Affordable production of pathogen inactivated platelet concentrates
Is it possible to implement pathogen inactivation in a cost neutral (or even cost saving) way?

- Introduction
- Automated production of buffy coat derived platelets (BCPs) (based on 2014)
- Why pathogen inactivation?
- Challenges!
- Manual production of BCPs in combination with pathogen inactivation (based on 2015)
- Changes and their effect
- Lessons learned
- Future improvements
- Summary and conclusions
Introduction to the blood process at Karolinska

Collection of **80,000** whole blood units (WB) a year.

Production of **9,000** units of buffy coat platelets (BCPs)
(In addition: 1,500 apheresis platelets)
**Blood collection**
- 4 fixed donation sites and 5 mobile units
- From 7.30 am – 7 pm, Monday – Saturday

**Transport** to the **Unit of Blood Component Production, Huddinge**
- On cooling plates in isolated boxes
- Our own designated drivers
- 2 – 3 times a day from each site
Fractionation
- WB arrives between 12 pm – 8.30 pm
- 5 - 6 persons 12:30 pm - 9 pm (evening shift)
- 1 – 2 persons 7 pm – 6 am (night shift)
- No over-night storage of WB

One production line
- One production site
- One blood bag system (NTP6280LE, MacoPharma)
- One centrifugation program
- One press (Macopress Smart Revo, Macopharma)
  + one separation program

Simple and effective!
- One production line
- 100% (RBCs + plasma + BC)

Maximum number of available buffy coats!
2014 – What did our BCP procedures look like?

Production summary
– **8,669** production procedures
– **8,669** produced BCPs

Production system
– **OrbiSac** System (automated)
– **Single doses** (5 BC + 300 mL PAS-E)

Safety measures
– **100%** γ-irradiated BCPs
– Bacterial screening with **eBDS** (enhanced Bacterial Detection System)

% safety measures at transfusion:

- **22 %** none
- **23 %** started
- **55 %** completed
### 2014 – What did our BCP procedures look like?

#### Quality

**BCPs**
- 342 ± 32 × 10⁹ plt/unit
- 359 ± 13 mL

**RBCs**
- 46 ± 4 g Hb/unit
- 253 ± 14 mL

**Plasma**
- 248 ± 15 mL

#### Staff

- 2 persons for BCP production (8 am – 4.30 pm)
- 1 person for safety measure (8 am – 4.30 pm)

#### Storage time

- 7 days with eBDS
- 5 days without eBDS

#### Outdating rate

- 5.5%

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We aim for an outdating rate of 6 – 8% to avoid a shortage of platelets.
2014 – Timeline

DAY 0
8 AM - 2 PM
BCP production
OrbiSac

DAY 1
2:30 PM
Release

DAY 2
2:30 PM - 4 PM
Irradiation
8 AM - 12 AM
Safety measure
eBDS - start

DAY 3
From 8 AM
Safety measure
eBDS - finished

Single dose
8,669
BCP procedures

100%
22% No eBDS
55% eBDS completed
23% eBDS not completed
Why did we want to change production system?

- We wanted to implement pathogen inactivation as a safety measure, because
  - It is cool!
  - It is part of modern blood banking technology
  - Possibility to reduce risk of spreading new viruses and other pathogens
  - Faster safety measures to allow 100% of BCPs to be treated before transfusion

- Also:
  - OrbiSac was falling apart
  - Spare parts were hard to find

...so we needed to change our production system anyway – and why not aim for something safer?
What were the criteria for implementation?

- Criteria imposed by The Department of Clinical Immunology and Transfusion Medicine:
  - **Production + safety measure** must not be more expensive than the present production system.
  - **No new staff** could be hired.
  - **Quality** must still be above quality limits.

There was a real challenge in meeting these criteria!
But then again… who can resist a good challenge?

We gave it a shot!
What needed to be done to keep it economically viable?

- The INTERCEPT™ Blood System was the pathogen inactivation system of choice
- To be affordable it had do be combined with production of double dose BCPs (DD-BCPs)

What is a DD-BCP?

A platelet concentrate with:

- double the amount of platelets
- double the volume of a BCP.

The DD-BCP is Intercept-treated and after treatment divided into two transfusion units of BCP.
However …

There is a **volume limit** for the INTERCEPT™ treatment!
- Max: 420 mL
- Min: 385 mL

Challenge!

Increase concentration of platelets in the concentrate so that it contains enough platelets for two transfusion doses in a smaller volume than before!!!
What do our BCP procedures look like now?

**Production summary**
- 4,632 production procedures
- 9,264 produced BCPs

**Production system**
- **Manual** production:
  - Pooling
  - Centrifugation
  - Separation on automatic blood component separator
- **Double doses**
  (8 BC + 280 mL PAS-E)

**Safety measures**
- Pathogen inactivation with INTERCEPT™ Blood System
- 2% γ-irradiated BCPs

% safety measures at transfusion:
- 2 % none
- 98 % completed
2015 – What do our BCP procedures look like now?

**Quality**

**BCPs**
- 239 ± 40 × 10⁹ plt/unit
- 189 ± 40 mL

**RBCs**
- 46 ± 4 g Hb/unit
- 255 ± 13 mL

**Plasma**
- 246 ± 15 mL

**Storage time**
- 7 days with PI
- 5 days for γ-irradiated BCPs

**Staff**
- 3 persons for BCP production/start of safety measure (8 am – 4.30 pm)
- 1 person for finishing safety measure (12.30 pm – 9 pm)

**Outdating rate**
- 5.5 %

We aim for an outdating rate of 6 – 8 % to avoid a shortage of platelets.
2015 – Timeline

DAY 0 → DAY 1 → DAY 2

8 AM - 11 AM
BCP production
Manual

9:30 AM - 12 PM
Pathogen inactivation
Start

4 PM - 9 PM
Pathogen inactivation
Finished
Division
Release

4,632
BCP procedures

2% irradiated

98 % INTERCEPT™

2x single doses

All done in the same day!
<table>
<thead>
<tr>
<th>Comparison</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of BCP produced</td>
<td>8,669 a year</td>
<td>9,264 a year</td>
</tr>
<tr>
<td>Production system</td>
<td>Automatic system</td>
<td>Manual system</td>
</tr>
<tr>
<td></td>
<td>Single doses</td>
<td>Double doses</td>
</tr>
<tr>
<td></td>
<td>5 BC PAS-E</td>
<td>8 BC PAS-E</td>
</tr>
<tr>
<td>Safety measures</td>
<td>eBDS™</td>
<td>INTERCEPT™</td>
</tr>
<tr>
<td>Storage time</td>
<td>7 days with safety measure</td>
<td>7 days with safety measure</td>
</tr>
<tr>
<td>Outdating rate</td>
<td>5.5 %</td>
<td>5.5 %</td>
</tr>
<tr>
<td>Staff</td>
<td>2 + 1 persons</td>
<td>3 + 1 persons</td>
</tr>
<tr>
<td>Quality</td>
<td>$342 \pm 32 \times 10^9$ plt/unit</td>
<td>$239 \pm 40 \times 10^9$ plt/unit</td>
</tr>
</tbody>
</table>
Changes and their effect!

- Manual production instead of automated
  - ↓ 21 % material cost
  - ↑ +8 % cost for extra quality control

- Double dose compared to single dose
  - ↓ PLT content from 342 to $239 \times 10^9$ plt/unit
  - However... transfusion quality unchanged
    - limit: >$200 \times 10^9$ plt/unit
    - ~7800 BCP transfusions both 2014 and 2015.

- Shorter procedure for safety measures (6 hrs vs 16+24 hrs)
  - 1 extra shift required
  - ↑ +10 % labour cost

- One less BC per transfusion unit
  - more available raw material
  - possible to produce more BCPs
Overall results

Safety measures
- The % of BCPs that are subjected to safety measures increased from 55 % to 98 %, mostly due to shorter overall production time.

\[ +43\% \]

Gamma irradiation
- Only 2 % of BCPs are \( \gamma \)-irradiated, since the rest are pathogen inactivated.

\[ -98\% \]

Bacterial sepsis
- No adverse effects due to bacterial sepsis since implementation of PI. 2 cases reported during previous 24 months.

\[ -100\% \]

Cost / BCP unit
- Overall cost savings are 16%.

\[ -16\% \]

No. of transfusions
- Platelets per unit -30%
- Number of BCP transfusions is unchanged → same clinical effectiveness

\[ \pm 0\% \]
Are we satisfied?

YES!

Can we do better?

YES!
Lessons learned

– Manual systems:
  – More sensitive to fluctuation.
  – Harder to standardise.

Changing from an automated to a manual system requires:
– More time spent on instructing and supervising the staff
– Frequent status check-ups and feedback loops

– Procedures that work well in a small scale are not necessarily optimal for a larger production scale.

It is important to:
– Monitor the process closely and detect early signs that it needs adjustment
– Encourage the staff who work in the everyday process to suggest improvements.
Future improvements

– **Improve raw material**
  – **Harder centrifugation of WB**
    – Increased recovery of platelets in BCs
    – Fewer BCs per transfusion unit
    – More efficient use of resources

– **Revise SOPs**
  – further *standardise* procedures
  – get rid of *unnecessary steps*

– **Further education** of production staff
  – deeper *understanding* of the process
  – reduce risk of *shortcuts*
Future improvements

- Optimisation of **packing** in the **centrifugation liners**.
  - Pivotal for platelet **volume** and **colour**

- Optimisation of the **pooling bag**.
  - **New bag** streamlined for our production

- **LEAN**

  - Prolong incubation to **16 hrs** → **reduce labour costs**
    - 6 hrs incubation → **3** day persons + **1** evening person
    - 16 hrs incubation → **2** day persons + **1** evening person

- Reduction of extra quality control based on previous experience
To answer the initial question...

It is absolutely possible to implement pathogen inactivation in a cost neutral way.

We even did it cost saving!!

Starring: Hanna-Stina Ahlzén and Linda Larsson
Fabulous photo: Liza Larsson
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