Coating Line Operations for the Production of Drug-Containing Transdermal Patches

Presented by:
Ken Glade
Director of Engineering
LTS Lohmann Therapy Systems

Kenneth.glade@lts-corp.com
+1 (973) 396-5384
Abstract

- What does the operation of a coating line look like in a GMP regulated world?

- For the newcomer to GMP production, a review of the FDA regulations that apply to medical and pharmaceutical products often leaves the newcomer with more questions than answers.

- Rather than providing a top-down analysis of the regulations, this paper presents a real-world example of the production of a typical coated web batch under GMP conditions to ensure its safety, integrity, strength, purity and quality.

- General requirements for proper documentation will be presented including logbooks, SOP’s, batch records, change controls and deviation management.
Topics

• What is a transdermal patch?

• What are Good Manufacturing Practices?

• How do GMPs apply to transdermal patches?

• What needs to be done before, during and after a coating batch to comply with GMP requirements?
Transdermal Patch

- Backing Layer
- Drug Adhesive Layer
- Release Liner
What are GMPs?

• FDA wrote GMPs in the Code of Federal Regulations (CFR)
  • They are laws
  • FDA enforces with possible shutdown or jail time
  • No legal advice here

• GMP is really cGMP
  • The “c” means current
  • to keep pace with advances in
    • Equipment
    • Processes

Simple, clear purpose and principles give rise to complex, intelligent behavior. Complex rules and regulations give rise to simple and stupid behavior.

Dee Hock
Why have GMPs?

- Consumers expect their medicines to be safe and effective
- The cGMPs remove worry and the need to self investigate
- SISPQ: Safety, Integrity, Strength, Purity, Quality
What GMPs apply?

• 21 CFR Part...
  210, Current Good Manufacturing Practice In Manufacturing, Processing, Packing, Or Holding Of Drugs; General
    • Overview and definitions
  211, Current Good Manufacturing Practice For Finished Pharmaceuticals
    • Personnel, buildings and facilities, equipment
  820, Quality System Regulation
    • Internal processes
  11, Electronic Records; Electronic Signatures
    • Computerized records
Before, Before the Batch

- Quality Unit must exist (820.20)
- Validation Master Plan (820.70, 820.75)
- People, places and things must be qualified (211.xx)
  - Capable
  - Used properly
  - Qualification must be documented
- Systems must be in place to handle
  - Changes (211.100)
  - Deviations and Investigations (820.90)
  - Corrective and Preventive Actions (CAPAs) (820.100)
  - Customer complaints (211.198)
Before, Before the Batch

• Procedures must be written, Standard Operating Procedures (SOPs) (211.100)

<table>
<thead>
<tr>
<th>SOP No.</th>
<th>Title</th>
<th>SOP No.</th>
<th>Rev.</th>
<th>Page 1 of 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ</td>
<td>Equipment</td>
<td>EQ-127</td>
<td>03</td>
<td></td>
</tr>
<tr>
<td>127</td>
<td>Preventive Maintenance Program</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>03</td>
<td>Effective 27 April 2017</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1. RESPONSIBLE  Engineering

2. REFERENCE 21CFR: 211.67, 211.180, 211.182

3. PURPOSE
Just Before the Batch

- Production Planner creates Working Batch Record from Master Batch Record
- Typically 30 – 40 pages, several hundred spaces for data entry
- Once started, Working Batch Record becomes Executed Batch Order

<table>
<thead>
<tr>
<th>For: Transdermal Coating</th>
<th>Master Batch Record No. 104-654-99 rev 02</th>
<th>Date: 09.09.18</th>
<th>Page 34 of 38</th>
</tr>
</thead>
<tbody>
<tr>
<td>Working Batch No.</td>
<td>090918-10465499</td>
<td>Equipment: Coating Line No 7</td>
<td></td>
</tr>
<tr>
<td>Step</td>
<td></td>
<td>Operator</td>
<td>Checked</td>
</tr>
<tr>
<td>1. Verify that coating line is clean and ready to use. Attach cleaning tag.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Verify that pump, hoses and fittings are BOM ASSY 22-44369</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Just Before the Batch

- Materials and Equipment are verified
  - Materials passed QC testing
  - Equipment as specified, in good working condition
  - Logbook and calibration check
    - Cleaning swab passed

<table>
<thead>
<tr>
<th>Date</th>
<th>Description</th>
<th>Performed By (Initials / Date)</th>
<th>Checked By (Initials / Date)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.4.18</td>
<td>Cal pm 50V CAL-4229</td>
<td>18.4.18</td>
<td>14/9/18</td>
</tr>
</tbody>
</table>
Just Before the Batch

• Room conditions are OK (Temp / RH)
  • Logbook check for excursions that might effect the batch
• Set up the coating line per the Pre-Production Set-up SOP
  • Line clearance
  • Line challenges
During the Batch

- Start coating
- In Process Controls (IPC)
  - Coat weights per sampling plan
- Monitor and record Critical Process Parameters
  - Drying conditions, e.g. airflows and temperatures
  - Written or electronically collected
    - If electronic, must be Part 11 compliant
- If all goes well, stop when desired linear length has been produced
  - Start “After the Batch” work
  - Start reconciliation calculations
During the Batch

- If something doesn’t go as expected,
  - Start deviation process
  - Flag the web, capture and document observations and supporting data
  - QA starts a formal investigation with written investigation report
  - Logbook check for excursions that might effect the batch
  - The batch is placed in Quarantine until the investigation is complete and “no impact” was the conclusion
After the Batch

• Shut down the coating line per the SOP
• Close out the batch record
• Perform post-batch calculations
  • Exact time elapsed during batch
  • Does the time make sense?
  • Unit conversions
  • How much coating solution is left over?
  • Does it make sense?
• Bag, Tag and Brag
Batch Quarantine & Release

- All rolls are considered suspect until proven acceptable
- Quality Control performs post-batch testing
  - Coat weights
  - Drug content (total, uniform)
- Quality Assurance triple checks batch documentation
  - Complete
  - Correct
  - Correctly Formatted
  - Deviations shown to be “no impact”
- Batch can be released
Conclusions

• cGMP compliance is a system wide process

• FDA provides the guidance, but the coater bears the burden of proof

• Document, document, document

• The prep work is the barrier to entry that gives you the competitive advantage
Questions?
Thank You

Coating Line Operations for the Production of Drug-Containing Transdermal Patches

Presented by:
Ken Glade
Director of Engineering
LTS Lohmann Therapy Systems

Kenneth.glade@lts-corp.com
+1 (973) 396-5384