NHS
Blood and Transplant

Bacterial Screening of NHSBT Platelet Components

Dr. Carl McDonald
Head of Bacteriology
National Bacteriology Laboratory
NHS Blood and Transplant

NHS
Blood and Transplant

Overview

- Impact of bacterial transmission
- Why PCs are the greatest risk
- NHSBT Strategy
- Impact diversion and improved donor arm disinfection
- NHSBT protocol Bacterial Screening
- NHSBT results Bacterial Screening
- Added value Bacterial Screening
- Future development

NHS Blood and Transplant

Bacterial Mortality Worldwide

USA	2005-2015	38 deaths	(FDA)
France	1994-2015	36 deaths	(Haemovigilance)
Germany	1997-2014	14 deaths	(Haemovigilance)
U.K.	1994	3 deaths	(Pre-SHOT)
U.K.	1996-2016	11 deaths	(SHOT)

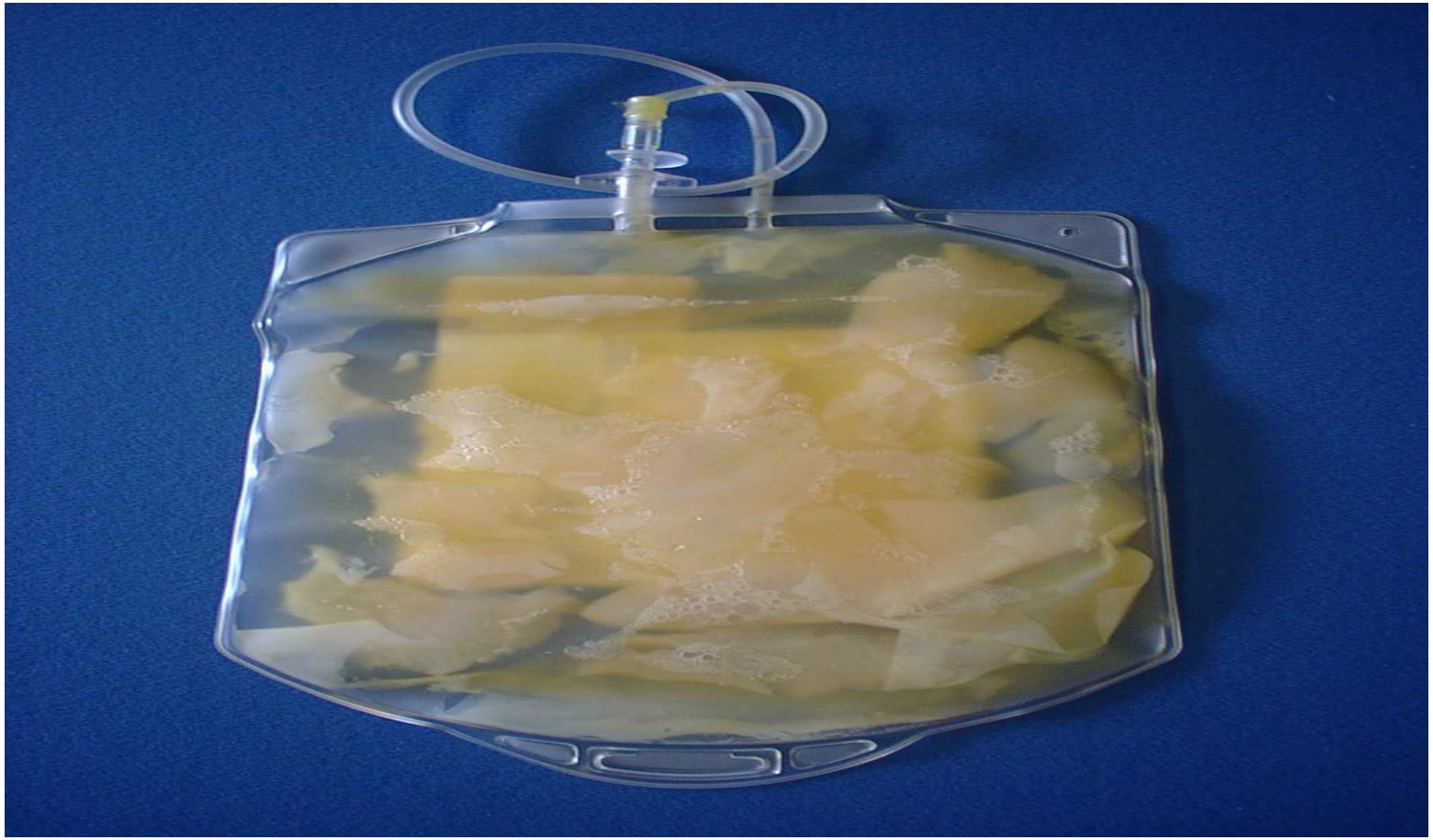
NHS
Blood and Transplant

Platelet Components Are The Greatest Risk!

- **USA: (FDA) 2005 – 2015 platelet components comprised 87% (33/38) bacterial fatalities**
- **UK: (SHOT) 1996 – 2016 platelet components comprised 84% (37/44) cases**

NHS
Blood and Transplant

Klebsiella oxytoca



NHS
Blood and Transplant

NHSBT Strategy

- Improved donor arm disinfection
- Diversion
- Bacterial Screening

NHS Blood and Transplant

Interventions Introduced

- **Improved Donor Arm Disinfection – implemented nationally 2007**
- **Diversion – implemented nationally 2003**
- **In combination 77% reduction in contamination**

McDonald, C.P. *et al.*, Relative Values of the Interventions of Diversion and Improved Donor-Arm Disinfection to Reduce the Bacterial Risk from Blood Transfusion: Vox Sanguinis (2004), 86:178-182

NHS
Blood and Transplant

Post Implementation Improved Donor Arm Disinfection and Diversion (2006 – 2010)

- 7 contamination incidents in PC
- 10 patients affected
- 3 deaths
- 5 near misses

NHS
Blood and Transplant

NHSBT Bacterial Screening

NHS
Blood and Transplant

Bacterial Screening of Platelet Components in NHSBT

- NHSBT Board Meeting in January 2010
- Decision was made to implement bacterial screening within 12 months
- February 2011 rolled out
- July 2011 all components screened

NHS
Blood and Transplant

NHS
Blood and Transplant

BacT/ALERT System

NHS
Blood and Transplant

Bacterial Screening Laboratory

NHS
Blood and Transplant

Bacterial Screening Laboratory

NHS
Blood and Transplant

Bacterial Screening Laboratory

NHS
Blood and Transplant

NHSBT Test Protocol
(1 test, Extension Shelf Life to 7 Days)

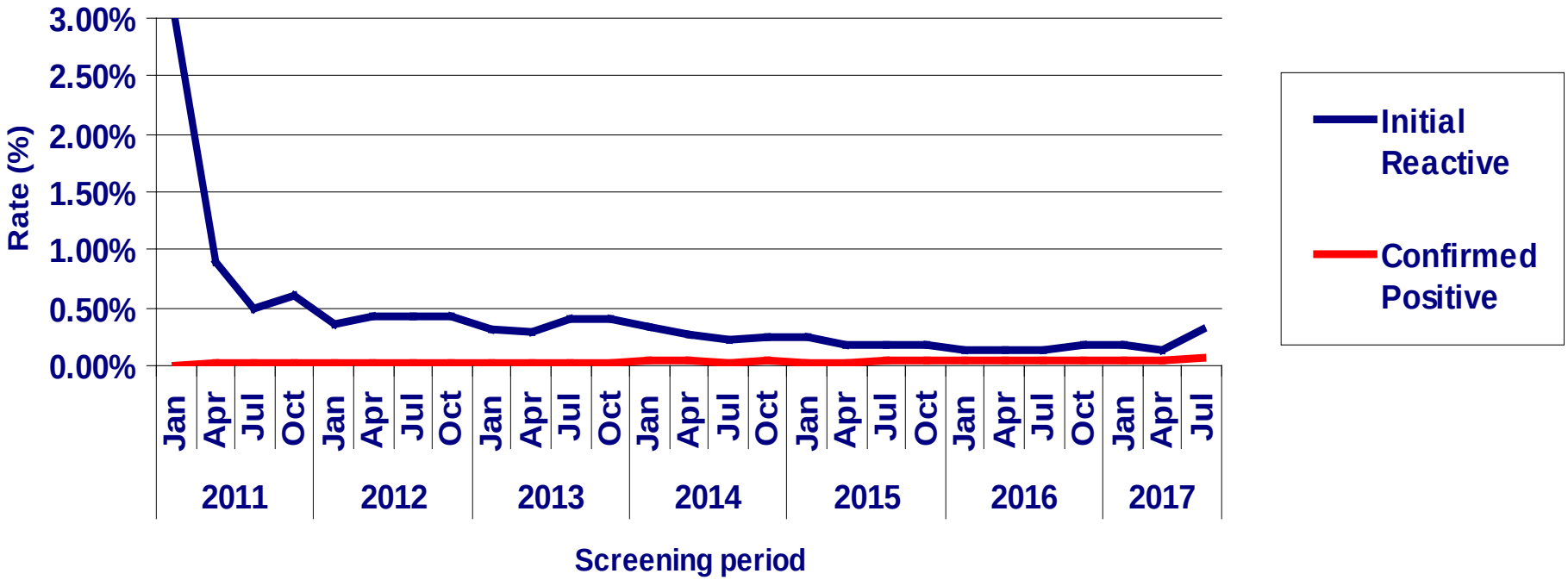
1. Platelet components held for ≥ 36hrs – 48hrs after collection
2. Platelet components sampled and tested
3. Held for 6hrs
4. Released with a 7 day shelf life
5. Monitored for the component shelf life
6. Positives recalled

NHS
Blood and Transplant

What Happened?

NHS
Blood and Transplant

Quarterly Bacterial Screening Rates (February 2011 - Sept 2017)



NHS Blood and Transplant

Initial Reactive and Confirmed Positive Rates (Cumulative Feb 2011 – Sept 2017)

	Number	Initial Reactive Rate	Confirmed Positive Rate
Apheresis*	1,285,959	0.33%	0.02%
Pooled*	530,804	0.25%	0.07%
Total	1,816,763	0.31%	0.04%

*Apheresis platelets screened from Feb 2011
*Pooled platelets screened from May 2011

NHS
Blood and Transplant

Initial Screen: Bottle Reactivity

(February 2011 – Sept 2017)

Bottle Type	Initial Reactive	False Positive
Anaerobic	73.8%	77.9%
Aerobic	21.3%	21.7%
Both	4.8%	0.4%

NHS
Blood and Transplant

Confirmed Positives - Bottle Type (February 2011 – Sept 2017)

- Anaerobic bottle 65%
- Aerobic bottle 7%
- Both bottles 28%

NHS
Blood and Transplant

Confirmed Positives (February 2011 – Sept 2017)

- 666 confirmed
- 640 Gram positives
- 26 Gram negatives

Confirmed Organisms (February 2011 – Sept 2017)

Gram Positives (n=640):

Propionibacterium spp. = 346
Staphylococcus spp. = 163
Streptococcus spp. = 105
Gemella spp. = 6
Listeria monocytogenes = 4
Corynebacterium spp. = 3
Enterococcus spp = 3
Lactobacillus casei = 2
Bacillus cereus = 2
Granulicatella adaciens = 2
Lactococcus lactis = 1
Peptostreptococcus micros = 1
Finegoldia magna = 1
Misc. Gram Positive bacilli = 1

Gram Negatives (n=26):

Escherichia coli = 9
Serratia marcescens = 5
Klebsiella spp. = 5
Enterobacter spp = 2
Pseudomonas aeruginosa = 1
Haemophilus aphrophilus = 1
Bacteroides vulgatus = 1
Proteus mirabilis = 1
Campylobacter lari = 1

NHS Blood and Transplant

Confirmed Positive Gram Positive 'Pathogenic' Organisms (Feb 2011 – Sept 2017)

Organisms	n	Detection Time Range (hours)	Total Contaminated Components
Streptococcus dysgalactiae (Group G/C)	24	2-19	32
Staphylococcus aureus	17	2-21	21
Streptococcus pneumoniae	12	10-13	16
Streptococcus agalactiae (Group B)	6	6-16	5
Listeria monocytogenes	4	14-20	5
Bacillus cereus	2	11-14	2

Total cases with pathogenic organisms: 65
Total number of contaminated components: 81

NHS Blood and Transplant

Confirmed Positive Gram Negative 'Pathogenic' Organisms (Feb 2011- Sept 2017)

Organisms	n	Detection Time Range (hours)	Total Contaminated Components
Escherichia coli	9	3-14	19
Serratia marcescens	5	3-13	8
Klebsiella oxytoca	3	3-10	4
Klebsiella pneumoniae	2	4-11	3
Proteus mirabilis	1	14	1
Pseudomonas aeruginosa	1	15	1
Campylobacter lari	1	32	1

Total cases with pathogenic organisms: 22
Total number of contaminated components: 37

NHS Blood and Transplant

Number of Splits Contaminated in Confirmed Positive Apheresis Donations (Feb 2011 – Sept 2017)

	Total number of splits positive per investigation		
Splits per donation	1	2	3
2	47.9% (69)	52.1% (75)	N/A
3	50% (16)	18.8% (6)	31.2% (10)

NB: when all components returned for confirmatory/reference testing

NHS
Blood and Transplant

Near Misses and Transmissions

NHS
Blood and Transplant

Transmissions and Near Misses

- **1 transmission: 1 x *Staphylococcus aureus***

- **4 near misses: 3 x *S. aureus***

  1 x *Serratia marcescens*

NHS
Blood and Transplant

Near Miss 1: 2013

- Apheresis platelet donation (2 splits)
- Large clumps reported in pack 2 by Hospital A
- Pack 1 issued to Hospital B but not transfused. No clumps present
- Both units received by NBL

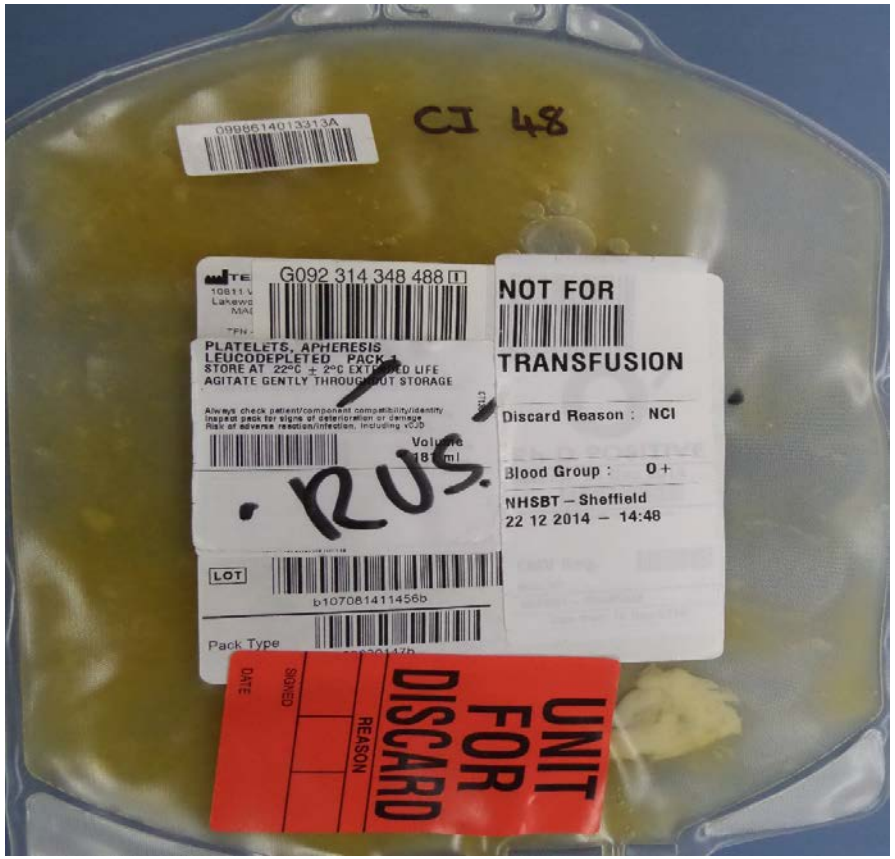
NHS
Blood and Transplant

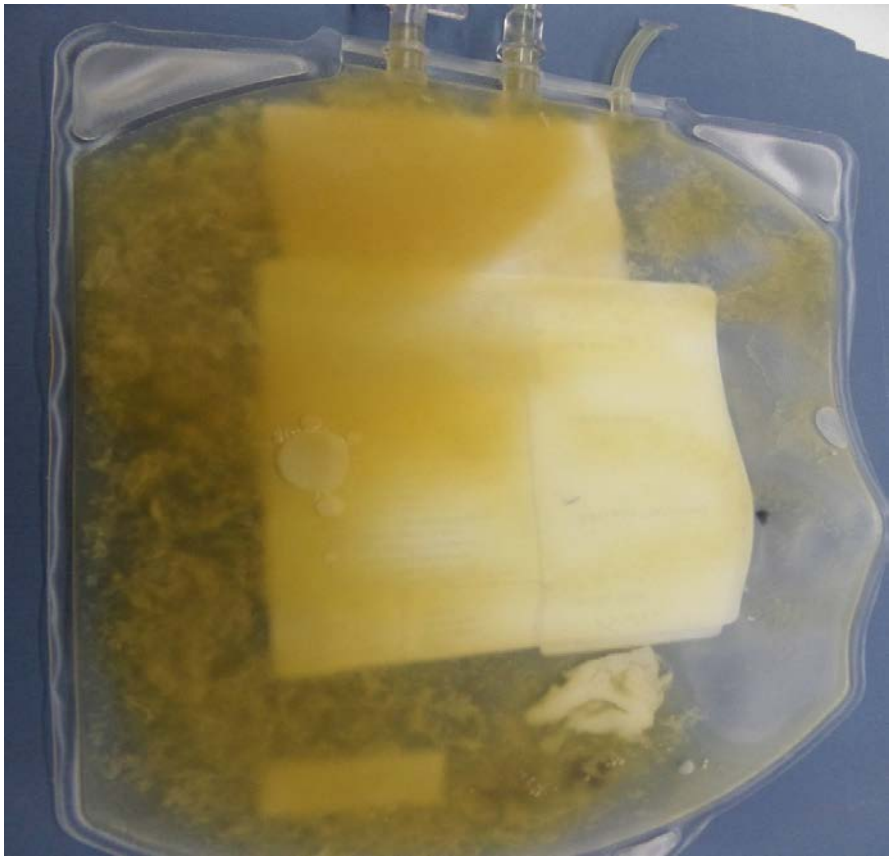
Near Miss 1: 2013 (cont'd)

- No clumps visible in pack 2, but were present in pack 1
- BacT/ALERT cultures for both units positive in 3.8hr
- *Staphylococcus aureus* isolated
- Investigation of donor found *S. aureus* colonisation
- Strain typing of PC and donor isolates were indistinguishable

NHS
Blood and Transplant

Near Miss 3





NHS
Blood and Transplant

BacT/ALERT Culture Bottles

NHS
Blood and Transplant

Near Miss 4: 2015

- Apheresis unit – 2 splits
- Clumps observed in split 1 by SHU
- Packs and BacT/ALERT screening bottles sent to NBL

NHS
Blood and Transplant

Near Miss4: 2015

Pack 1

Pack 2

NHS
Blood and Transplant

Near Miss 4: 2015 (cont'd)

- **Gram from pack 1 – Gram negative rods**
- **Gram from pack 2 – negative**
- **Clotted pack 1 – positive on BacT/ALERT 3.7h**
- **Unclotted pack 2 – negative on BacT/ALERT**
- ***S. marcescens* identified from pack 1**

NHS
Blood and Transplant

Near Miss 4: 2015

Inoculated **Uninoculated**

NHS Blood and Transplant

Near Miss 4: 2015 (cont'd)

- **BacT/ALERT bottles – Gram stain negative (both packs)**
- **BacT/ALERT bottles subcultured into new bottles – negative**
- **Screening bottles inoculated *S. marcescens* – positive**

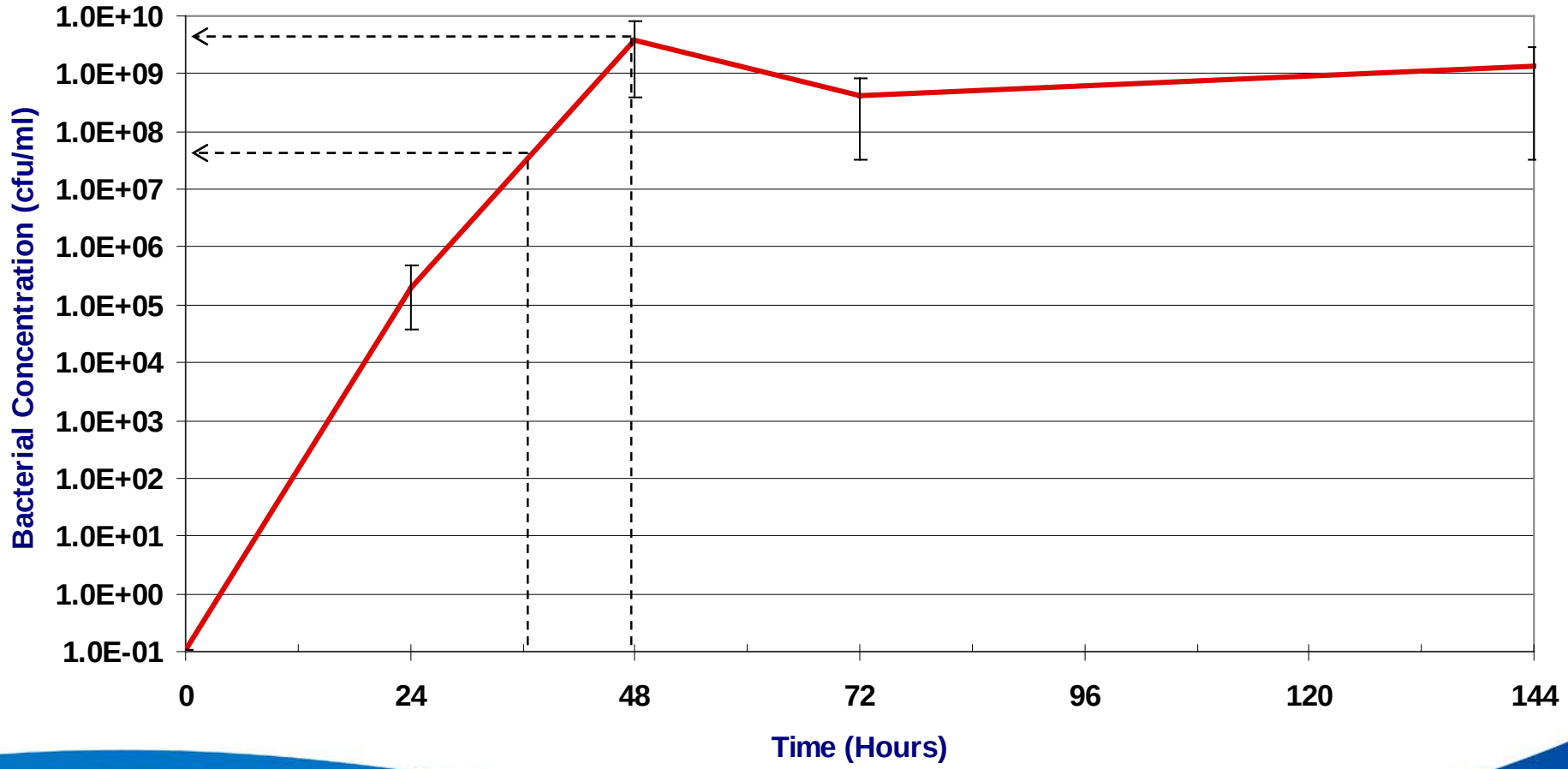
NHS
Blood and Transplant

Near Miss 4: Conclusion

- Not a BacT/ALERT failure
- Insufficient bacteria at sampling time?
- Contamination post screening?

NHS
Blood and Transplant

Growth Kinetics of *S. marcescens* in Platelets Suspended in Plasma



NHS Blood and Transplant

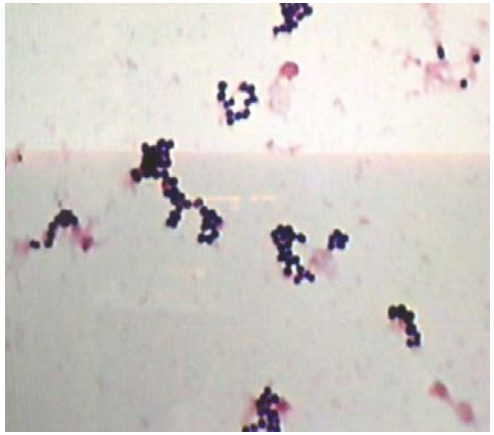
Confirmed Transfusion-Transmitted Infection (TTI) 2015

- Pooled platelet unit transfused into AML patient
- After 15 mins, the patient became agitated and suffered rigors, tachycardia and pyrexia
  - Temperature rose to 38.7°C, then 40°C overnight
- Patient cultures grew *Staphylococcus aureus*

NHS Blood and Transplant

Confirmed TTI: 2015 (cont'd)

- Platelet unit received by NBL
- Unit was leaking through open port, sealed with a capped needle
- Remaining contents (~3ml) appeared 'cloudy'
- Gram stain showed heavy contamination with GPC
- BacT/ALERT cultures positive in 3.8h



NHS Blood and Transplant

Confirmed TTI: 2015 (cont'd)

- ***S. aureus*** **isolated, strain type matched the patient isolate**
- **All 4 associated red cells units were cultured by NBL and remained negative after 7 days incubation**
- **2/4 Donors investigated – both had *S. aureus* in multiple sites**
- **Strain typing of 1st donor isolates showed a distinct strain (no match)**
- **Strain typing of 2nd donor showed closely-related Spa type and matching DNA fingerprint**

NHS
Blood and Transplant

Bacterial Screening: Added Value

NHS
Blood and Transplant

Donor Healthcare Benefits Bacterial Screening

- ***Streptococcus bovis*** **(n=4): donor's colonic polyps**
- ***Streptococcus constellatus*** **(n=3) and P. micros: dental**

McDonald, C. *et.al*., Transfusion, 2013,53:2117-2119

Lee, CK. *et.al*., Transfusion, 2013,53:2205-2208

NHS
Blood and Transplant

Bacterial Screening Provides Insight into Possible Source of Contamination

- **Pseudomonas spp. – poor hygiene facilities**
- **Staphylococcus spp. – inadequate donor arm disinfection**

NHS
Blood and Transplant

Future

NHS
Blood and Transplant

BacT/ALERT Virtuo

Virtuo Advantages

- Superior performance to BacT/Alert 3D
  - Faster detection times
  - Potentially lower false positive rates
  - Automated loading and unloading

NHS
Blood and Transplant

NHSBT Screening (February 2011 to March 2017)

- **1 transmission in >1.8million PC screened (*S.aureus*)**
- **4 near misses *(3 S. aureus and S. marcescens)***
- **False negative rate 1 in 360,000 (0.0003%)**
- **1 CP in 6015 TE platelets screened *(S. pneumoniae)***

NHS
Blood and Transplant

Success NHSBT Bacterial Screening

- Delayed sampling
- High volume tested (5-7%)
- Screening of apheresis splits
- Use of a two bottle system

NHS
Blood and Transplant

Conclusion

Bacterial Screening within NHSBT has proven to be extremely successful risk reduction intervention!

NHS
Blood and Transplant

Bacterial Screening of Platelet Components by National Health Service Blood and Transplant, an Effective Risk Reduction Measure

C. McDonald, J. Allen, *et al.,*

Transfusion 2017;57;1122-1131

NHS
Blood and Transplant

Acknowledgements

- Jennifer Allen
- Kate Aplin
- Su Brailsford
- Richard de Ritis
- Rachael Morrison
- Tyrone Pitt
- Mariza Vasconcelos
- Tracy Ward

NHS
Blood and Transplant

THANK YOU

carl.mcdonald@nhsbt.nhs.uk