HFA pMDI Manufacturing Techniques

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HFA pMDI Manufacturing Techniques
Key Challenges for CFC-HFA Change

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1 Typical pMDI Filling and Packing Line Configurations

Typical Filling Line Configuration
1 Typical pMDI Filling and Packing Line Configurations

Typical Packing Line Configuration

2 Typical pMDI Formulations and Filling Techniques
2 Typical pMDI Formulations and Filling Techniques

Two stage CFC filling process

- Liquid propellant 70%
- Solvent 28%
- Drug Solids 2%
### 2 Typical pMDI Formulations and Filling Techniques

#### Single or two stage HFA filling process

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid propellant</td>
<td>93%</td>
</tr>
<tr>
<td>Solvent</td>
<td>5%</td>
</tr>
<tr>
<td>Drug Solids</td>
<td>2%</td>
</tr>
</tbody>
</table>

#### Single stage HFA filling process

<table>
<thead>
<tr>
<th>Component</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liquid propellant</td>
<td>98%</td>
</tr>
<tr>
<td>Drug Solids</td>
<td>2%</td>
</tr>
</tbody>
</table>
Filling Techniques for different Formulations

2 Typical pMDI Formulations and Filling Techniques

Two Stage CFC Filling

- Open Can Product Fill
- Place Valve
- Crimp Valve
- Pressure Fill Propellant
CFC MDI Filling on DH Micromat

Two Stage HFA Filling

- Open can product Fill
- Place Valve
- Crimp Valve
- Pressure Fill propellant

1. Fill Product Suspension or Solution
2. Place Valve
3. Crimp Valve
4. Fill HFA Propellant
2 Typical pMDI Formulations and Filling Techniques

Two Stage HFA Filling (if purging required)

- Purge open can with liquid propellant
- Open can product fill
- Place valve
- Crimp valve
- Pressure fill propellant

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2 Typical pMDI Formulations and Filling Techniques

Two stage HFA Filling on DH Macromat
2 Typical pMDI Formulations and Filling Techniques

GSK Patented Dual Filling

- Place valve
- Purge through valve
- Crimp valve
- Fill 2 stage pressure

GSK Patented Dual Filling Nozzle
2 Typical pMDI Formulations and Filling Techniques

Dual Filling on DH MacroElcomat

Single Stage HFA Filling (trough valve purge)

- Place valve
- Purge through valve
- Crimp Valve
- Aspirator fill

Fill HFA Suspension then suck away residue with vacuum
2 Typical pMDI Formulations and Filling Techniques

Single Stage HFA Filling (vacuum purge)

- Place valve
- Vacuum crimp
- Aspirator fill

Two Stage HFA Pressure Filling (vacuum purge)

- Place valve
- Vacuum crimp
- Aspirator fill
- Propellant fill
2 Typical pMDI Formulations and Filling Techniques
Single Stage Filling – Aspirator Nozzle
3 Mixing and Process Equipment

HFA Suspension Manufacturing – Single Stage Filling

- Manufacturing and filling carried out at room temperature
- Product kept under pressure at 20°C
- 134a pressure at 20°C – 5.7 bar
- 227 pressure at 20°C – 3.9 bar
- Product suspension pumped to filling heads at 10 bar pressure to keep it in its liquid state
- Recirculation path back to mixing vessel.
3 Mixing and Process Equipment
HFA Suspension Manufacturing

Typical HFA Suspension Manufacturing System

- Main Vessel
- Pre-mix vessel
- Tandem diaphragm pump
- Propellant top up system

3 Mixing and Process Equipment
HFA Suspension Manufacturing

Mobile pre-mix vessel taken to dispensary to add product/formulation

- Main Vessel
- Pre-mix vessel being taken to dispensary
Pre-mix vessel connect back to mixing skid
Product/formulation mixed with homogeniser/agitator
depending on manufacturing method
Propellant can be added to concentration prior to mixing

Mobile pre-mix vessel connected to hoist and
elevated above main vessel
3 Mixing and Process Equipment

HFA Suspension Manufacturing

- Pre-mix vessel docked on top of main vessel
- Propellant supply connected to pre-mix vessel
- Hose connected between pre-mix vessel and main vessel

- Contents of pre-mix vessel emptied into main vessel
- Propellant charged to main vessel through pre-mix vessel
- Rinsing all product/formulation out of pre-mix vessel
- Product kept in suspension by agitator in main vessel
Pre-mix vessel connected to hoist and removed from main vessel

- Lifting mechanism
- Main Vessel
- Pre-mix vessel

Tandem diaphragm pump pumps HFA suspension in recirculation to filling machine
Propellant top up system replaces propellant in main vessel as level descends

- Tandem diaphragm pump
- Propellant top up system