Filling of Nested Vials
A Logical Step in Fill-Finish Production?

Pharmpur GmbH
Messerschmittring 33
D-86343 Königsbrunn
Germany
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Pharmpur GmbH - Facts & History

Pharmpur GmbH was founded 1991 in Augsburg as special lab for ultra purification of technical grade materials. Soon after, an own analytical department was established and R&D activities became part of Pharmpur’s daily business.

In 1998, Pharmpur started fill & finish production of ophthalmic medical devices. As a Contract Manufacturing Organization with the focus on sterile liquid dosage forms, Pharmpur produces niche products for a global market.

The former premises in Augsburg soon became too small wherefore Pharmpur moved in 2005 to Messerschmittring, Königsbrunn. In 2009, the manufacturing site was further extended.

Today, Pharmpur is a FDA approved contract manufacturer of medical devices and medicinal products with about 60 employees and customers all over the world.

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Pharmpur GmbH - Certificates & Standards

ISO 13485 since 2001
21 CFR 820 since 2000
21 CFR 211 since 2004
AMG since 2011

Although Pharmpur has proprietary Technical Files since 2003, Pharmpur does not distribute these products under its own brands.

Pharmpur has approvals acc. to MDD 93/42 EEG for
- Ocular endotamponades
- Pharmpur HPMC

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Services offered by Pharmpur

Ultrapurification & Chemical Synthesis

Analytics

Fill & Finish

Research & Development

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Pharmpur’s “all under one roof”-concept

• Ultrapurification of technical-grade materials
• Chemical synthesis and pharmaceutical preparation
• Fill & Finish:
  ◦ compounding
  ◦ filling
  ◦ labeling
  ◦ assembling
  ◦ sterilization
  ◦ packaging
• Analytical services (routine characterization, troubleshooting)
• Stability studies
• Manufacturing transfer, scale-up of developed processes

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Contract Manufacturing

Customer → CMO → Product

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Contract Manufacturing

Customer A
Customer B
Customer C
Customer D

Product A
Product B
Product C
Product D
Contract Manufacturing – the tale of ideal customers...

Customer A
Customer B
Customer C
Customer D

Product A
Product B
Product C
Product D

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Contract Manufacturing –
...and the Egg laying wooly milk pig
Contract Manufacturing of individual Niche Products – meeting the needs of the customer

Modular Manufacturing Processes

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Modular Manufacturing Processes - Advantages

- Reduced investments
- Increased flexibility
- Higher degree of automation
- Less validation/qualification work
- Focused Personnel qualification

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Inova SV 122 as Central Element of a Modular Filling Concept – 10 years ago

Filling of nested syringes:

- Flexibility in the Primary Container
- Standardization of the syringe nest and packaging

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Aseptic Filling of Nested Vials

Sterile closure
Sterile container
Sterile drug product

Class A
Aseptic filling
sterile filled product
Aseptic Filling of Nested Vials

• A primary container must be:
  ◦ Sterile
  ◦ Pyrogen free
  ◦ Particle free

Manual loading of the nest with cleaned and sterile vials
The reusable nest for preparation and filling of vials

- A primary container must be:
  - Sterile
  - Pyrogen free
  - Particle free

- Rinsing overhead
- Sterilization and Depyrogenization by dry heat
The Fedegari Washer-Sterilizer

- In 2009, the idea of a functional trolley, specifically designed for Pharmpur’s reusable steel nest was born
- Planned as pass-through process

✓ Ideal solution for medium demand
✓ Discussed with glass vendors as entry concept to make pre-sterilized vials available
✗ Not realized
**Outsourced preparation – nested ready to fill vials**

- In 2011, nested pre-sterilized vials became available
  - D2F®-Vials from NSGG (former MGläs)
  - EZ-fill™ Vials from Nuova Ompi
  - Others will follow
- All advantages of ready to fill formats
- Abbreviated validation concepts for new products possible
- Modular pre-processing units can be used
## Preparation of nested vials: Overview

<table>
<thead>
<tr>
<th></th>
<th>Nest</th>
<th>Sterilizing agent</th>
<th>Media supply</th>
<th>Format compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual Pharmpur process</td>
<td>re-usable</td>
<td>dry heat</td>
<td>---</td>
<td>only to nest-filler</td>
</tr>
<tr>
<td>Fedegari Washer-Sterilizer</td>
<td>re-usable</td>
<td>steam</td>
<td>purified steam, sterile pressurized air</td>
<td>only to nest-filler</td>
</tr>
<tr>
<td>Pre-sterilized vials</td>
<td>disposable</td>
<td>ETO</td>
<td>ETO, sterile pressurized air</td>
<td>Pharmaceutical Standard for pre- and post-processing</td>
</tr>
</tbody>
</table>
Filling of nested vials

Video
Post-processing of nested vials:

How to cope with Annex 1?

118. The container closure system for aseptically filled vials is **not fully integral until the aluminium cap has been crimped** into place on the stoppered vial. Crimping of the cap should therefore be performed as soon as possible after stopper insertion.

120. Vial capping can be undertaken as an aseptic process using sterilised caps or as a clean process outside the aseptic core. Where this latter approach is adopted, vials should be protected by **Grade A conditions up to the point of leaving the aseptic processing area**, and thereafter stoppered vials should be protected with a **Grade A air supply** until the cap has been crimped.
Filling and post-processing in a line filler

Class A

Aseptic filling

sterile filled product

Sterile container

Class A

Class A

Class A

Filling

Crimping
Filling with nest filler and manual post-processing

- Fully compliant to Annex1, but transfer time should be controlled
- Individual process steps can be performed separately
- No advantages in post-processing by the use of nests
Filling with nest filler and post-processing line

- Fully compliant to Annex1, but transfer time should be controlled
- Standard post-processing line technology can be applied
- No advantages in post-processing by the use of nests but denesting necessary
Filling and post-processing in nest format

- Fully compliant to Annex1
- No glass to glass contact
- High throughput by the use of nests
- Standard technologies are applicable
## Post-processing of nested vials: Overview

<table>
<thead>
<tr>
<th></th>
<th>Compliance to Annex 1</th>
<th>Throughput</th>
<th>Format compatibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manual</td>
<td>transfer time needs to be controlled</td>
<td>low</td>
<td>only to nest-filler</td>
</tr>
<tr>
<td>Line</td>
<td>transfer time needs to be controlled</td>
<td>high</td>
<td>Transfer from nest standard to line standard</td>
</tr>
<tr>
<td>Nest</td>
<td>Fully compliant</td>
<td>high</td>
<td>Nest standard for post-processing needs to be established based on standard technologies</td>
</tr>
</tbody>
</table>
Conclusion

- Nested Ready-to-fill vials complete ideally the modular fill-finish platform and increase the format diversity
- Nested vials can be processed in full compliance to Annex 1 with available standard technologies
- Post-processing technology should be extended to process nested vials in line
Thank you for your kind attention!
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Highest quality for your niche products

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