in critically ill patients?

Cécile Aubron[1,10*], Andrew W. Flint[1,9], Michael Bailey[1], David Pilcher[1,3], Allen C. Cheng[5,6], Colin Hegarty[8], Antony Martinelli[8], Michael C. Reade[7,9], Rinaldo Bellomo[1,4] and Zoe McQuilten[1,2]

risk of infection



risk of bacteremia



ca. 19000 Patients

Conclusions: After adjustment for confounders, including patient severity and other blood components, platelet transfusion was independently associated with ICU-acquired infection.

Summary

- risk mitigation for bacterial contamination of platelet concentrates can be implemented through screening by growth-based methods or pathogen reduction technologies

- late (>36 h after donation) sampling strategy seem to be more effective than early sampling

- whenever possible the microbiological control strategy should be implemented, since frequency of transfusion septic incidents might be much higher as hemovigilance data suggest

- necessity of harmonization of the microbiological strategies among EU member states

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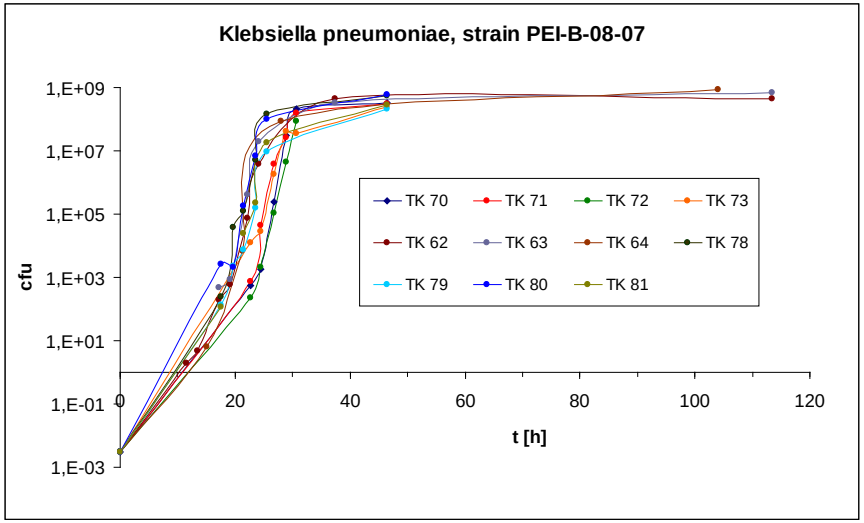
Health is our focus

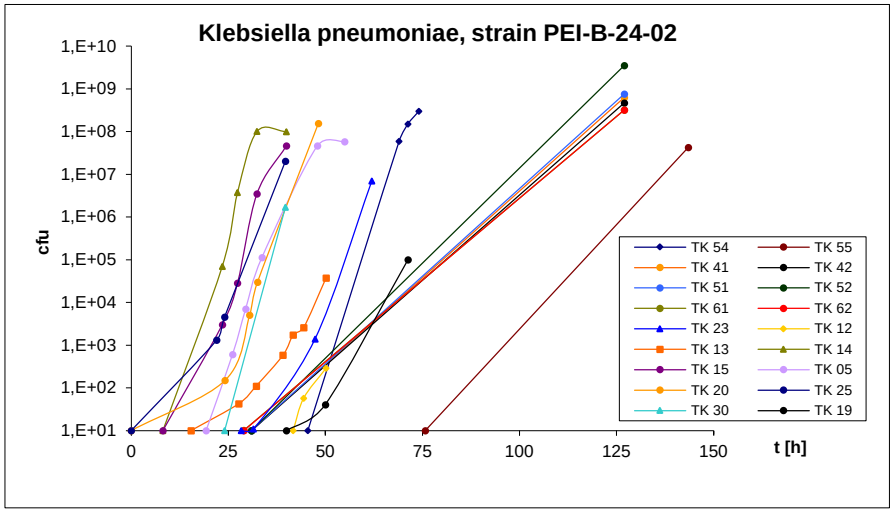
Thank you for your attention !

Section Microbial Safety: Ingo Spreitzer, **Marcel Prax,** Holger Lößner, Oliver Karo, **Birgit Blissenbach**, **Anja Schneider, Marie Anders-Mauer**, Bjorn Becker, **Philipp Windecker**

Growth kinetics *K. pneumoniae* Strains

Low titer spiking (ca. 30 CFU / Unit) of PCs from different donors
Colony count determination over time (22.5°C, agitation)





relevant differences between strains of the same bacterial species