Trends in Industry for parenteral Fill-finish

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groninger & co.gmbh
Future customers’ request in 10 years

Outcome of discussion yesterday evening

“round table” Pharmaceutical company - supplier

Growing market

- Impact of product
- Impact of material
- Impact of technology
- Impact of new therapies
- Impact of new regulation
- Impact of cost pressure

\[ \rightarrow \text{complexity} \]
Decontamination

Transfer of cfu into sterile container

Inside contaminated due to transport damage (e.g. pinholes)

Typical material: Tyvek™, HDPE, LDPE

(assuming a proper sterilization and packaging closure)
Decontamination

Transfer of cfu into sterile container

Contaminant is carried over from the outside into a primary container during opening process

A spore made it into a syringe
APPENDIX 1: ASEPTIC PROCESSING ISOLATORS
(“Contains Nonbinding Recommendations”)

D. Decontamination

2. Efficacy

The decontamination method should render the inner surfaces of the isolator free of viable microorganisms... Process development and validation studies should include a thorough determination of cycle capability. The characteristics of these agents generally preclude the reliable use of statistical methods (e.g., fraction negative) to determine process lethality (Ref. 13). An appropriate, quantified Biological Indicator (BI) challenge should be placed on various materials and in many locations throughout the isolator, including difficult to reach areas. ... Normally, a four- to six-log reduction can be justified depending on the application. ... For example, demonstration of a four-log reduction should be sufficient for controlled, very low bioburden materials introduced into a transfer isolator, including wrapped sterile supplies that are briefly exposed to the surrounding cleanroom environment. ...
## Decontamination

<table>
<thead>
<tr>
<th>procedure</th>
<th>note</th>
</tr>
</thead>
<tbody>
<tr>
<td>zone concept</td>
<td>no disinfection</td>
</tr>
<tr>
<td>spraying alcohol</td>
<td>not sporicidal; difficult validation; $10^2$ kill</td>
</tr>
<tr>
<td>Aerosol (VHP) / wetting by $\text{H}_2\text{O}_2$</td>
<td>15min - 6h erosion of material residuals (Tyvek)</td>
</tr>
<tr>
<td>E-beam</td>
<td>Radicals; oxidation; radiation</td>
</tr>
<tr>
<td>UV-light</td>
<td>max. killing rate $10^3$ shadowing effects</td>
</tr>
<tr>
<td>Plasma</td>
<td>New technology</td>
</tr>
</tbody>
</table>
Plasma Decontamination
Single-use-systems in (BioTech) - Manufacturing
Single-use

Components for disposable systems
Single-use

Single-use not available yet
- Mass Flow
- Time Pressure

Single-use already standard
- Peristaltic Pump

Single-use an option
- Diaphragm Pump
- Rotary Piston Pump incl. Filling Needle
Benefits of single-use fill finish

- Reduce investment costs
- Reduce change over time
- Eliminate CIP / SIP
- Eliminate Cross-Contamination
- Reduce (re)-validation activities
- Reduce qualification activities
- Reduce time to market
Complete single-use product path, installed on filling line
# Single-use

## Single-use vs. traditional approach

<table>
<thead>
<tr>
<th>CUSTOMER DATA</th>
<th>CIP/SIP</th>
<th>Single Use System</th>
</tr>
</thead>
<tbody>
<tr>
<td>Investment in</td>
<td>$500,000 (incl. $200,000 ancillary costs)</td>
<td>-- (even less equipment costs)</td>
</tr>
<tr>
<td>equipment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Setup (incl.</td>
<td>2 hours</td>
<td>45 minutes</td>
</tr>
<tr>
<td>connections)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CIP + SIP-cycle</td>
<td>40 + 75 minutes</td>
<td>-- (arrives ready to use)</td>
</tr>
<tr>
<td>Cool down cycle</td>
<td>75 minutes</td>
<td>-- (ready to go)</td>
</tr>
<tr>
<td>cleanup</td>
<td>1 hour</td>
<td>15 minutes</td>
</tr>
<tr>
<td>Post-Use CIP</td>
<td>40 minutes</td>
<td>-- (throw it away)</td>
</tr>
<tr>
<td>Summary</td>
<td>~ 7 hours and $500k (qualification and</td>
<td>1 hour and cost of assembly (easy storage)</td>
</tr>
<tr>
<td></td>
<td>re-validation efforts are not included)</td>
<td></td>
</tr>
</tbody>
</table>
Nested objects – Syringes
## Nested objects - Vials

### EZ-fill™ Vial Range: Nest & Tub configuration

<table>
<thead>
<tr>
<th>Format</th>
<th>dm</th>
<th>h</th>
<th>F</th>
<th>pcs</th>
<th>Nest &amp; Tub</th>
</tr>
</thead>
<tbody>
<tr>
<td>2R</td>
<td>16</td>
<td>35</td>
<td>13</td>
<td>120</td>
<td>Available</td>
</tr>
<tr>
<td>4R</td>
<td>16</td>
<td>45</td>
<td>13</td>
<td>120</td>
<td></td>
</tr>
<tr>
<td>6R</td>
<td>22</td>
<td>40</td>
<td>20</td>
<td>32</td>
<td>By Q3 2014</td>
</tr>
<tr>
<td>8R</td>
<td>22</td>
<td>45</td>
<td>20</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>10R</td>
<td>24</td>
<td>45</td>
<td>20</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>20ml</td>
<td>26,5</td>
<td>63</td>
<td>20</td>
<td>32</td>
<td></td>
</tr>
<tr>
<td>20R</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>To Be Defined</td>
</tr>
</tbody>
</table>

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*EZ-fill™ | Courtesy of Nuova Ompi glass division

Connecting People, Science and Regulation®
Nested objects - Cartridges

EZ-fill™ Cartridge Range: Nest&Tub configuration

<table>
<thead>
<tr>
<th>Format</th>
<th>dm</th>
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<th>Nest &amp; Tub</th>
</tr>
</thead>
<tbody>
<tr>
<td>3ml ISO</td>
<td>11.6</td>
<td>62.3</td>
<td>7</td>
<td>100</td>
<td>By Q2 2014</td>
</tr>
</tbody>
</table>

Cartridge is available in 3 formats:

- Only cartridge (no components)
- Capped Cartridge
- Cartridge + plunger

EZ-fill™ | Courtesy of Nuova Ompi glass division
Nested objects - Polymers

Daikyo Crystal Zenith®

Vials
0.5, 1, 3, 5, 10, 20, 50mL

Syringes
5mL Luer Lock
1 mL Insert Needle

Cartridges
1, 3mL

Available only in EZ-fill N&T format
Nested objects

SCHOTT adaptiQ™
THE FUTURE FAST FORWARD

Afton Scientific
Ready-to-Fill®

Connecting People, Science and Regulation®
Small batch filling

Business strategy

Small batch to midsize production
• Clinical trials
• Start-up phase
• New markets & New products
• High margin / low volume production

Flexibility / Easy adaption to changes of:
• Containers, Processes, Performance, Layout, Location, Regulatory requirements, ...

Small batches: modular concept

- 3 standardized isolators
- Modular filling equipment designed for isolator

Additional adaption by format parts:
- Peristaltic and/or rotary piston pump
- Single-use system
- Vacuum filling and stoppering
- Container dimensions made of polymer or glass by several suppliers

Sketch not to scale!
Small batches: modular concept
Small batches: Requirements

Keep:
- Known processes
- Approved solutions
- Product quality
- Product safety

Reduce:
- Footprint
- Training
- Quali. / Vali.
- Investment

Gain:
- Flexibility
  - on container
  - on location
- Reproducibility
  - on equipment
  - on processes
- Investment safety
Flexibility & bulk objects

Processing bulk material
Flexibility & nested objects

Processing nested objects -classical-
Flexibility & nested objects

- All objects (syringes, vials, cartridges)
- Flexible modular concept
- 100% IPC up to 400/min
Future customers’ request in 10 years

Inspection of “all” processes

Parametric release to fulfill future regulations

Electronic batch documentation
Future customers‘ request in 10 years

No human intervention

Source: t3n.de
Future customers‘ request in 10 years

Flexibility?

Systems with full flexibility for all kind of containers inside isolators
Future customers’ request in 10 years

Movable factory?

Source: prozesstechnik-online.de
Future customers' request in 10 years

Advanced Therapy Medical Products

The next “monoclonal Antibodies” ?
Future customers’ request in 10 years

Outcome of discussion yesterday evening
“round table” Pharmaceutical company - supplier

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<th>In progress</th>
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<td>Decontamination</td>
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<tr>
<td>Impact of material</td>
<td>Single-use</td>
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<tr>
<td>Impact of technology</td>
<td>Nested container</td>
</tr>
<tr>
<td>Impact of new therapies</td>
<td>Small batch</td>
</tr>
<tr>
<td>Impact of new regulation</td>
<td>Process control</td>
</tr>
<tr>
<td>Impact of cost pressure</td>
<td>No human intervention</td>
</tr>
<tr>
<td>Location</td>
<td>ATMP</td>
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=> Flexibility into the future

Thank you very much for your attention!

We fill Visions with Life.

Wenzel Novak
Director pharmaceutical research and development
groninger & co.gmbh