Working Party Transfusion-Transmitted Infectious Diseases (WP-TTID)

Subgroup Bacteria

Chair: Thomas Montag, Germany

Co-Chair: Erica Wood, Australia

Annual Report 2008/9

WP-TTID, Subgroup Bacteria
Annual Report 2008/9

Extraordinary organisational topics in 2008:

1. Extraordinary Meeting of Subgroup Bacteria
   Montreal, Canada (AABB October 2008)
   "Preparation of WHO ISBT International Validation Study on Blood Bacteria Standards – discussion of scientific and logistical details"

   (financed by WP-TTID, budget of Subgroup Bacteria)

2. Regular phone conferences
   - Started in April 2008
   - Erica Wood, Melanie Stoermer, Carl McDonald, Thomas Montag

   (financed by Australian Red Cross)

WP-TTID, Subgroup Bacteria
Annual Report 2008/9

Working Schedule 2008/9

1. Preparation of an international survey on transfusion-transmitted bacterial infections.

2. Review on Bacterial Safety of Cellular Blood Components.

3. WHO ISBT International Validation Study on Blood Bacteria Standards.

WP-TTID, Subgroup Bacteria
Annual Report 2008/9

Working Schedule

1. **Preparation of a international survey on transfusion-transmitted bacterial infections.**

   -> draft questionnaire (topics of relevance) prepared by Thomas Montag, Melanie Stoermer, Erica Wood, and Carl McDonald
   -> model questionnaire provided by Silvano Wendel (BEST, Chris Prowse)
   -> agreement with Kurt Roth to implement the inquiry on transfusion-transmitted bacterial infections into the electronic questionnaire of Subgroup Virology
   -> to be continued in 2009

2. **Review on Bacterial Safety of Cellular Blood Components.**

3. **WHO ISBT International Validation Study on Blood Bacteria Standards.**

WP-TTID, Subgroup Bacteria
Annual Report 2008/9

Working Schedule 2008/9

1. Preparation of a international survey on transfusion-transmitted bacterial infections.

2. Review on Bacterial Safety of Cellular Blood Components.

   -> outline prepared by Carl McDonald, Erica Wood, Melanie Störmer and Thomas Montag
   -> installation of a writing group (several members of WP-TTID)
   -> to be continued in 2009

3. WHO ISBT International Validation Study on Blood Bacteria Standards.

WP-TTID, Subgroup Bacteria
Annual Report 2008/9

Working Schedule 2008/9

1. Preparation of a international survey on transfusion-transmitted bacterial infections.

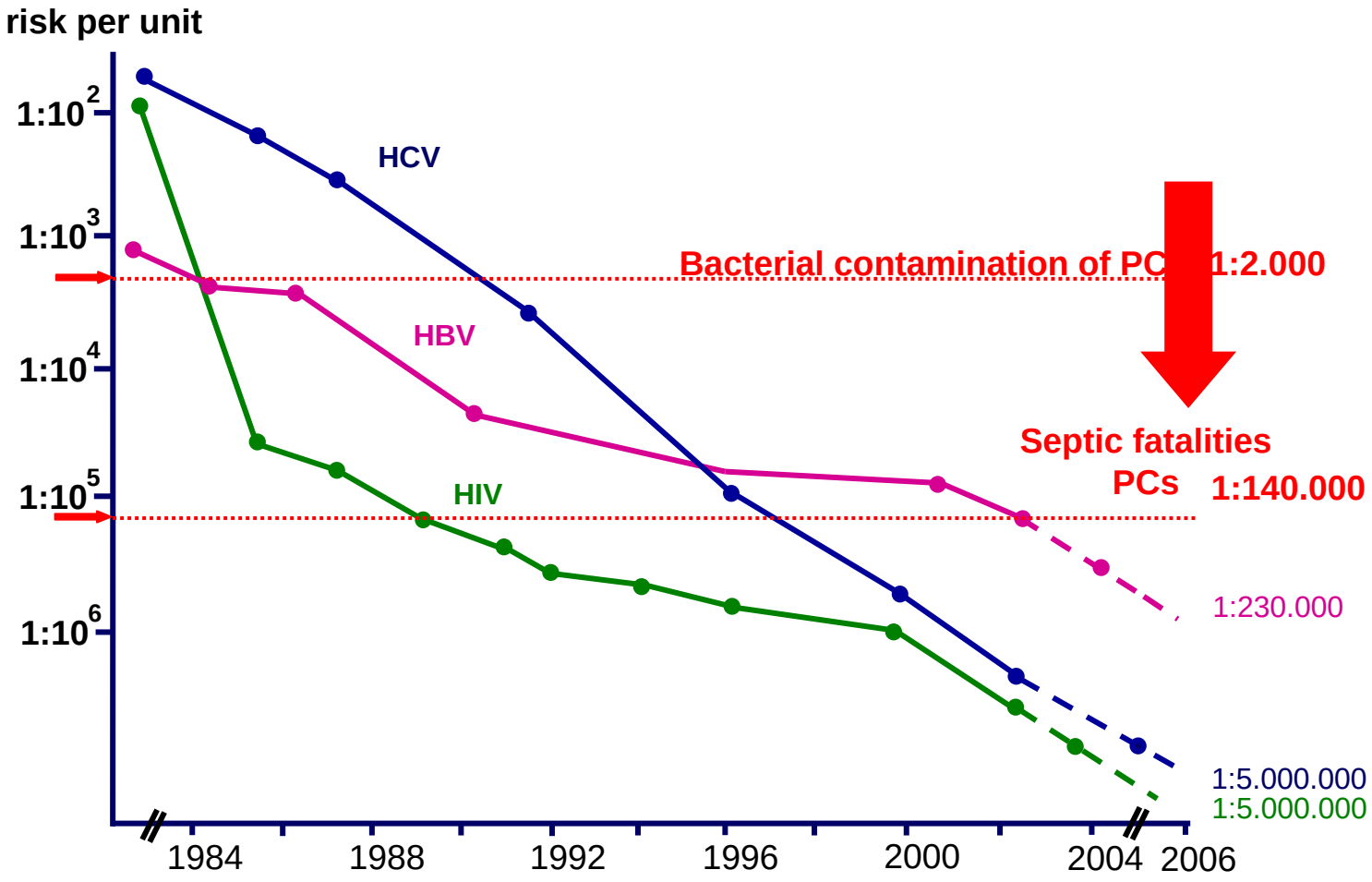
2. Review on Bacterial Safety of Cellular Blood Components.

3. **WHO ISBT International Validation Study on Blood Bacteria Standards.**

Background of WHO ISBT International Validation Study on Blood Bacteria Standards

Why do we need a panel of transfusion-relevant bacteria?

Infection Risk in Platelets: bacterial vs viral

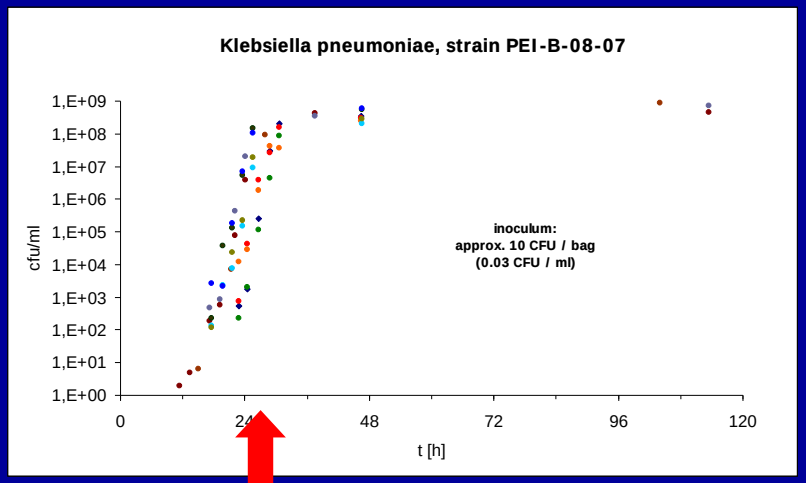


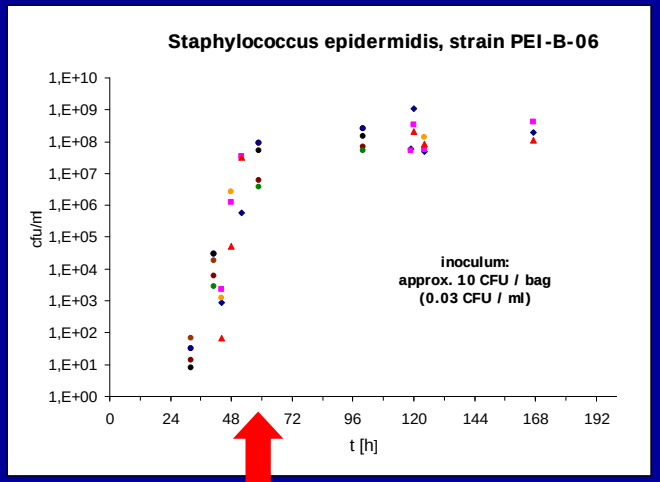
according to Mike Busch, modified

Crux in Bacterial Contamination of Blood Components

Usually, bacteria are contaminating blood donations in a very low count (10 to 100 CFU per bag corresponding to 0.03 to 0.3 CFU / ml).

Thereafter, they can grow up in platelets to 10^8 to 10^9 CFU / ml (in dependency on species and strain).





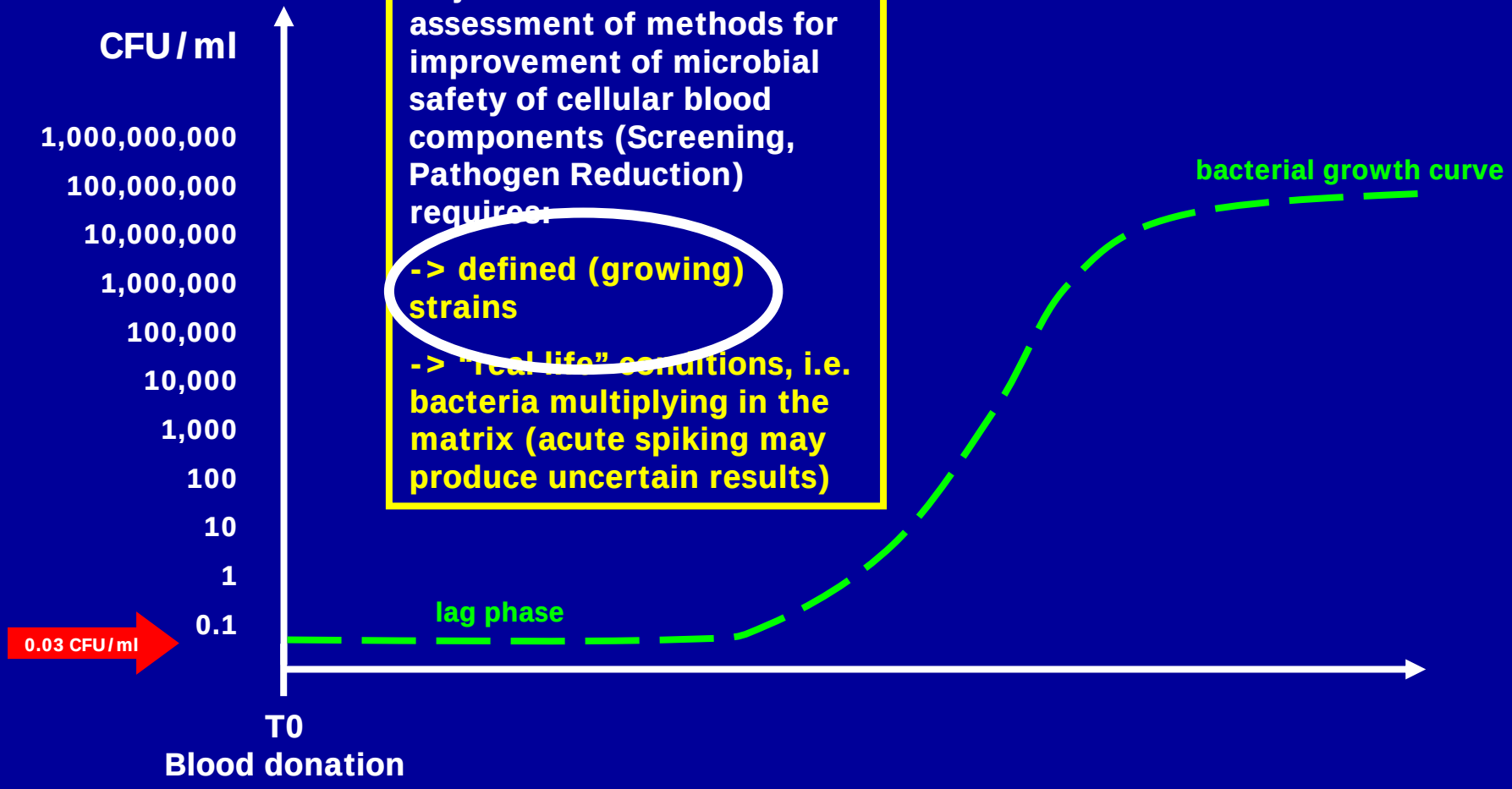
Artificial contamination of platelets imitating "real life" conditions:
-> contamination with 0.03 CFU / ml
-> storage at 22.5 °C under agitation

Kinetic of microbial growth in blood components

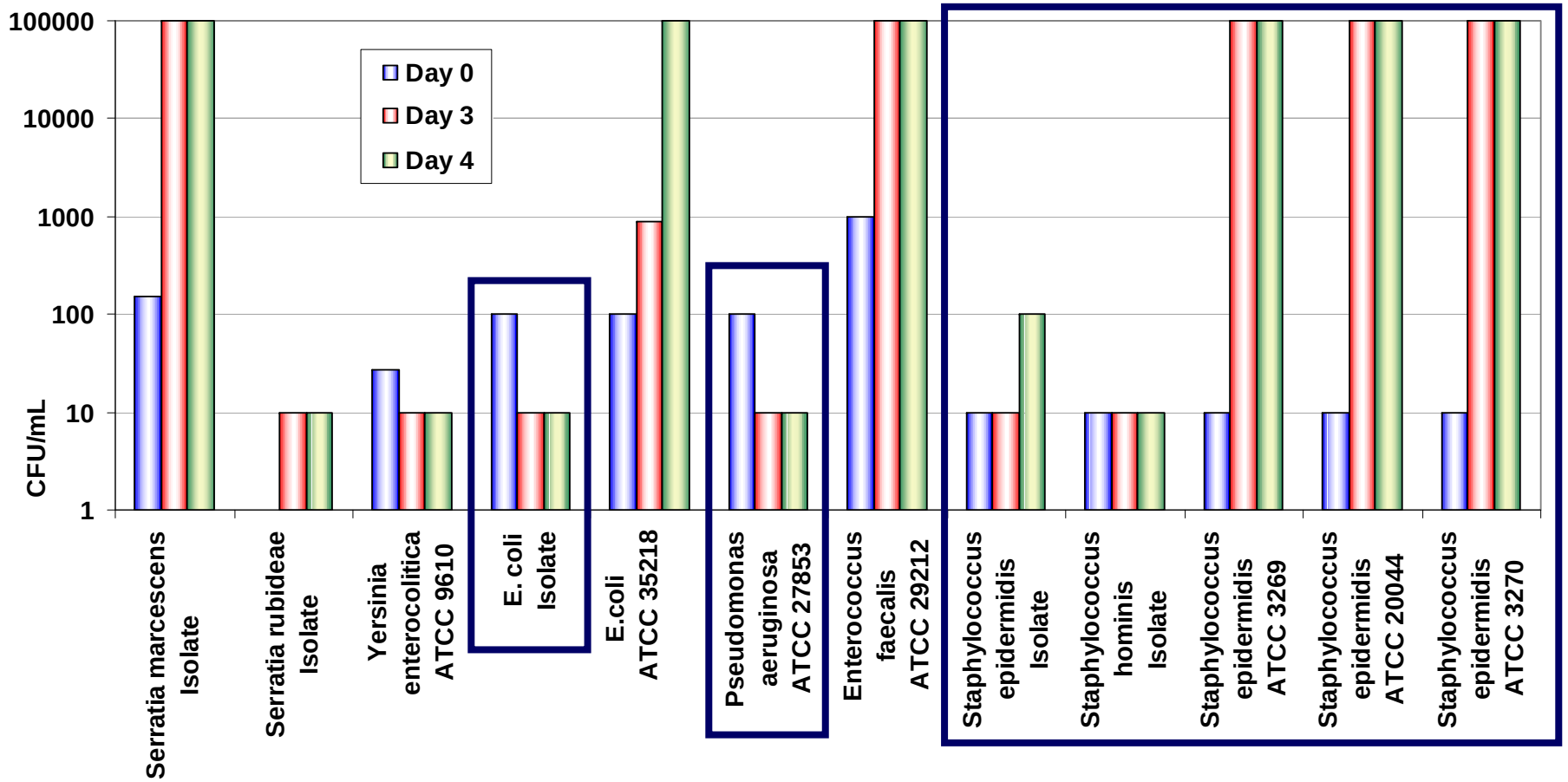
Objective validation and assessment of methods for improvement of microbial safety of cellular blood components (Screening, Pathogen Reduction) requires:

-> defined (growing) strains

-> "real life" conditions, i.e. bacteria multiplying in the matrix (acute spiking may produce uncertain results)



Growth of different bacteria strains in platelet concentrates



Consequence:

The established bacterial reference strains (e.g. from ATCC) are not (automatically) applicable for validation studies regarding methods for improvement of microbial safety of cellular blood components.

What kind of reference bacteria do we need ?

- Selected strains (not species !)
- Should grow / multiply in platelets
- Should grow independent on donor's blood (plasma)
- Should enable "real life" contamination, i.e. 10 CFU per platelet bag corresponding to 0.03 CFU per millilitre
  in order to allow objective method validation

Consequence:
Development of Blood Bacteria Standards during the past 10 years

What are Blood Bacteria Standards ?

1. Blood Bacteria Standards (References) are able to grow in PCs up to high counts (what is not automatically given in case of reference strains like ATCC strains).
2. Strains grow up in PCs independent on donor properties (tested for relevant multiplication in PCs from at least 100 different donors).
3. The standards are deep frozen, ready to use, stable, and shippable (manufactured by a special procedure).
4. They are defined in count and consist mainly of living cells (as a rule > 95 % living cells).
5. The standards allow "real life" spiking of blood components, i.e. artificial contamination with ~ 10 CFU per bag corresponding to 0.03 CFU per millilitre.
6. Thus, Blood Bacteria Standards are a feasible tool for objective validation and assessment of methods for screening and pathogen reduction in blood components.

Prototype Certificate of one of the Blood Bacteria Standards

Working Party on
Transfusion-Transmitted Infectious Diseases

WHO-ISBT International Validation Study

Certificate

Blood Bacteria Standard

Species: *Staphylococcus epidermidis*
Code: PEI-B-06-Charge
Lot: PEI-B-06-07

store below -70°C

Developed by: Paul Ehrlich Institute
Federal Agency for Sera and Vaccines
Division Microbial Safety
Paul-Ehrlich-Strasse 51-59
63225 Langen

Generated:
Date: 2005/09/28

Approved:
Date: 2008/02/06

Lot: PEI-B-06-07

Species: *Staphylococcus epidermidis*

Isolated from: platelet concentrate (PC)

Supplied as: deep frozen in 10% Human Serum Albumin in saline (150 mM NaCl)

Volume: 1.5 mL

Bacterial load: 2.18 ± 0.29 x 10^8 CFU/mL

Growth in PC: Blood Bacteria Standard *Staphylococcus epidermidis* PEI-B-06 grows donor independently in PCs.

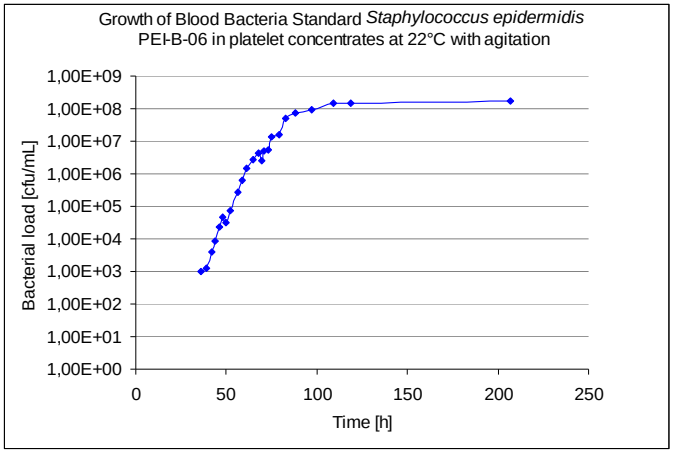


Fig.1 In the in vitro study pooled PCs (n=4) were inoculated with 0.03 CFU/mL of Blood Bacteria Standard PEI-B-06 of isolate *Staphylococcus epidermidis*. Sampling was performed during aerobic storage at 22°C and the presence of bacteria was assessed by plating culture.

Prototype Certificate of one of the Blood Bacteria Standards

2. Bacterial Strain (Blood Bacteria Standard)

Phylum:	Firmicutes
Class:	Cocci
Order:	Bacillales
Family:	*Staphylococcaceae*
Species:	*Staphylococcus epidermidis*
Collection no.:	none (isolate)
Isolated from:	platelet concentrate
Characteristics:	GRAM-positive cocci (0.7 - 1.2 µm), colonies are often surrounded by a clear zone of haemolysis (beta haemolysis) due to production of haemolysins tissue invasive, produce purulent (pus-filled) lesions, nonsporeforming, facultative anaerobic, obligatory pathogenic, grows at 6.5°C to 46°C at pH 4.2 - 9.3.

3. Microbiological identification

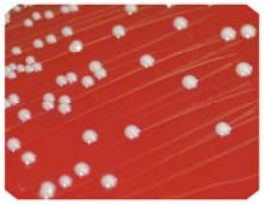


Fig. 2 *St. epidermidis* (PEI-B-06) on sheep blood agar after 24 hours incubation at 37°C

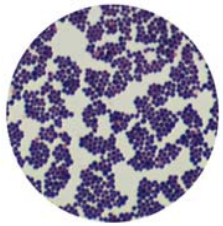


Fig. 3 GRAM-stain of *St. epidermidis* (PEI-B-06)

Colonies: small, white or yellow color, approx. 1-2 mm in diameter after overnight incubation; no haemolysis

GRAM-stain: GRAM-positive

4. Molecular genetic identification (16S rDNA Sequence)

Automated microbial DNA sequencing was performed by using the MicroSEQ® Microbial Identification System (Applied Biosystems).

Name	Resultat MicroSeq	Match	Specimen Score	Consensus Length
PEI-B-06	*St. epidermidis* ATCC 12228	100 %	46	1469

Staphylococcus epidermidis 16S rDNA sequence

GAACGCTGGCGGCGTGCCTAATACATGCAAGTCGAGCGAACAGACGAGGAGCTTGCTCCTCT
GACGTTAGCGGCGGACGGGTGAGTAACACGTGGATAACCTACCTATAAGACTGGGATAACTT
CGGGAAACCGGAGCTAATACCGGATAATATATTGAACCGCATGGTTCAATAGTGAAAGACGG
TTTTGCTGTCACTTATAGATGGATCCGCGCCGCATTAGCTAGTTGGTAAGGTAACGGCTTAC
CAAGGCAACGATGCGTAGCCGACCTGAGAGGGTGATCGGCCACACTGGAACTGAGACACGGT
CCAGACTCCTACGGGAGGCAGCAGTAGGGAATCTTCCGCAATGGGCGAAAGCCTGACGGAGC
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GTGTAAGTAACTATGCACGTCTTGACGGTACCTAATCAGAAAGCCACGGCTAACTACGTGCC
AGCAGCCGCGGTAATACGTAGGTGGCAAGCGTTATCCGGAATTATTGGGCGTAAAGCGCGCG
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AGCGTGGGGATCAAACAGGATTAGATACCCTGGTAGTCCACGCCGTAAACGATGAGTGCTAA
GTGTTAGGGGGTTTCCGCCCCTTAGTGCTGCAGCTAACGCATTAAGCACTCCGCCTGGGGAG
TACGACCGCAAGGTTGAAACTCAAAGGAATTGACGGGGACCCGCACAAGCGGTGGAGCATGT
GGTTTAATTCGAAGCAACGCGAAGAACCTTACCAAATCTTGACATCCTCTGACCCCTCTAGA
GATAGAGTTTTCCCCTTCGGGGGACAGAGTGACAGGTGGTGCATGGTTGTCGTCAGCTCGTG
TCGTGAGATGTTGGGTTAAGTCCCGCAACGAGCGCAACCCTTAAGCTTAGTTGCCATCATTA
AGTTGGGCACTCTAAGTTGACTGCCGGTGACAAACCGGAGGAAGGTGGGGATGACGTCAAAT
CATCATGCCCCTTATGATTTGGGCTACACACGTGCTACAATGGACAATACAAAGGGYAGCGA
AACCGCGAGGTCAAGCAAATCCCATAAAGTTGTTCTCAGTTCGGATTGTAGTCTGCAACTCG
ACTATATGAAGCTGGAATCGCTAGTAATCGTAGATCAGCATGCTACGGTGAATACGTTCCCG
GGTCTTGTACACACCGCCCGTCACACCACGAGAGTTTGTAACACCCGAAGCCGGTGGAGTAA
CCATTTGGAGCTAGCCGTCGAAGGTGGGACAAATGATTGGGGT

5. Production

5.1 Production principle

After the bacterial identification process using microbiological, biochemical (using the API Staph multitest identification system, bioMérieux) and molecular genetic methods (16S rDNA sequencing, RAPD-PCR), an impedance-monitoring system is used to characterize bacterial growth kinetics of Blood Bacteria Standard PEI-B-06 under

Prototype Certificate of one of the Blood Bacteria Standards

defined conditions (e.g. media, temperature). Following, bacteria are removed during the logarithmic phase, enumerated and frozen in 10% Human Serum Albumin in saline (150 mM) at -80 °C. Viability control is performed 24 hours after production while stability control is performed quarterly. The bacterial identity of each charge of Blood Bacteria Standard PEI-B-06 is confirmed by biochemical and molecular genetic methods, including 16S rDNA sequencing and DNA fingerprinting (RAPD-PCR).

5.2 Master Bank

Bacteria of Blood Bacteria Standard PEI-B-06 are cultured on appropriate agar media to a sufficient bacterial count. Under aseptic conditions bacteria are transferred to six vials of a Cryobank system to the manufacturer`s instructions and stored at -80 °C. Cryobank tubes contain a medium for suspending the bacterial culture and 25 colour-coded ceramic beads. The suspending medium comprises trypticase soy broth supplemented with glycerol and sucrose. Cryobank systems offer a reliable, convenient and versatile system for storing and preserving fastidious bacteria over long periods.

6. Batch Quality Control

6.1 Viability

To affirm the viability of the Blood Bacteria Standard PEI-B-06, vials of PEI-B-06 are thawed 24 hours after production and enumerated as described in the application section.

6.2 Stability

The stability of the Blood Bacteria Standard PEI-B-06 is confirmed quarterly by thawing and enumerating as described in the application section.

		Production		Last Stability control	
Species	**Charge**	**Date**	**Bacterial load [cfu/mL]**	**Date**	**Bacterial load [cfu/mL]**
Staphylococcus epidermidis	PEI-B-06-07	28.09.2005	2.18 ± 0.29E+08	06.02.2008	1.56 ± 0.33E+08

6.3 Identity (Fingerprint)

Random amplified polymorphic DNA analysis (RAPD) was performed using different single oligonucleotide primers of arbitrary sequence.
PCR products underwent electrophoresis on an agarose gel (2%) and were visualized using ethidium bromide staining.

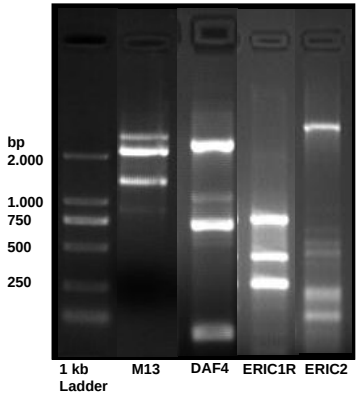


Fig. 4 RAPD-PCR (DNA-Fingerprint) of *St. epidermidis* PEI-B-06 using different single oligonucleotide primers (n=4).

7. Application

7.1 Storage

The vials of the Blood Bacteria Standard PEI-B-06 have to be stored immediately below 70°C after arrival. To assure the viability of bacteria of the Blood Bacteria Standard PEI-B-06 the cold chain must not be interrupted.

7.2 Utilization

Before use, transfer the vials of the Blood Bacteria Standard PEI-B-06 directly from the deep freezer to a dry incubator and defrost the vials at 37ºC for 10 minutes. If ice crystals are still evident, the vial should be warmed in the hand until the crystals have melted. Vortex the vial for 15 seconds to be sure that all bacteria are evenly spread. Dilution steps and determination of the bacterial count have to be performed as described in the study design protocol.

Partners of WHO-ISBT Validation Study on Blood Bacteria Standards

Study coordinating group

Thomas Montag / Melanie Stoermer, Paul Ehrlich Institute, Germany
Carl McDonald, NBS, United Kingdom
Erica Wood, ARCBS, Australia
Ana Padilla, WHO
Cohava Gelber/ Marian McKee, American Type Culture Collection (ATCC), USA
Dirk de Korte/ Henk Reesink, Sanquin, The Netherlands

Partners

Institution	Country	Contact	asked	con-firmed
Blood Centre Linz	Austria	Christian Gabriel	+	yes
Canadian Blood Service, Ottawa	Canada	Sandra Ramirez-Arcos	+	yes
CaridianBCT, Lakewood CO	USA	Ray Goodrich	+	yes
Case Western Reserve University, Cleve-land	USA	Roslyn Yomtovian Michael R. Jacobs	+	yes
German Red Cross Blood Transfusion Ser-vice Springe, Partner Lab of BD Biosciences	Germany	Thomas Mueller	+	yes
German Red Cross Blood Transfusion Ser-vice, University of Frankfurt/Main	Germany	Michael Schmidt	+	yes
Hong Kong Red Cross Blood Transfusion Service	Hong Kong SAR China	Cheuk-Kwong Lee	+	yes
National Blood Service, London	United Kingdom	Carl McDonald	+	yes
National Blood Transfusion Centre,	México	Julieta Rojo	+	yes
Regional Centre for Transfusion Medicine, Bialystok	Poland	Piotr Radziwon	+	yes
South African National Blood Service, Weltevreden Park	South Africa	Tshilidzi Muthivhi	+	yes
St. Elisabeth Ziekenhuis, Tilburg	The Netherlands	Jan Marcelis	+	yes
VU University Medical Centre, Amsterdam	The Netherlands	Annika Pettersson	+	yes
Walter Reed Army Medical Center, Washington DC	USA	David G. Heath	+	yes

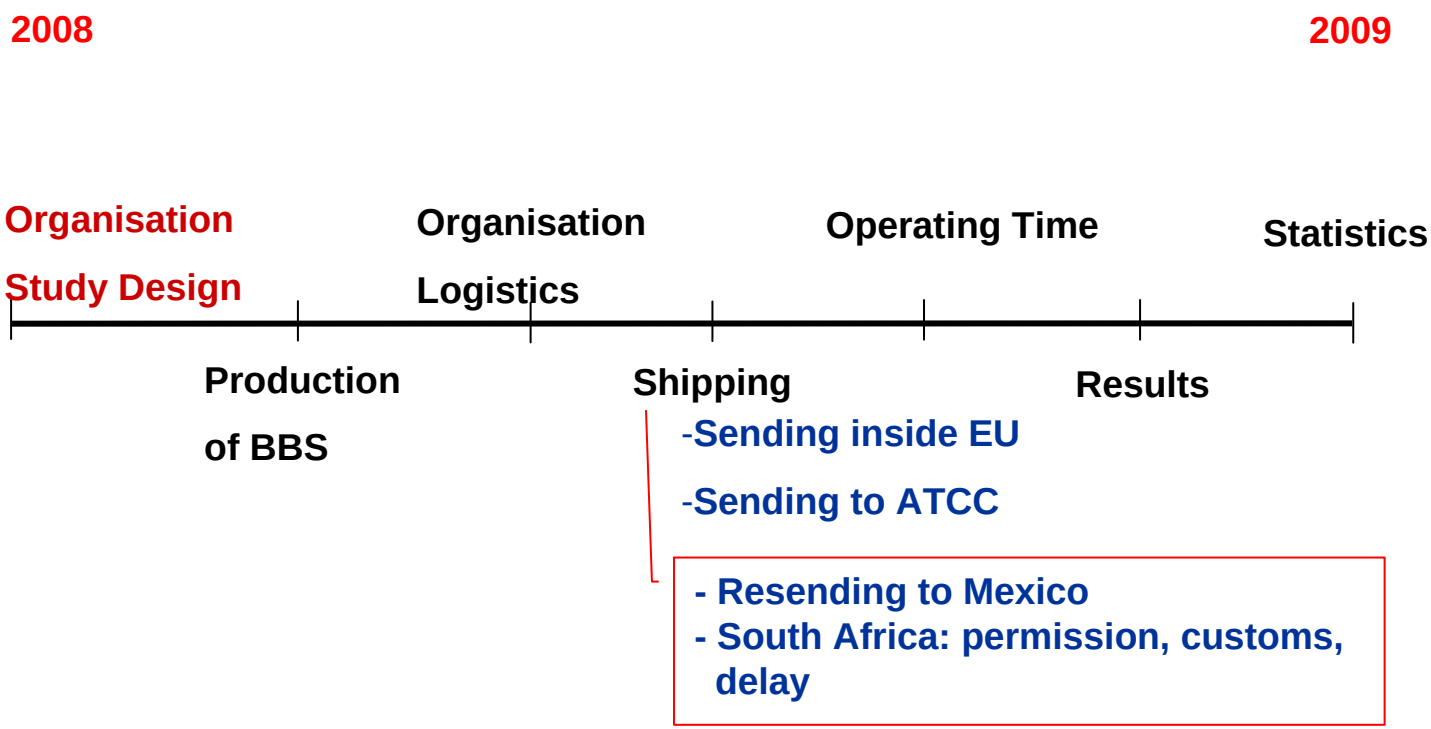
Logistics

1. **Shipping**
   - complicated to bring **living (blinded) pathogenic bacteria** through the customs
   - re-decision on deadline because of delay
   - Europe and Canada: shipping by PEI
   - Hong Kong, Mexico, South Africa, USA: shipping by ATCC
   - sometimes repetition of shipping necessary
   - shipping successful with the exception of South Africa

   data provided yesterday (bacteria meeting) by Tshilidzi Muthivhi

2. **Data receiving**
   - successful in all cases ~~(with exception of South Africa)~~
   - in one case too late for being able to perform the complete statistic calculation before Cairo meeting

Time schedule of WHO ISBT International Validation Study on Blood Bacteria Standards



Study Design

Phase 1 Four different blinded Blood Bacteria Standards (BBS) are sent to the partner labs

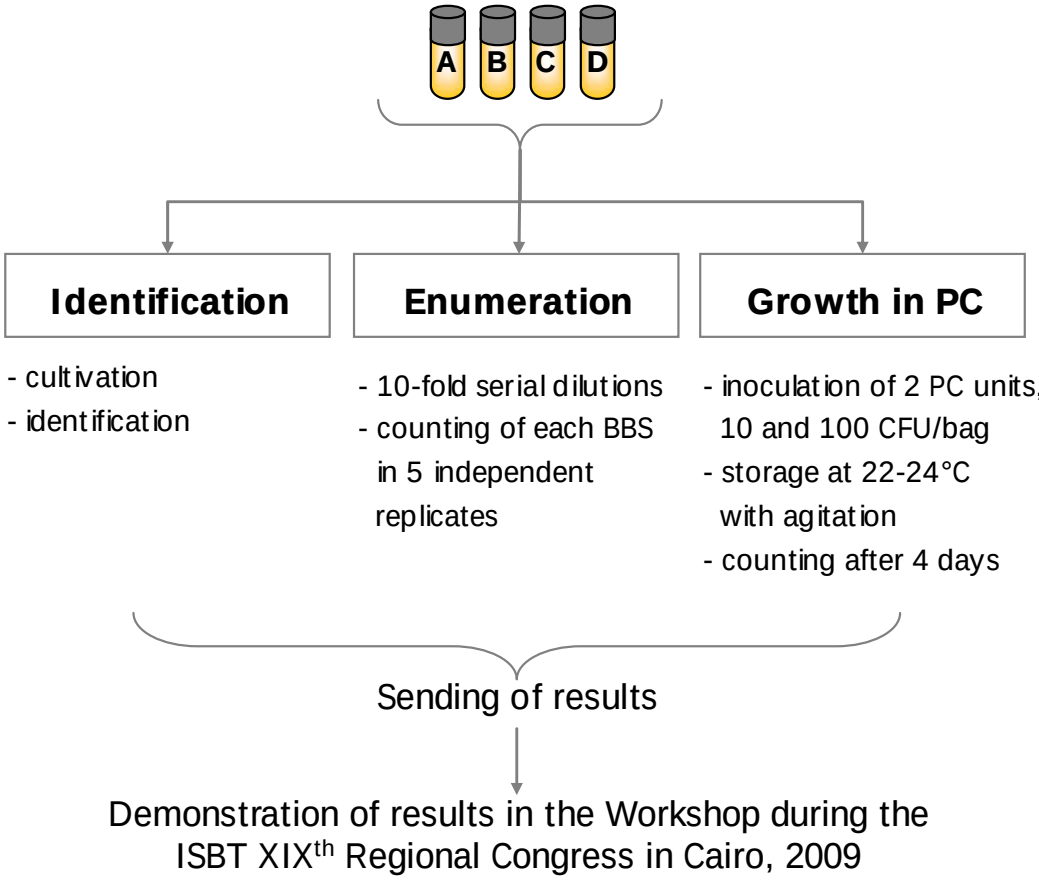
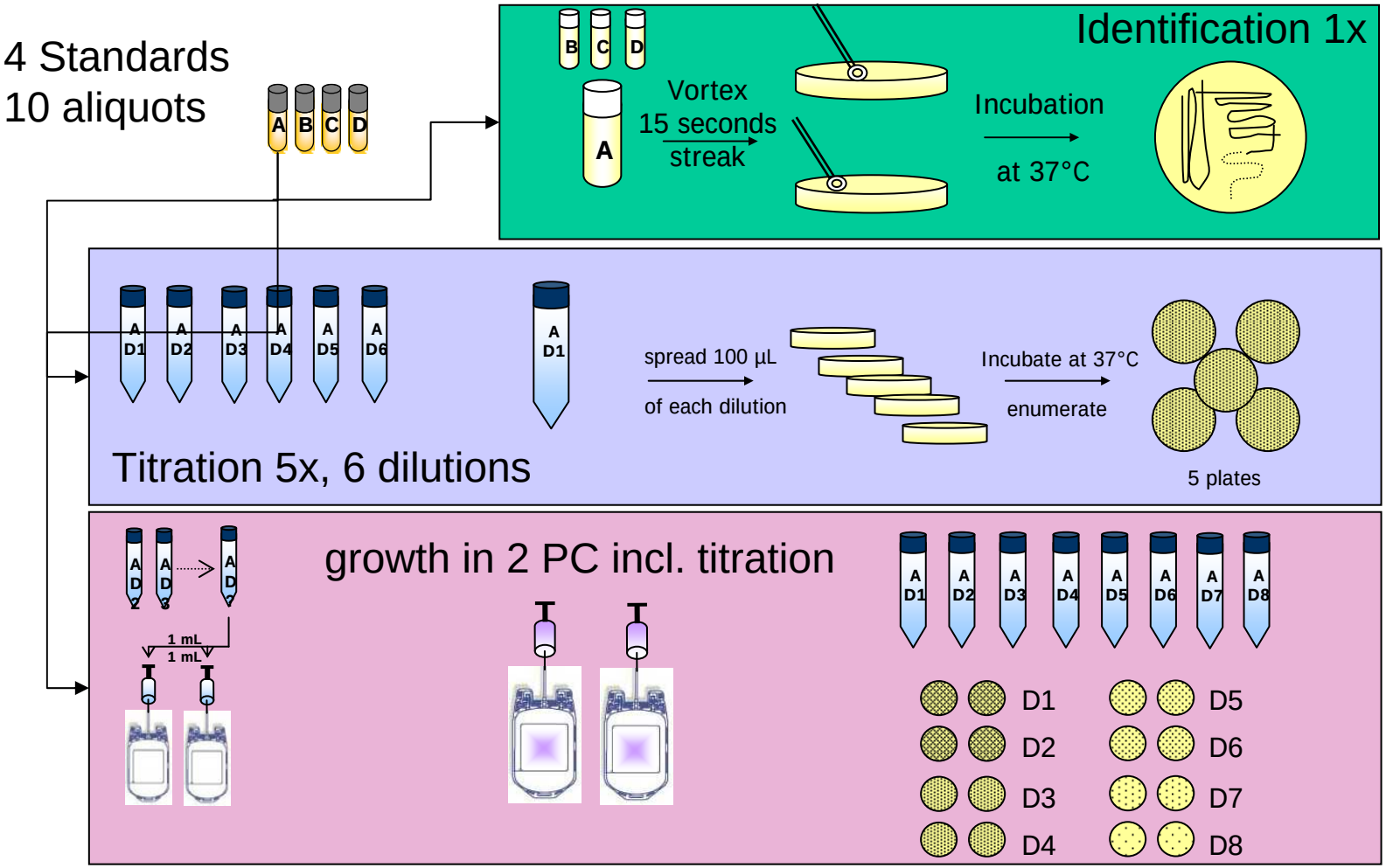


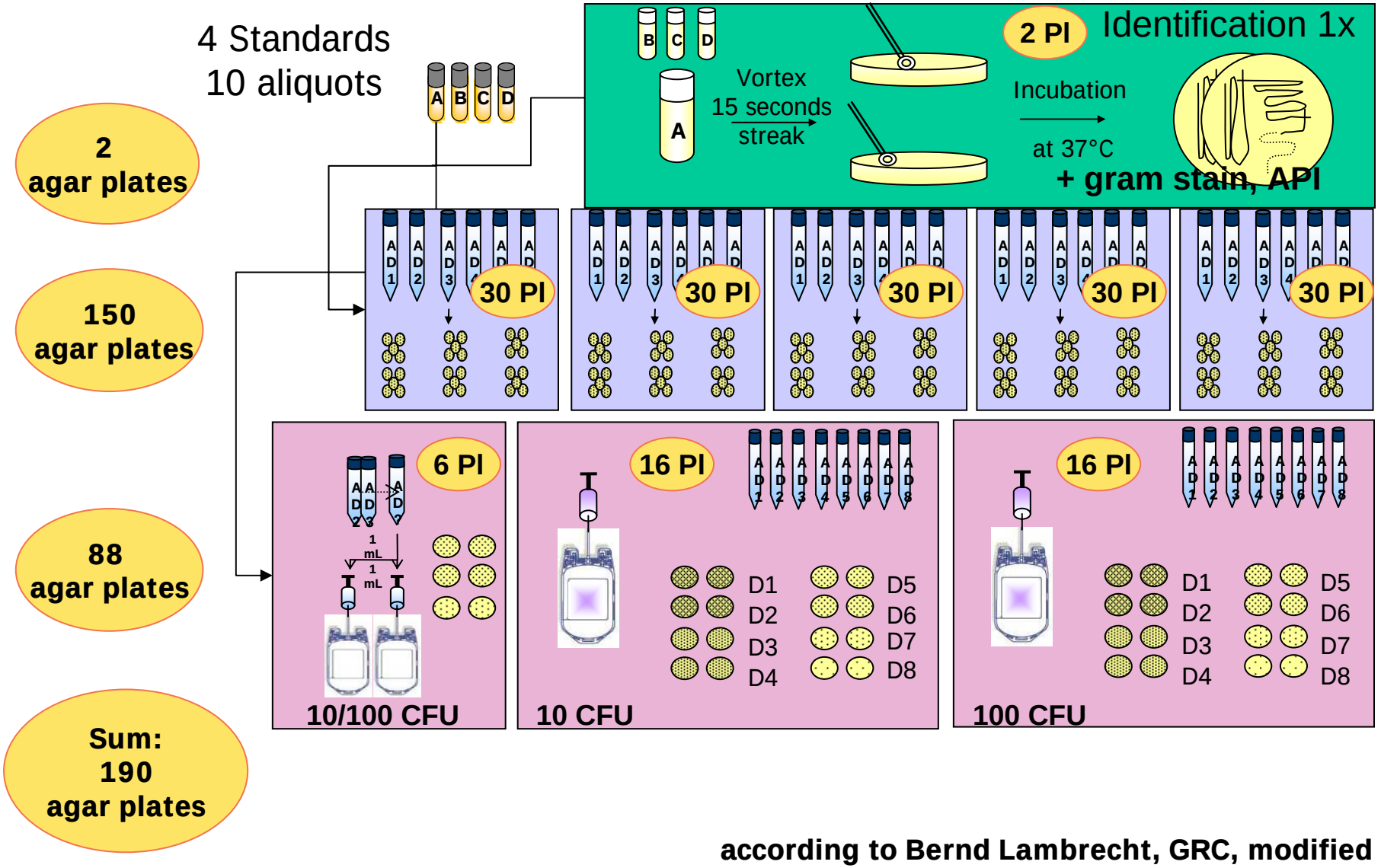
Fig. 1 Principle and Subject of Validation Study Phase 1

Study Protocol



according to Bernd Lambrecht, GRC, modified

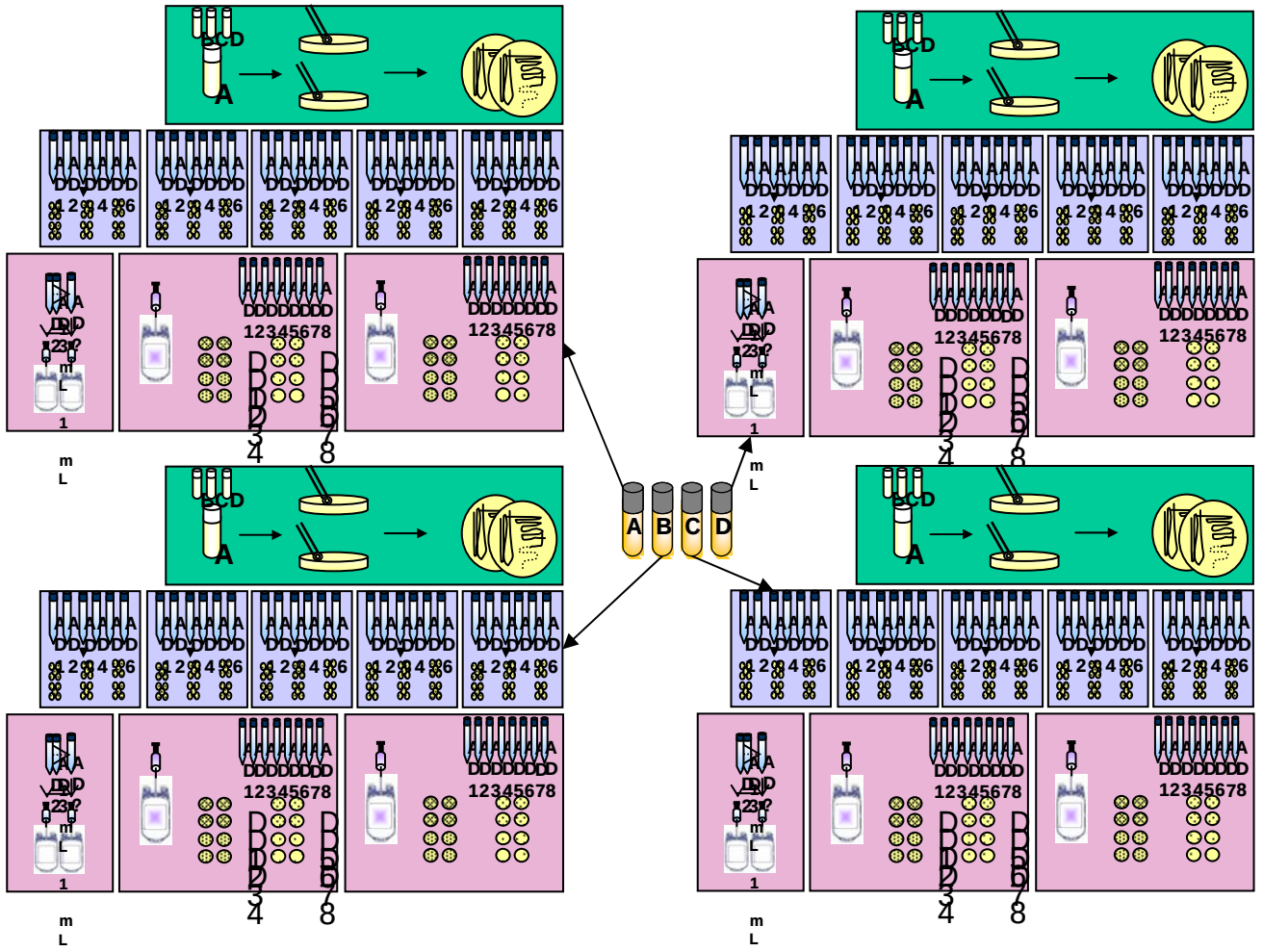
Protocol for 1 of the bacteria standards in detail



according to Bernd Lambrecht, GRC, modified

Complete protocol (4 standards)

Sum:
4 x 190
=
760
agar
plates



according to Bernd Lambrecht, GRC, modified

Results of

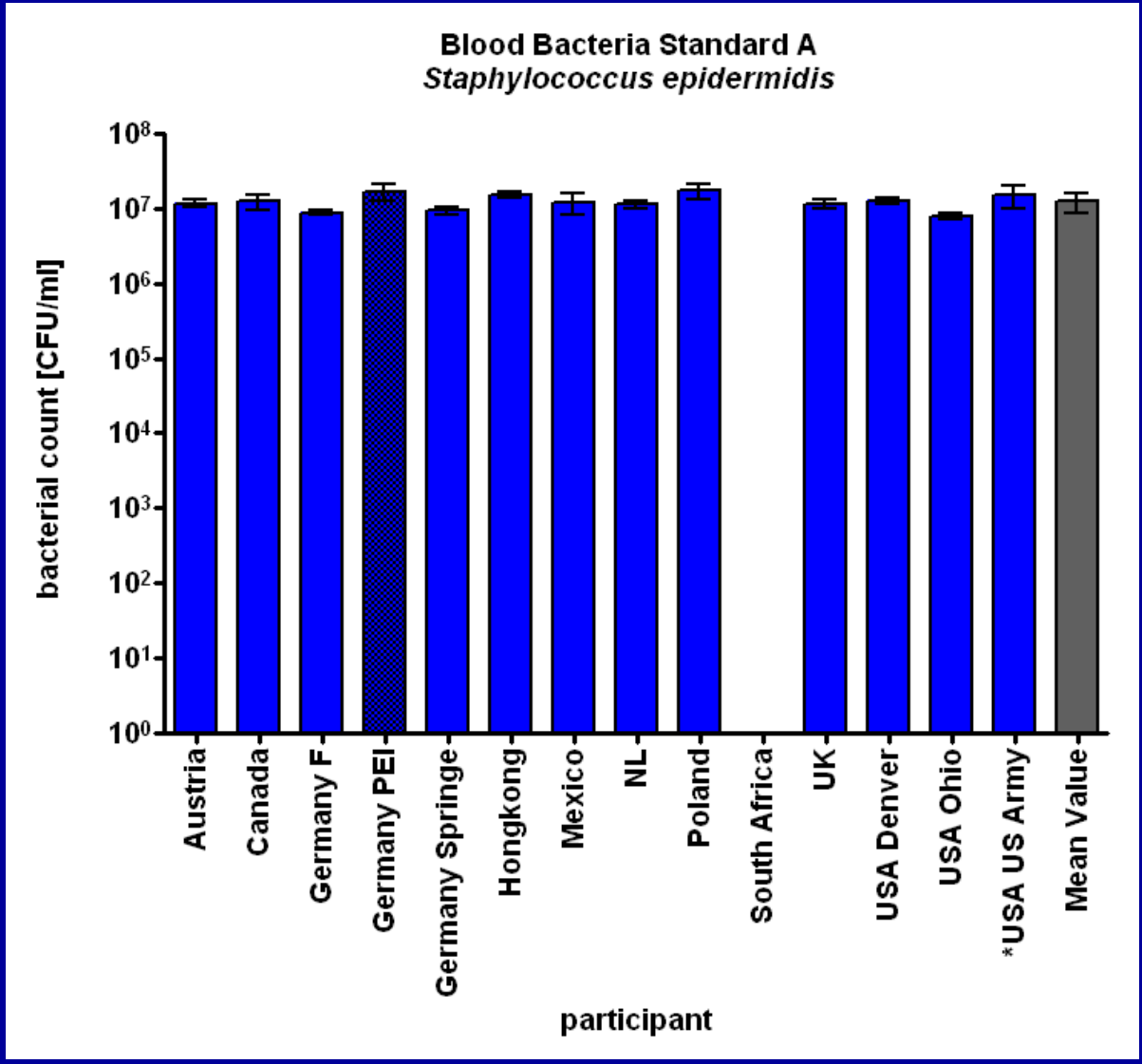
WHO ISBT International Validation Study on Blood Bacteria Standards

Part 1
Identification of blinded Bacteria Standards

Code	Bacteria species	Partners												
		1	2	3	4	5	6	7	8	9	10	11	12	13
A	*Staphylococcus epidermidis* (PEI-B-06-08)	+	+	+	+	+	+	+	+	+	+	(+)*	+	+
B	*Streptoccoccus pyogenes* (PEI-B-20-06)	+	+	+	+	+	+	+	+	+	+	+	+	+
C	*Klebsiella pneumoniae* (PEI-B-08-10)	+	+	+	+	+	+	+	+	+	+	+	+	+
D	*Escherichia coli* (PEI-B-19-06)	+	+	+	+	+	+	+	+	+	+	+	+	+

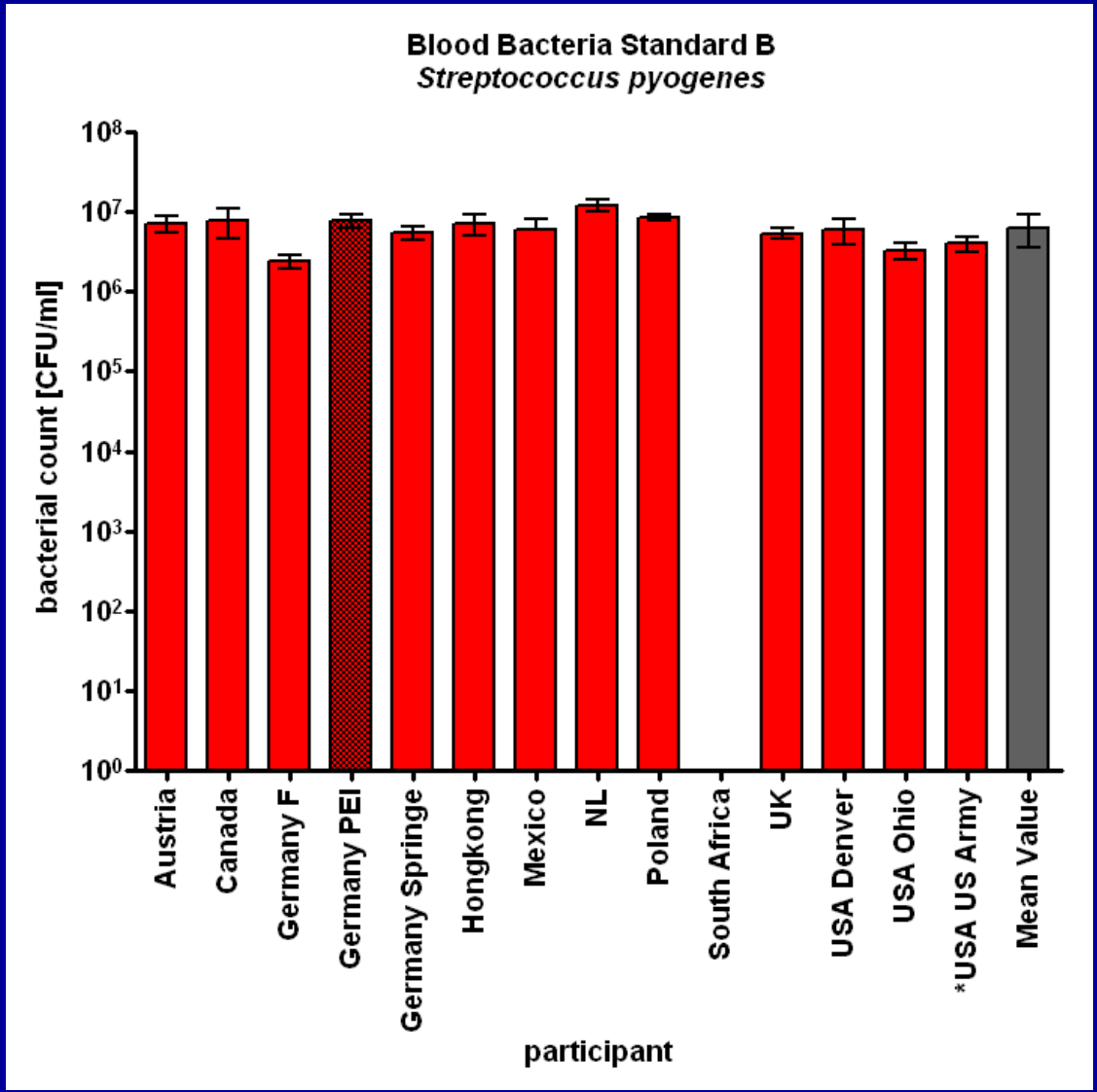
* In one case, determination as *Staphylococcus delphinii* instead of *Staphylococcus epidermidis* (most likely to the commercial identification kit used) but identified at least as coagulase-negative Staphylococcus.

Part 2
Enumeration of Blood Bacteria Standards



Data from South Africa to be added.

Part 2
Enumeration of Blood Bacteria Standards



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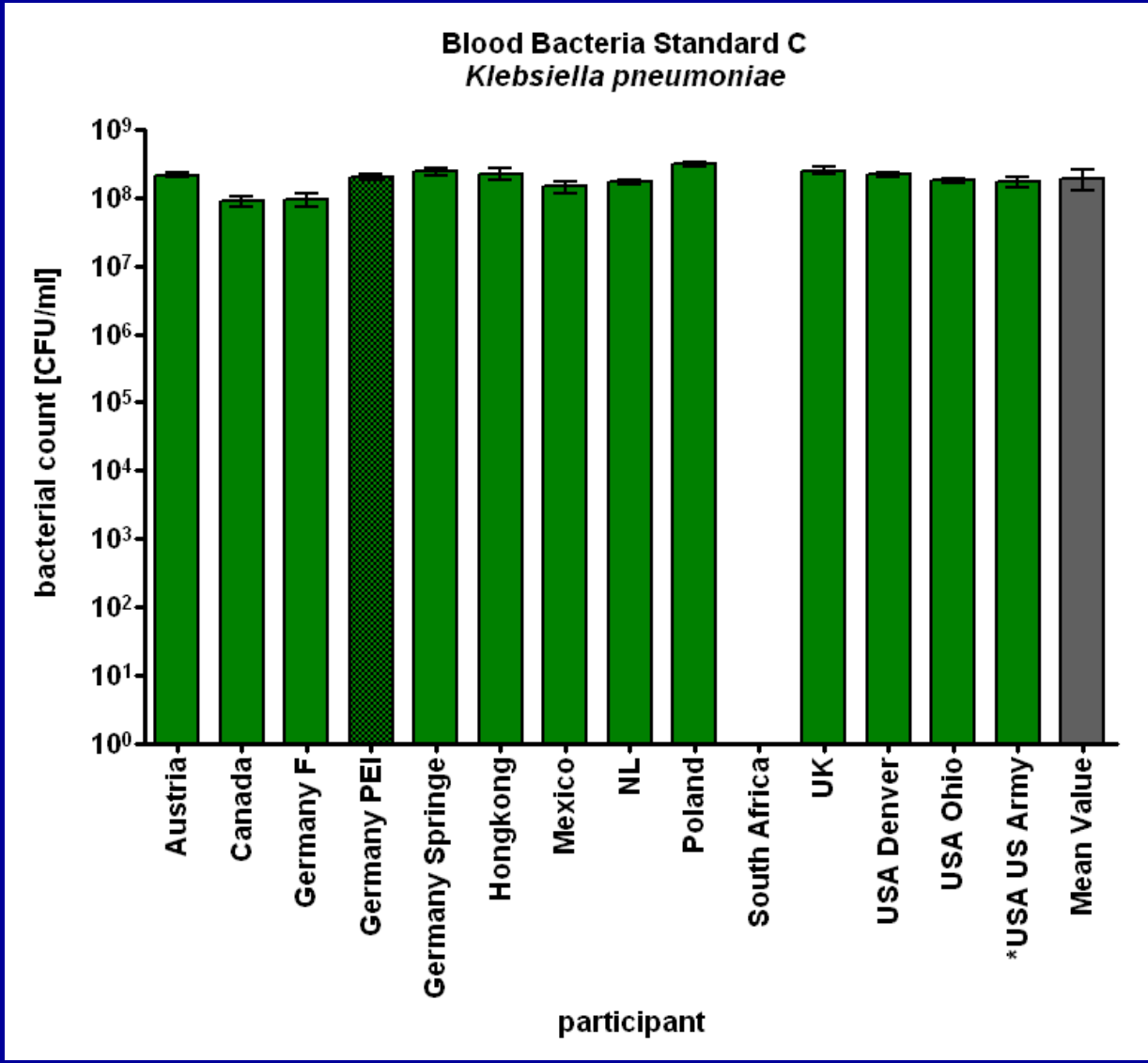

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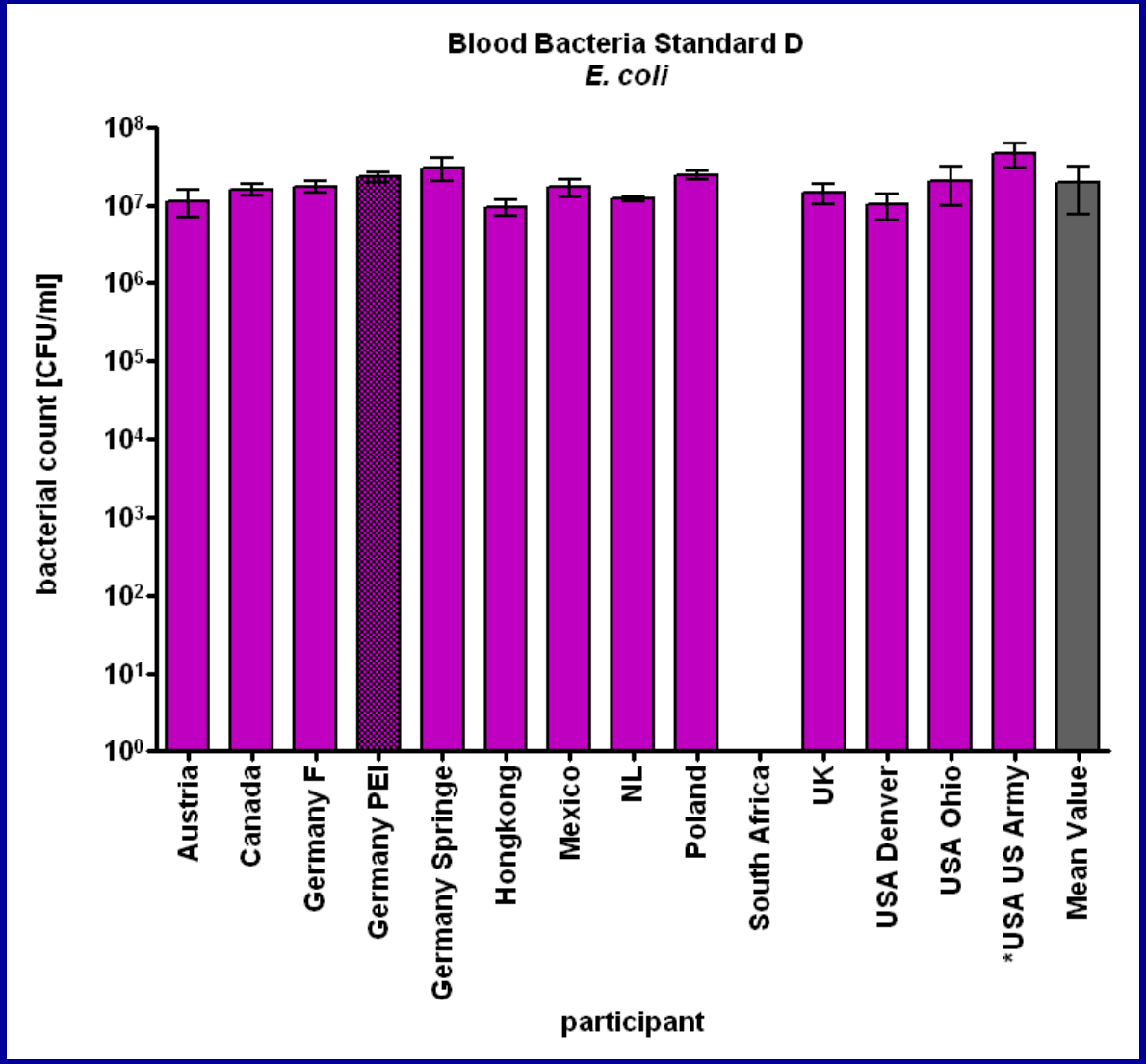

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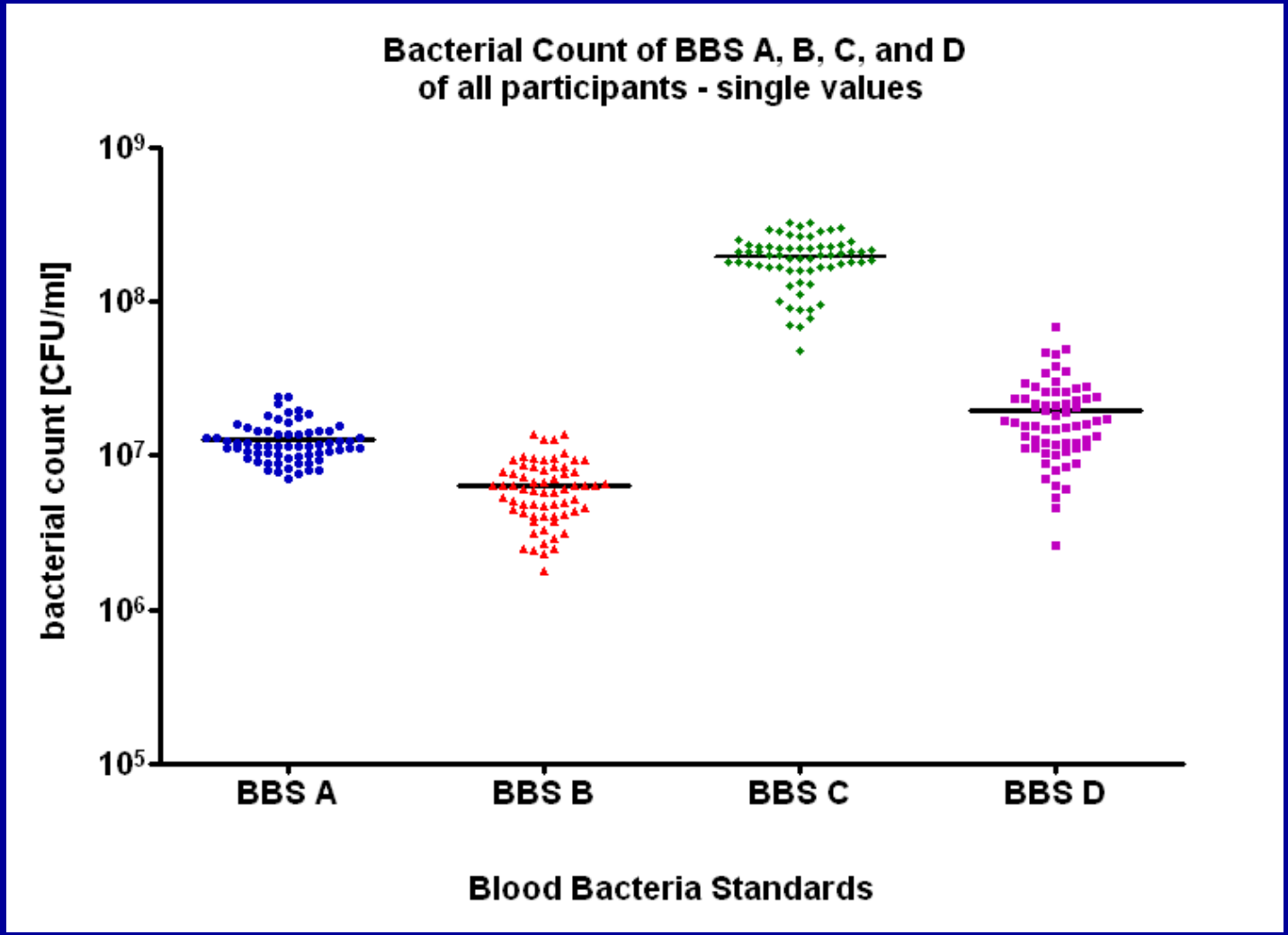

Part 3
Growth of Blood Bacteria Standards in PC
(summarised results)

Code	Groth in PC after contamination using 10 to 100 bacteria per bag corresponding to 0.03 to 0.3 CFU / ml	Partners												
		1	2	3	4	5	6	7	8	9	10	11	12	13
A	*Staphylococcus epidermidis* (PEI-B-06-08)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
B	*Streptoccoccus pyogenes* (PEI-B-20-06)	yes	yes	yes	yes	yes	yes	no	yes	yes	yes	yes	yes	yes
C	*Klebsiella pneumoniae* (PEI-B-08-10)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes
D	*Escherichia coli* (PEI-B-19-06)	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes	yes

Table does not consider all details, e.g. growth in case of contamination of PCs applying 100 CFU per bag but no growth applying 10 CFU per bag, repetitions, pooled or apheresis PCs (will be described in detail in study report).

Costs of study

Topic	Remarks / Details	Borne by:	Sum (circa):
Shipping of deep frozen Bacteria Standards	PEI to: Canada, Germany (2x), Poland, The Netherlands, United Kingdom PEI to ATCC, ATCC to: Hong Kong, Mexico, South Africa, USA (2x)	PEI	~ 4,000 Euro
Costs of partners		study partners	
Materials	Microbiology: ~ 150 Euros per Standard, sum: ~ 600 Euros (600 x 13 = 7800)		~ 7,800 Euros
PCs	at least 8 Pcs (outdated possible) e.g. prices in Germany: 1 Pool PC ~ 300 Euros 1 Apheresis PC ~ 600 Euros		(2400 – 4800 Euros)
Staff	(calculated by Piotr Radziwon, Poland)		1,150 Euros
Sum	without PCs (in worst case with PCs)		~ 13,000 Euros (15,500 to 18,000 Euros)

Many colleagues worldwide volunteered for the study without any funding and without hesitating to invest a substantial amount of hard work.

WHO ISBT International Validation Study on Blood Bacteria Standards

ISBT Meeting 2006, Cape Town, South Africa	ISBT Working Party Transfusion-Transmitted Infectious Diseases (WP-TTID) decides on Validation Study
WHO CC Meeting 2007, Bethesda MD, USA	Official proposal to WHO to install Blood Bacteria Standards
ISBT Meeting 2007, Madrid, Spain	Agreement between WHO (Ana Padilla) and ISBT WP-TTID on a Collaborative Validation Study
ISBT Meeting 2008, Macao, China	Kick-off Meeting Validation Study, ISBT WP-TTID, Subgroup Bacteria
AABB Meeting 2008, Montreal, Canada	Extraordinary Meeting of Subgroup Bacteria, discussion of study details
WHO CC Meeting 2009, Langen, Germany	Update Blood Relevant Bacteria Panel Decision on start of formalised procedure for submission of topic to WHO Expert Committee for Biological Standardisation (ECBS)
ISBT Meeting 2009, Cairo, Egypt	Annual Meeting of Subgroup Bacteria, Evaluation of Study, decision on follow ups

Outcome of study:

WHO Collaborative Centres Meeting
2009 February 17th to 19th
Langen, Germany:

Decision on start of formalised procedure for submission of topic to WHO Expert Committee for Biological Standardisation (ECBS).

Outcome of Subgroup Bacteria meeting yesterday

1. Follow-up of study
   - report to WHO ECBS by end of June 2009
   - abstract submissions to AABB and ISBT meetings
   - manuscript submission to Vox Sanguinis
2. List of transfusion relevant bacteria/fungi
   - discussion via e-mail inside Subgroup Bacteria including the study partners
   - afterwards harmonisation (WP-TTID, ISBT, FDA ....)
3. Enlargement of panel of Blood Bacteria Standards
   - discussion of first draft in Subgroup Bacteria 

First draft: further candidates for Blood Bacteria Standards

Discussion paper:
List of transfusion-relevant microbial species / strains

No.	Species	Strain	Remarks
Gram-positive Bacteria			
1.	*Staphylococcus epidermidis*	PEI-B-06	FDA
2.	*Staphylococcus aureus*	PEI-B-23	FDA
3.	*Streptococcus pyogenes*	PEI-B-20	FDA
4.	*Streptococcus viridans*	*Str. bovis* (NBS)	FDA
5.	*Streptococcus faecalis*		???
6.	*Streptococcus agalactiae*		fatal case
7.	*Propionobacterium acnes*	PEI-B-22	FDA
8.	*Corynebacterium species*		FDA, ???
9.	*Bacillus cereus*	PEI-B-07	FDA
10.	*Bacillus cereus, spores*	PEI-B-07-S	
11.	*Bacillus subtilis*		FDA
12	*Bacillus subtilis, spores*		
13.	*Clostridium perfringens*	PEI-B-25	FDA
14.	*Clostridium perfringens, spores*	PEI-B-25-S	
Gram-negative Bacteria			
1.	*Klebsiella pneumoniae*	PEI-B-08	
2.	*Klebsiella oxytoca*		FDA
3.	*Escherichia coli*	PEI-B-19	FDA
4.	*Serratia marcescens*		FDA
5.	*Yersinia enterocolitica*	DSM 11502	
6.	*Salmonella cholerae suis*		fatal case
7.	*Proteus vulgaris*		???
8.	*Pseudomonas aeruginosa*		FDA
9.	*Pseudomonas fluorescence*		
Fungi			
	Candida albicans	PEI-B-21	
	Aspergillus species		???, species?

Outcome of Subgroup Bacteria meeting yesterday

1. Follow-up of study
   - report to WHO ECBS by end of June 2009
   - abstract submissions to AABB and ISBT meetings
   - manuscript submission to Vox Sanguinis
2. List of transfusion relevant bacteria/fungi
   - discussion via e-mail inside Subgroup Bacteria including the study partners
   - afterwards harmonisation (WP-TTID, ISBT, FDA ....)
3. Enlargement of panel of Blood Bacteria Standards
   - discussion of first draft in Subgroup Bacteria
   - will be discussed and completed by e-mail
4. Continuation:
   - preparation of survey
   - review on microbial safety of blood components

Relevant remark:

The Blood Bacteria Standards are applicable for the novel Advanced Therapy Medicinal Products (ATMPs), e.g. Cell Based Medicinal Products.

Additional outcome of study:

The Blood Bacteria Standards are applicable for the novel Advanced Therapy Medicinal Products (ATMPs), e.g. Cell Based Medicinal Products.

Thus, Subgroup Bacteria will have a meeting here in Cairo with colleagues from BEST in order to discuss a draft design of a study on sterility testing of stem cells.
It is intended to start the study in the next time applying a panel of Blood Bacteria Standards.

I have to say “Thank you very much!” to:

PEI

- **Melanie Stoermer**
- **Utta Schurig**
- **Sven-Boris Nicol**
- **Julia Brachert**
- **Ute Sicker**
- **Rekia Beshir**
- **Christian Schneider**

The study partners

The study coordinating group

WHO

- **Ana Padilla**
- **Gabriele Unger**
- **Michael Chudy**
- **Heiner Scheiblauer**

and to you for attention