RESULTS AND DISCUSSION (cont’d…..)

### MATERIALS AND METHODS (cont’d…..)

**Purpose:**

In the course of development, solithromycin 200 mg capsules were manufactured for use in clinical studies. To continue product development, a confirmation batch at the same scale as the planned registration batches was manufactured. A Design of Experiments (DOE) study was conducted to optimize the critical process parameters identified at the 5-kg scale, using a Design of Experiments (DOE) approach, consistent with Quality by Design (QbD) principles. In preparation for registration batches manufacture, it was essential to demonstrate that the process optimized at the 5-kg scale was scalable to the 200-kg scale.

### RESULTS AND DISCUSSION

**Material Passes Through (API and excipients)**

- 10-mesh: 100.0%
- 40-mesh: 22.5%
- 80-mesh: 51.3%
- 140-mesh: 72.9%
- 200-mesh: 89.3%
- 270-mesh: 93.4%

**Dry mixing (VG 200)**

- 40-mesh: 30.2%
- 80-mesh: 59.4%
- 140-mesh: 72.9%
- 200-mesh: 89.3%
- 270-mesh: 93.4%

**Impeller = 125 RPM 100 - 160 RPM 2 minutes Cross Screw = 2500 RPM 2000 - 3000 RPM**

- **Dry batch:**
  - Moisture (LOD) NMT 2.5%
  - Moisture: 1.24 - 2.32%
  - Moisture: 1.64 - 2.32%
  - Moisture: 1.48 - 1.96%
  - Moisture: 1.60 - 1.76%

**Impeller = 125 RPM 100 - 160 RPM 4 minutes Cross Screw = 2500 RPM 2000 - 3000 RPM**

- **Dry batch:**
  - Moisture (LOD) NMT 2.5%
  - Moisture: 1.24 - 2.32%
  - Moisture: 1.64 - 2.32%
  - Moisture: 1.48 - 1.96%
  - Moisture: 1.60 - 1.76%

**Microcrystalline Cellulose**

- Pan: 100.0%
- 40-mesh: 22.5%
- 80-mesh: 51.3%

**Sodium Lauryl Sulfate**

- Pan: 100.0%
- 40-mesh: 22.5%
- 80-mesh: 51.3%

**Milling (Comil; 0.5 mm screen)**

- Only steel granulation retained on 18-mesh sieve

**Wetting  (Granulation)**

- Only steel granulation retained on 18-mesh sieve

**Screening**

- (API and excipients)
- Only steel granulation retained on 18-mesh sieve

**Results for the scale-up batch**

- All three registration batches met the acceptance criteria for related substances and the Microbial Limits Test for the drug product specification during release testing.

- The encapsulation yield for the scale-up and registration batches is listed in Table 3.

**Table 3. Encapsulation Yield for the Bulks Samples (Release Testing)**

<table>
<thead>
<tr>
<th>Process</th>
<th>Test</th>
<th>Specification</th>
<th>Batch (200 mg)</th>
<th>Batch (200 mg)</th>
<th>Batch (200 mg)</th>
</tr>
</thead>
<tbody>
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<td>UCL 100%</td>
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</tr>
</tbody>
</table>

**Conclusion**

The physical and analytical data for solithromycin capsules 200 mg from the Stratifed scale-up batch and the three registration batches met the acceptance criteria of the drug product specification. This demonstrated that the manufacturing process is able to produce drug product that meets specifications and quality standards. Since these batches met all specifications, they were deemed suitable.