New Solutions for Cleaning, Sterilization and Decontamination of Process Equipment for Aseptic Sterile, Biotech and Vaccine Manufacturing

Process Cleaning & Sanitizing, and Continuous Thermal Decontamination of Effluents.

By Ole T. Madsen  otm@McFlusion.com
Agenda

Present Solution
Inline CIP/SIP of Filling Machine
Continuous Decontamination of Effluents
Comparison to Present Solution
Agenda

Present Solution

Inline CIP/SIP of Filling Machine

Continuous Decontamination of Effluents

Comparison to Present Solution
Present Solution
Filling Machine

• After batch is ended, filling machine is hooked up to WFI line for a rinse sequence to remove active ingredients.
• Filling machine is disassembled and parts are cleaned manually e.g. in parts washer outside classified area.
• Before parts are returned to classified area they are sterilized (steam or dry heat sterilizer)
• After re-assembly filling machine is ready for Sterilization-in-Place.
Present Solution

Filtration Station

- Integrity testing is performed.
- Rinse by WFI
- Filter is removed / housing is cleaned in parts washer
- Returned to classified area through sterilizer
- Reassembled
- Sterilization-in-Place
- Integrity test
(Mobile) Filling Vessel

• Cleaned either manually outside classified area or by a central CIP system.
• SIP performed either in sterilizer or inline with rest of line.
Holding Tank for Process Waste Water

- Holding tank is used as buffer or active sterilization and neutralization tank for a batch kiln system.
Agenda

Present Solution

Inline CIP/SIP of Filling Machine—*MORK solution*

Continuous Decontamination of Effluents

Comparison to Present Solution

Conclusion
MORK Solution
**Filling Machine and Filtration Station**

- Flexible hose or spool piece is connected to filtration station (this manual handling will secure any Class C cross-contamination issues).
- Filters from previous batch are removed (or complete product filter arrangement is removed and replaced by a spool piece).
- CIP program initiated from stand-alone CSD OIT or from integrated control OIT.
- Thermal decontamination of effluents integrated with CIP process.
- Filters with filter housings are inserted inline.
- SIP is performed and air removed
- Filling machine pressurized with nitrogen.
MORK Solution
**MORK Solution**

**Integration Between Filling Machine and CSD Unit**

- One supply line between Filling Machine and CSD Unit for media, vacuum, steam, air and nitrogen.
- One return line between Filling Machine and Decontamination Unit for CIP and process waste—conductivity, temperature and pressure are measured.
- PLC-PLC interaction via Ethernet, or potential free contact hard wired.
- CIP Unit can also function as utility server—sterile air, nitrogen, hot and cold WFI, clean steam, detergent 1 and 1, and vacuum.
MORK Solution

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MORK Solution

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**MORK Solution**

**Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit**

The operation of the CIP/SIP unit can be fully automated and is performed in accordance with predefined validated recipes.
MORK Solution

Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

Sequences can be included or left out:

- Pre-rinse, cold
- Pre-rinse, hot
- Wash (caustic cleaning agent + water)
- Rinse
- Wash (Acidified cleaning agent + water)
- Post Rinse
- Final rinse (USP water)
- Drain and purge with heated air
- Pressure test before sterilization
- Vacuum
- Sterilization
- Drying/Cooling
Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

- System is programmed to flush all incoming utilities to drain prior to start-up to prevent contamination.

- Heated drain and air purge sequence can be performed after each sequence and at the end of each cycle to ensure that all parts of the CIP/SIP Unit and associated piping is emptied and left in dry condition.
Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

- All sequences can be performed in “once-through” (single-pass) or “re-circulation” modes, except for final rinse, which always will be performed as “once-through.”
Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

- The final rinse of the cleaning process is monitored by conductivity.

- The sterilization process, which can be chosen as part of the CIP cycle or started as an independent cycle, begins with a vacuum cycle to remove any air in the vessel. The vacuum cycle can be repeated as many times as needed.
Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

The CIP/SIP unit uses the temperature sensor on the return line to calculate the $F_0$ value. This is reached with a temperature of approximately 121 °C in the time required to obtain $F_0 > 15$.

$$F_0 = \int_{T_1}^{T_2} 10^\left(\frac{T_0 - 121}{10}\right) \, dt$$

$T_0$-Product temperature at the time $t$

A minimum log 12 reduction of spores is achieved.
Filling Vessel and/or Other Portable Vessels can be Integrated to Same Unit

- The SIP cycle will sterilize the filling system and the portable vessels, e.g. 121°C until either a programmable $F_0$ value is achieved at the coldest point or until a programmable time limit is achieved.
Agenda

Present Solution

Inline CIP/SIP of Filling Machine

Continuous Decontamination of Effluents

Comparison to Present Solution
Large Scale Continuous Decontamination

• 80-8,000 gallons/hour.
• Suitable for BSL 1, 2 & 3.
Large Scale Continuous Decontamination

• Effluents continuously collected in a collecting tank.
• Decontamination begins when level set point is reached.
• When the treatment temperature is reached, effluents are pumped and continuously treated before disposal.
• In the event of power failure or at the end of the cycle, effluents flow back to the collecting tank.
• The system is then automatically cleaned, sanitized and ready for a new decontamination cycle.
Continuous Decontamination

Contaminated effluents

Treated effluents

CIP preparation or sanitization

Water inlet

Vent

Collecting tank

Product inlet

Product outlet

Heating section

Holding energy recovery section

Pumps
Large Scale Continuous Decontamination

Time and temperature for 30 lethality rate:

• 30 minutes at 121 °C.
• 3.9 minutes at 130 °C.
• 72 seconds at 135 °C.
• 24 seconds at 140 °C.
• 8 seconds at 145 °C.
Self-Contained Unit

1) Collecting Tank; 2) Double secured pump system; 3) Thermal section; 4) Control cabinet.
Small Scale Decontamination

- 15-160 gallons/day; 57-600 liters/day.
- Compact design, as small as 37” x 22” x 53”.
- For labs working on viruses, bacteria, prions, API or gmo.
- Effluents pressurized at 140°C.
- Real-time visual control, complete electronic records.
Small Scale Decontamination

1) Collection tank.
2) Heating system.
3) Cooling section.
4) Control cabinet.
Small Scale Decontamination

Contaminated effluents

Treated effluents
Continuous Decontamination

Additional Advantages With Small-Scale Continuous Thermal Biowaste Decontamination Unit:

• Internal electric pipe heating system...entire system is heated, no exposed elements to create scaling.
• Safe design: effluents are contained in event of power failure.
• cGMP design.
Agenda

Present Solution
Inline CIP/SIP of Filling Machine
Continuous Decontamination of Effluents
Comparison to Present Solution
Conclusion
## Comparison to Present Solution

**Complete GMP Documentation – CIP on one page**

<table>
<thead>
<tr>
<th>SP = Set point</th>
<th>Pre rinse 1</th>
<th>Pre rinse 2</th>
<th>Wash 1</th>
<th>Post rinse 1</th>
<th>Wash 2</th>
<th>Post rinse 2</th>
<th>Final rinse</th>
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</thead>
<tbody>
<tr>
<td>PV = Process value</td>
<td>SP</td>
<td>PV</td>
<td>SP</td>
<td>PV</td>
<td>SP</td>
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<td>Duration time [Sec]</td>
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<td>30</td>
<td>0</td>
<td>31</td>
<td>0</td>
<td>15</td>
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<tr>
<td>Temperature [°C]</td>
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<td>Cleaning agent 1 [Kg.]</td>
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<td>Cleaning agent 2 [Kg.]</td>
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<td>Drain CIP internal. [Sec]</td>
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<td>Drain w. pump [Sec]</td>
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<td>Operator Approval: Yes/No: Date:</td>
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<td>Supervisor Approval: Yes/No: Date:</td>
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</tr>
</tbody>
</table>

By Ole T. Madsen  otm@McFlusion.com
## Complete GMP Documentation – SIP Process

**SIP Report for Portable Vessel**  
**Printed on:** 24-02-2006

### Comparison to Present Solution

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SP</th>
<th>PV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vacuum repetitions</td>
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<tr>
<td>Minimum Vacuum pressure, 12PT01</td>
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<td>-0.9</td>
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<td>Steam heating pressure, 31PT01</td>
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<td>Sterilization duration time</td>
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<tr>
<td>Average temperature for air filter</td>
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<tr>
<td>F0 for air filter</td>
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<td>228.8</td>
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<tr>
<td>Average temperature for vessel</td>
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<tr>
<td>F0 for vessel</td>
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<td>Drying duration time</td>
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<td>Cooling duration time</td>
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<td>240</td>
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<tr>
<td>Nitrogen pressure in vessel after SIP</td>
<td>0.10</td>
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</tr>
</tbody>
</table>

### Additional Information

- **Start of SIP process:** 12/15/2005 12:16:10  
- **End of SIP process:** 12/15/2005 14:24:06  
- **Equipment:** Vessel 1  
- **User:** admin  
- **Recipe:** PV recipe 1  
- **Recipe version:** 1  
- **Cycle no.:** 89  

---

**Operator Approval:**  
**Yes/No:**  
**Date:**  
**Supervisor Approval:**  
**Yes/No:**  
**Date:**  

---

**By Ole T. Madsen  otm@McFlusion.com**
Comparison to Present Solution

CIP/SIP of Filling machine

Cleaning time can be reduced to less than 2 hours (batch to batch).

Total sterilization time can be reduced to 45 minutes (batch to batch).
Batch Processing of Effluents:

In a typical Class C installation, batch processing of effluents is common.

1) Large holding tanks for effluents.
2) Large volumes of steam are required.
3) Non-standard methods of decontamination.
4) There is increasing FDA scrutiny on what goes down the drain.
Continuous Processing of Effluents:

- Compact equipment.
- Reduced cost of maintenance and energy.
- Highly efficient continuous flow processing for more cost-effective production.
Continuous Thermal Processing of Effluents or Medias:

Continuous process has many options and benefits.

1) Small scale processing 15-160 gallons/day; large scale processing 50-8000 gallons per hour.

2) Suitable for virus or bacteria production (BSL 1, 2 & 3).

3) Creates an effective cGMP process with electronic records of essential parameters.

4) Increased production and reduced maintenance.
Continuous Thermal Processing of Effluents or Medias:

Options and benefits continued...

5) Less expensive investment.

6) Less energy consumption – 8 kW compared to 100 kW for a classic solution.

7) Compact installation, reduced space requirement.

8) Automatic descaling and descaling test.

9) No cooling water needed for continuous solution.
Comparison to Present Solution

Waste and Effluents Thermal Decontamination

Enclosed Room BSL 2 & 3
- Non-pressurized tank.
- Pump & agitator, standard lining.

Non-Enclosed Room BSL 2 & 3
- Pressurized starting tank.
- Secure thermal vent.
- Pump and agitator with magnetic drive.
- Radiography of welding.
- Double alarm security.