Outcomes of the European PVC-free blood bag project

What is next in the regulatory path?
Blood bags are medical devices

- Subject to EU current Directive and upcoming Regulation
- Classified as medium-high risk devices Class IIb
  - Unvaried in Regulation
- CE marked
  - by the legal manufacturer
Path to market

• Safety: Shall comply to
  – Essential requirements
  – International standards ISO

• Benefit
  – Shall give proof of consistent and statistically significant clinical data

• Consistent level of quality
  – Manufacturing as per good manufacturing practices
A new Essential Requirement
Reg. 2017/745 RES 7.4

• Attention to substances:
  – (a) substances which are carcinogenic, mutagenic or toxic to reproduction (‘CMR’),
  – (b) substances having endocrine-disrupting properties

• High contact devices: invasive, transport of fluids, storage of fluids- including blood bags

• Concentration higher than 0.1% weight by weight to be justified
Higher concentration justified
Reg. 2017/745 RES 7.4.2 (extract)

- (b) an analysis of **possible alternative substances**, materials or designs, including, where available, information about **independent research**, peer-reviewed studies, scientific opinions from relevant scientific committees and an analysis of the **availability of such alternatives**;
Possible alternative substance
PVC free Blood Bag

• All raw materials are 100% PVC free and contain no intentionally added phthalates.

• The bags are made of a 3-layered, polyolefin-based film.
  – Each layer is made of different types of modified polypropylene (polypropylene belongs to the wide family of polyolefins)

• The tubing is made of a 3-layered thermoplastic polyolefin elastomeric compound

• Additional components are made of Poly-propylene, Poly-ethylene, and Poly-carbonate,
  – Crucial components include: (1) the donor needle, made of steel, poly-carbonate and poly-propylene and (2) the whole blood leukocyte-reduction filter of poly-butylene terephthalate and Poly-carbonate

• All materials already approved for medical applications meeting the requirements of USP class VI and ISO 10993-5
Storage of red blood cells in a novel polyolefin blood container: a pilot *in vitro* study

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# Availability of alternatives

<table>
<thead>
<tr>
<th>No.</th>
<th>Ref. document</th>
<th>Observation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Technical File FT15 Rev. 0 of 2017-03-09</td>
<td>The OP and PQ phases of the process validation are not available for the bag moulding process and automatic assembly.</td>
</tr>
<tr>
<td>2</td>
<td>Technical File FT15 Rev. 0 of 2017-03-09</td>
<td>Documents for packaging validation and DM shelf life are not available.</td>
</tr>
<tr>
<td>3</td>
<td>Technical File FT15 Rev. 0 of 2017-03-09</td>
<td>Validation documents for gamma and steam sterilization processes are not available.</td>
</tr>
</tbody>
</table>
CE mark path

• The manufacturer quality system is available and ISO 13485 certified
• The technical file for CE mark is 80% complete
• Non conformities from Notified body due to EU founded project limits
Creating a technical file for CE mark: completed validations

- Compliance to international standards
  - Product mechanical features
  - Sterility
  - Stability over time
  - Interaction with blood
Creating a technical file for CE mark: completed evaluation of risk

• Risk analysis

• Clinical data evaluation and estimation of benefit/ usability
Creating a technical file for CE mark: draft information for the end user

- Instructions for use
- Label
- Training of operators

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With financial support from EU’s Life+ programme
quality system for CE mark: available

• Product traceability from raw materials to distribution
• High level of technical quality and quality control
• Industrial processes stability and repeatability
• Assurance of sterility

ISO 13485:2016

PVCfreeBloodBag.eu

With financial support from EU’s Life+ programme
What was done till now

- Compliance to international standards
- Risk analysis
- Technical drawing
- Sterility impact
- Evaluation of usability
- Industrial processes validation

With financial support from EU’s Life+ programme
What is missing

• Validation of sterilization cycle for commercial lots
• Stability testing
• Scale up
• Instructions for use and training