The impact of IPC on the residual risk of bacterial contamination of apheresis platelets

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SANBS Strategy

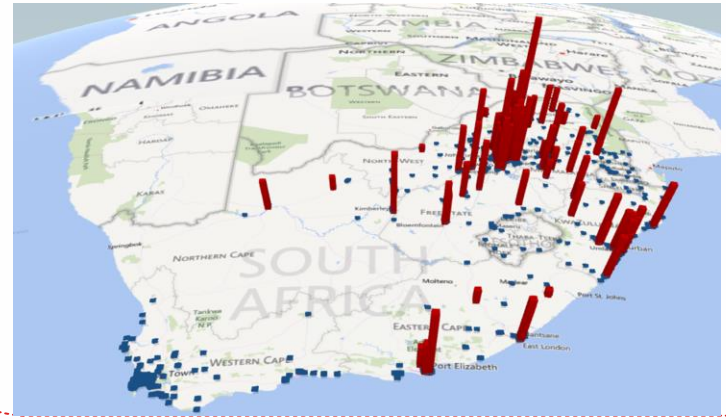
Our Purpose **“Trusted to Save Lives”**

Our mission

To **reliably** provide trusted blood products and services to **all** patients at a world class level of **cost** and **quality** while innovating new treatments to enhance human healthcare

Our Vision

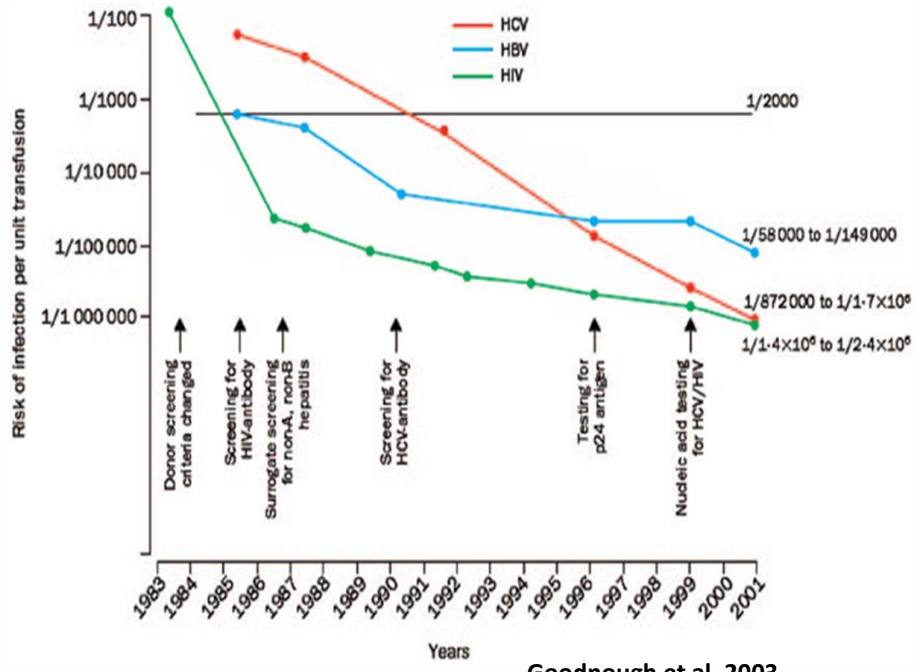
To be a cornerstone of healthcare services in South Africa, through the gift of life



- Private not for profit company operating on a fee for service
- Vein to vein blood transfusion service in 8 / 9 provinces
- 87 Donor Centres:
  - 900,000 units of blood collected annually from 450 000 donors
- 2 Donation blood testing centres:
  - Johannesburg and Durban
- 7 Blood Processing centres
- 84 blood banks managed by SANBS staff, serving > 600 hospitals
- Transport & cold chain logistics for distribution of blood
- SANAS accredited Specialized Labs

Background

- The residual risk of bacterial contamination of platelets remains a global problem.
- Residual Risk:
  - Developed Countries: static 1/2000
  - Africa: 2- 10%
- Mostly GP bacteria
- 1/10 will result in patient symptoms and a fatality rate of 1 / 1000 000
- Globally and locally in SA, bacterial sepsis is underreported



Goodnough et al. 2003

Transfusion Associated Sepsis (TAS)

- TAS accounts for approx. 10 % of transfusion deaths
  - 70 % Platelets
- Causal relationship difficult to prove
  - Recipient : immunosuppression, comorbidities
  - Diagnostic challenges : antibiotics
- Increased risk for a fatal outcome:

  GNB *(E.coli, Enterobacter spp, Serratia spp.)*

  GPC (*Staph aureus)*
- 50% drop of transfusion related mortality 2004:
  - bacterial screening
  - multiple donor pooled platelets → single donor apheresis platelets

BLOOD, 9 APRIL 2009 • VOLUME 113, NUMBER 15

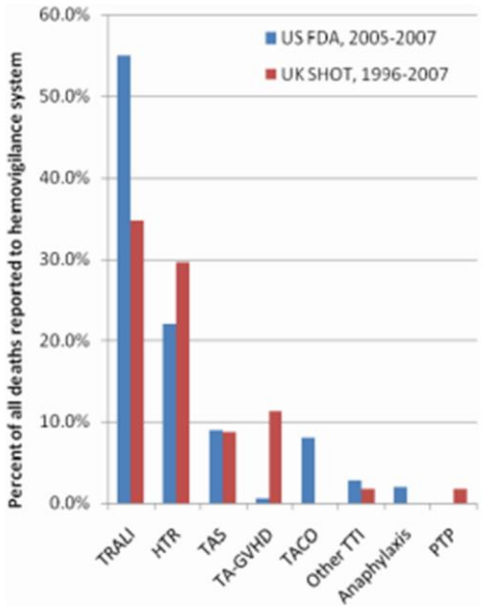
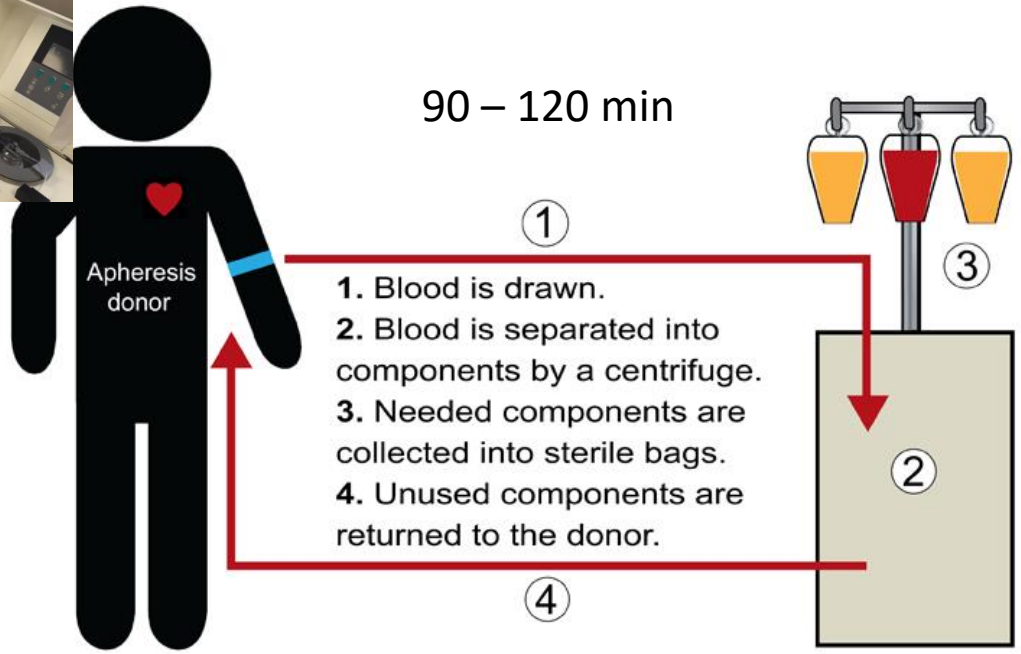


Figure 1. Causes of allogeneic blood transfusion–related deaths as a percentage of all deaths reported to SHOT (1996-2007)[4] or the FDA (2005-2007).[1] The figure shows the causes of death that accounted for at least 1% of all deaths in either of these 2 reports.[1,4] Transfusion-associated circulatory overload (TACO) was not

Collection of Apheresis Platelets



Why are platelets such high risk products?

- Platelet “media” is conducive for bacterial growth at 20 to 24 ^{0}C
- Aerobic condition in the absence of bactericidal factors
- Spiking studies:
  - 1 CFU / bag results in → 3 days > 10^{5} CFU/ml
- Pyrogenic substances (endotoxin)
- Biofilm formation
- Risk increases with age of platelets
  - Mortality occurs day 4 and 5 of stored platelets

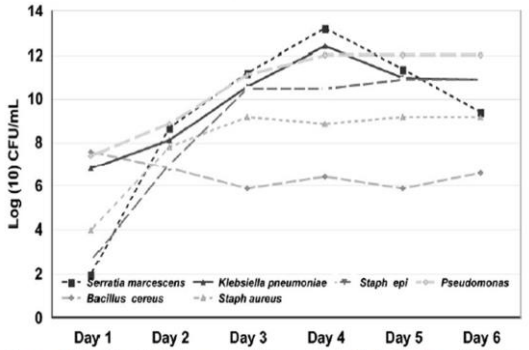


FIG. 3. Growth curves of six bacteria species (*S. marcescens*, $n = 7$; *K. pneumoniae*, $n = 21$; *S. epidermidis*, $n = 21$; *Pseudomonas* sp., $n = 15$; *B. cereus*, $n = 9$; *S. aureus*, $n = 22$) in 95 platelet units. All bacteria were inoculated on day zero at 10–50 CFU/ml (10).

Brecher, Hay 2005

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International Microbiological Bacterial risk control strategies

- AABB recommends:
  - all apheresis platelets (AP) be stored for 24 hours prior to sampling for sterility testing.
  - 4 – 8ml of the platelet component are drawn and inoculated into either one aerobic bottle or both aerobic and anaerobic bottles.
  - Product can be released for transfusion if negative after 24 hours incubation, the culture continued for the shelve life of the unit which is usually 5 days

- FDA - additional guidelines
  - Approved the use of Rapid tests for pre-release testing of platelets
  - Recommend the use of Pathogen Reduction Technologies for apheresis platelets
  - Sep 19: Large volume (16 ml) and delayed sampling (36hrs), aerobic and anaerobic culture

- Council of Europe: A QC procedure :
  - proportion of AP collections are tested for bacterial contamination

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FDA Guidance for Industry 2019

Intercept Pathogen Reduction Technology

within 24 hours of collection

No Primary Bacterial testing

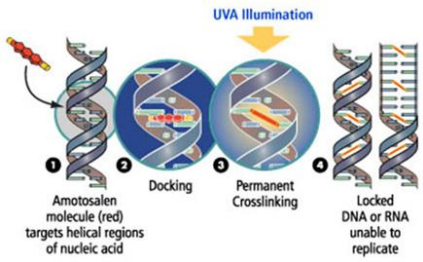
RELEASE UP TO DAY 5

Secondary Testing:

> Day 5 platelets

Rapid Device (Safety Device)

NEG: Release and transfuse within 24hrs (<= 7 D)



BacT/ALERT (Biomerieux)

16 ml ideal

Sampling : 36 hrs post collection

Aerobic bottle + AnO2

Duration : as per device if specified

RELEASE IF NEG

RECALL / ALERT if POS

Secondary Testing:

Day 4 and 5 stored platelets and culture still negative

Rapid Device

NEG: Release and transfuse within 24hrs

> Day 5 – Day 7:

Additional safety testing using a Rapid device

NEG: Release and transfuse within 24hrs (<= 7 days)

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SANBS Mitigation Strategies

- Donor screening and skin antiseptic technique (WHO)
- Diversion pouch
- Microbiological screening practices
  - 20% of platelets are screened with an approved bacterial culture system
  - Environmental screening across the value chain
  - Measures to alert collection site and clinician who transfused a positive platelet product

- Passive reporting haemovigilance system:
  - No reported cases of bacterial sepsis / mortality to date
- Continuous tracking and reporting of contamination rates

AIM and METHODS

- **Hypothesis** : Basic IPC measures focussing on hand and environmental hygiene are important cost effective measures to reduce the risk of bacterial contamination of blood product.
- Retrospective review of bacterial surveillance performed on a subset of apheresis platelets collected between 2011 and 2018.
- IPC improvements implemented from 2017
- Microbiological culture improvements from 2017 included increasing the culture volume to 4 ml in and reducing the incubation time to 7 days.

METHODS

- AP samples collected from 14 SANBS apheresis clinics across SA
- The sample is collected aseptically in a sterilely docked pouch.
- Transported at room temperature, processed 24 - 48 hours after collection.
- 4 ml of platelet product was cultured using the BacT/ALERT (Biomerieux) or BD BACTEC™
- Bacterial ID was done using standard microbiological procedures.

IPC Improvements and Interventions

Hand Hygiene

Technique

Effective sanitizers and antiseptics

chlorhexidine (CHX) / isopropyl alcohol (IPA)

Hand rub

Environmental hygiene

Environmental screening

Wipes for housekeeping in laboratories and donor clinics

National IPC awareness

International benchmarking

IPC policy and guidelines

Training and Auditing

IPC training

IPC audits

Microbiology laboratory optimization

Re-design, access control

Clean area

Testing aligned to international standards

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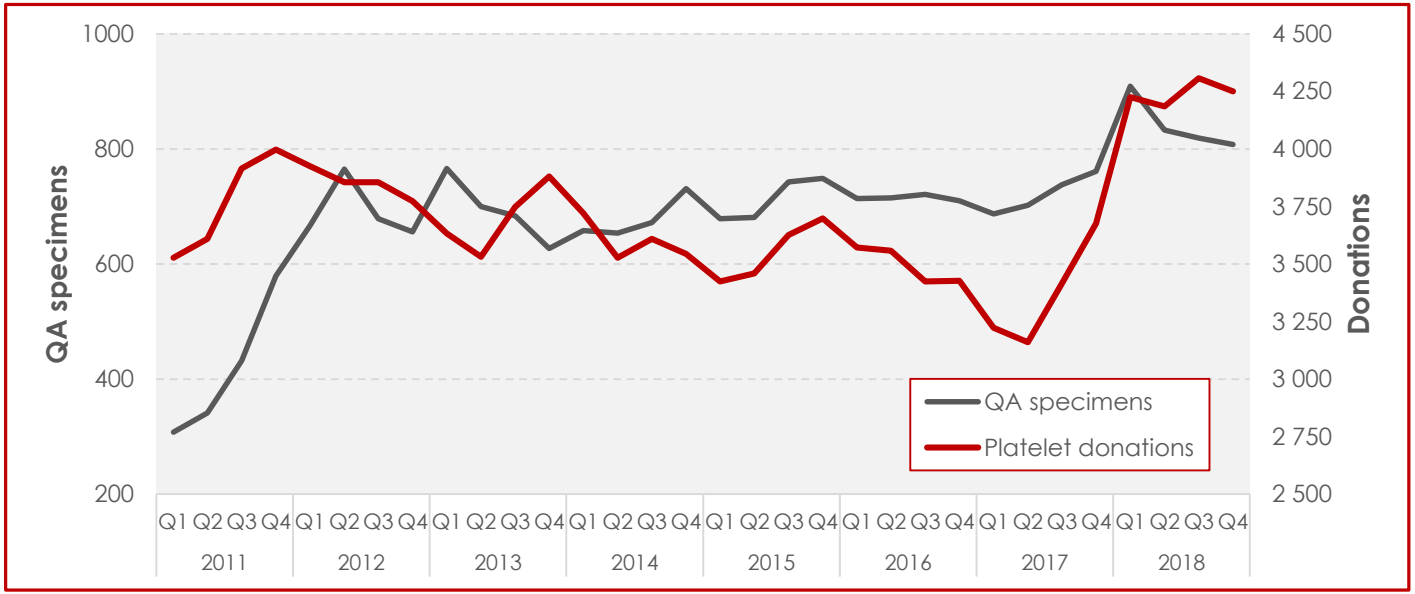
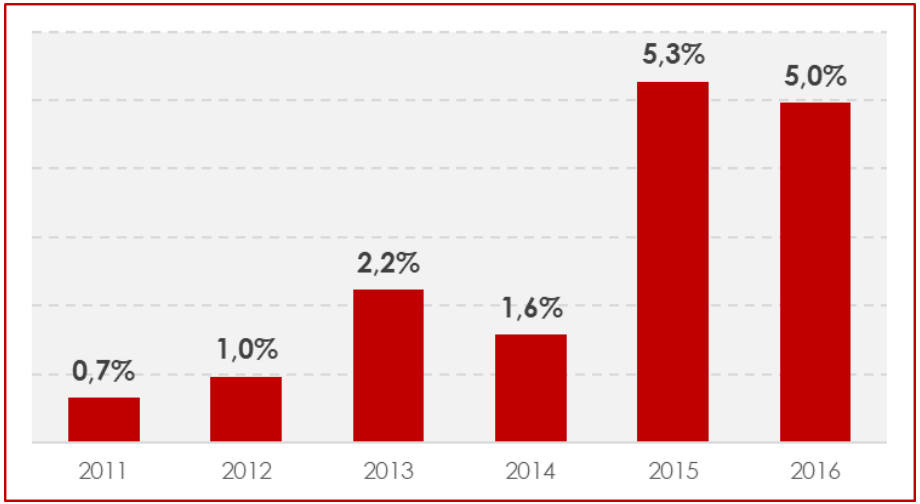
Results
Number of AP Collections and QC tests



- SANBS collected 118 287 AP units during the 8-year period
- Average annual collections range from 14 000 to 17 000 (n=118 287 over 8 years)
- The average percentage of AP platelets tested annually was 18,5% (n=21 888 over 8 years)

Bacterial Surveillance Pre-IPC Improvements

- Average prevalence of bacterial contamination 2011 – 2016 was 2.7%
- Annual rates ranging between 0.6% in 2011 and 5.22 % in 2015 indicating an overall increase between 2011 and 2015
- Two exogenous events of bacterial contamination were traced back to poor aseptic practice in 2015 and 2016.



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Bacterial Identification

- > 80% Gram positive skin commensals
  - *Cutibacterium acnes* (35%)
  - Coagulase negative *Staphylococci* (26%)
  - *Bacillus spp.* (8%), *Corynebacteria spp.* (8%)
  - *Micrococcus spp.* (7%).
- 9 highly pathogenic bacteria were isolated:
- 5 / 9 were GNB:
  - two *Acinetobacter spp*; one each of *Enterobacter spp., Serratia spp., Klebsiella spp*
  - One *Staph aureus* and three *Listeria spp*.
- Average time to positivity: 5.6 days
- Highly pathogenic bacteria were detected by day three.

Bacterial Species	Bacterial Isolates	Bacterial Isolates with known TTP	
	n (%)	n (%)	TTP
Gram positive bacteria	**269**	**166**	**6.0**
Cutibacterium spp	99 (34.7%)	63 (36.2%)	7.5
Coagulase negative *Staphylococci*	75 (26.3%)	41 (24.1)%	4.4
Staphylococcus aureus	1 (0.4%)	1 (0.8%)	2.0
Bacillus spp.	24 (8.4%)	19 (10.9%)	6.4
Corynebacterium spp.	23 (8.1%)	15 (8.6%)	5.7
Micrococcus spp.	19 (6.7%)	12 (6.9%)	3.6
Streptococcus spp.	13 (4.6%)	5 (2.9%)	7.8
Listeria grayi	3 (1.1%)	2 (1.2%)	5.5
Peptospstreptococcus spp.	3 (1.1%)	3 (1.7%)	5.6
Leuconostoc spp.	3 (1.1%)		
Other	6 (2.1%)	5 (2.9%)	5.6
Gram negative bacteria	**10**	**6**	**3.0**
Acinetobacter spp.	2 (0.7%)	1 (0.8%)	3.0
Enterobacter spp.	1 (0.4%)	1 (0.8%)	4.0
Klebsiella pneumoniae	1 (0.4%)	1 (0.8%)	3.0
Serratia liquefaciens	1 (0.4%)	1 (0.8%)	2.0
Other	5 (1.8%)	2 (1.2%)	2.7
Fungi	**6**	**2**	**12**
TOTAL	**285**	**174**	**5.6**

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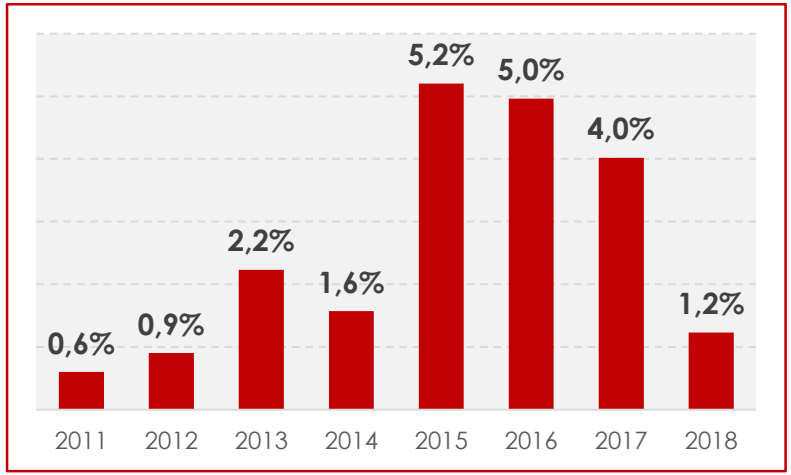
Bacterial Surveillance
Post IPC improvements



- In 2017, the bacterial contamination rate reduced to 4% (n=116).
- The reduction from 5% to 4% was significant (p=0.003).

- In 2018, a further significant decline in positive results was 1% (n=42) (p<0.003).
- 2019 data to date further decline (0.9%)

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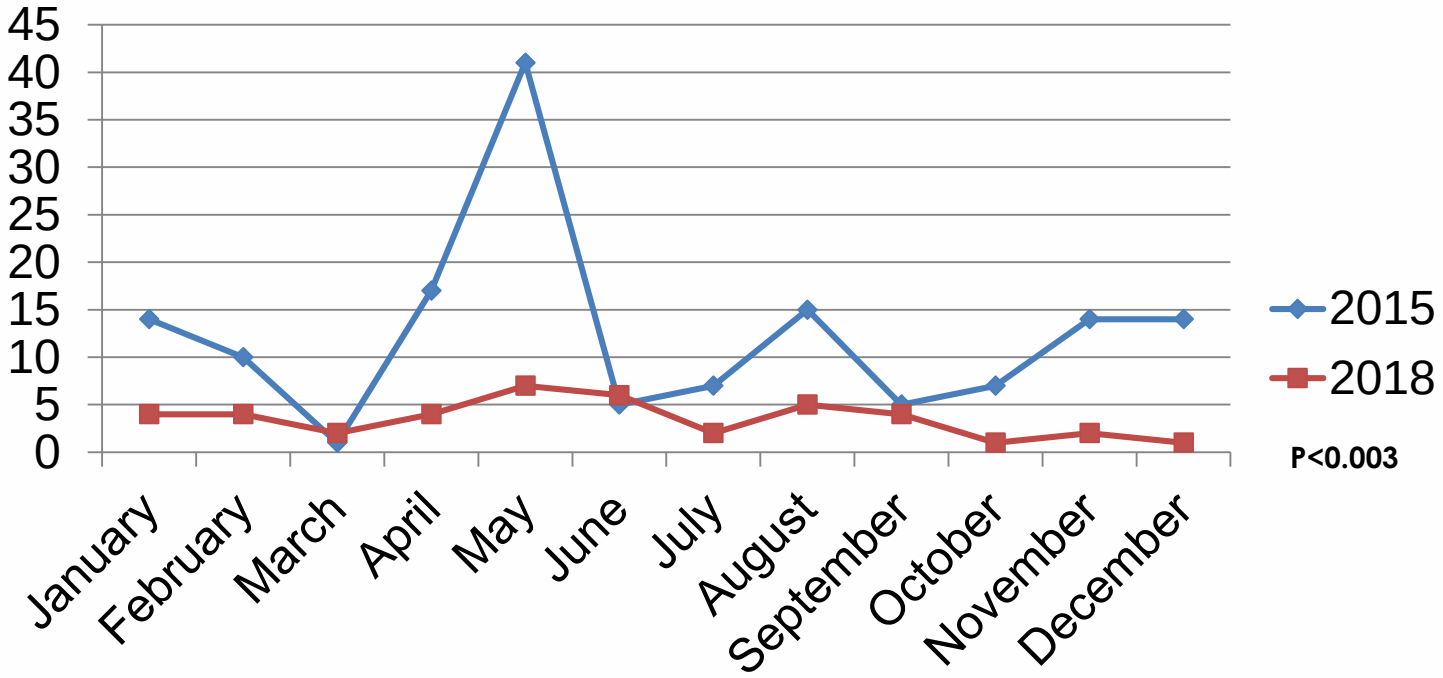
Bacterial Contamination Pre- (2015) vs Post-Improved (2018) IPC



Discussion

- Implementation of IPC processes have reduced the rate of bacterial contamination significantly from 5% to 1% between 2015 and 2018.
- In agreement with other publications gram positive skin commensals account for 80% of all bacteria isolated
- Due to limited AP stock, issuing of platelets early (by Day 3) is a good risk mitigation strategy
- The introduction of additional interventions such as pathogen inactivation should be explored to further reduce the residual risk of bacterial contamination

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- SANBS Colleagues:
  - Apheresis Collections Teams
  - Microbiology QC laboratory staff

- NHLS IPC team:
  - Lesley Devenish

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March 2016: FDA: Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion Draft Guidance for Industry
http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/default.htm

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Thank you