

| GMP SECTION   | ITEM  | COMMENTS | Rating |
|---|---|----------|--------|
| <b>4 QUALITY MANAGEMENT SYSTEMS-EXCIPIENT QUALITY SYSTEMS</b> |   |          |        |
| 4.1 General Requirements                                      |   |          |        |
| 4.2 Documentation Requirements                                |   |          |        |
| 4.2.1 General   |   |          |        |
| 4.2.2 Quality Manual  | <ul style="list-style-type: none"> <li>• Quality Manual</li> <li>• Quality Policy</li> <li>• GMP starting point</li> </ul>  |          |        |
| 4.2.3 Control of Documents                                    | <ul style="list-style-type: none"> <li>• Written manufacturing instructions</li> <li>• Process fully described</li> <li>• Verification of significant steps</li> <li>• SOP availability and control</li> <li>• Periodic review of SOPs</li> <li>• Electronic control</li> </ul>                       |          |        |
| 4.2.4 Control of Records                                      | <ul style="list-style-type: none"> <li>• Record retention SOP</li> <li>• Good Documentation Practices</li> </ul>  |          |        |
| 4.3 Change Control  | <ul style="list-style-type: none"> <li>• Change control procedure</li> <li>• Control of production changes</li> <li>• Independent approval of changes</li> <li>• Impact on qualification or validation</li> <li>• Change control log</li> <li>• Notification to customers &amp; regulatory</li> </ul> |          |        |
| <b>5. MANAGEMENT RESPONSIBILITY</b>                           |   |          |        |
| 5.1 Management Commitment                                     | <ul style="list-style-type: none"> <li>• Commitment to customer satisfaction</li> <li>• Commitment to GMP compliance</li> </ul>   |          |        |
| 5.2 Customer Focus  | <ul style="list-style-type: none"> <li>• Customer requirements</li> <li>• Customer audit policy</li> </ul>  |          |        |
| 5.3 Quality Policy  | <ul style="list-style-type: none"> <li>• Policy deployment, management support</li> <li>• Continual improvement</li> </ul>  |          |        |
| 5.4 Planning  | <ul style="list-style-type: none"> <li>• Measurable conformance objectives</li> </ul>   |          |        |
| 5.4.1 Quality Objectives                                      | <ul style="list-style-type: none"> <li>• Conformance objectives</li> </ul>  |          |        |
| 5.4.2 Quality Measurement System Planning                     | <ul style="list-style-type: none"> <li>• Adequate resources</li> </ul>  |          |        |
| 5.5 Responsibility, Authority and Communication               |   |          |        |

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| 5.5.1 Responsibility and Authority       | <ul style="list-style-type: none"> <li>• Reporting relationship of Quality Unit and Production (organization charts)</li> <li>• Job descriptions</li> <li>• Clarity of Quality Unit authority and responsibilities, delegation</li> <li>• Batch release</li> </ul>   |          |        |
| 5.5.2 Management Representative          | <ul style="list-style-type: none"> <li>• Periodic conformance reports to top management</li> </ul>   |          |        |
| 5.5.3 Internal Communication             | <ul style="list-style-type: none"> <li>• Quality system communication</li> <li>• Top management notification of quality critical issues</li> </ul>   |          |        |
| <b>5.6 Management Review</b>             |  |          |        |
| 5.6.1 General                            | <ul style="list-style-type: none"> <li>• Senior management quality system review</li> </ul>  |          |        |
| 5.6.2 Review Input                       | <ul style="list-style-type: none"> <li>• Defined</li> </ul>  |          |        |
| 5.6.3 Review Output                      | <ul style="list-style-type: none"> <li>• Resources and improvements identified</li> </ul>  |          |        |
| <b>6. RESOURCE MANAGEMENT</b>            |  |          |        |
| 6.1 Provision of Resources               | <ul style="list-style-type: none"> <li>• Adequate resources</li> </ul>   |          |        |
| <b>6.2 Human Resources</b>               |  |          |        |
| 6.2.1 General                            | <ul style="list-style-type: none"> <li>• Education, training, experience</li> <li>• Consultant qualifications</li> </ul>   |          |        |
| 6.2.2 Competence, Awareness and Training | <ul style="list-style-type: none"> <li>• Adequate training, experience, and qualifications</li> <li>• Training SOP</li> <li>• Training program</li> <li>• Trainer qualifications</li> <li>• GMP training records</li> <li>• GMP training frequency</li> <li>• Measure of training effectiveness</li> <li>• Communicating changing regulations</li> </ul> |          |        |
| 6.2.3 Personnel Hygiene                  | <ul style="list-style-type: none"> <li>• Personal hygiene training</li> <li>• Clothing</li> <li>• Reporting of illness</li> <li>• Loose items like jewelry and pens</li> <li>• Consumption of food, beverage, and tobacco products</li> <li>• Access control</li> </ul>  |          |        |

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| <b>6.3 Infrastructure (Facilities and Equipment)</b> |  |          |        |
| <b>6.3.1 Building and Facilities</b>                 | <ul style="list-style-type: none"> <li>• Space</li> <li>• Contamination control</li> <li>• Toxic products</li> <li>• Environmental controls</li> <li>• Laboratory facilities</li> <li>• State of repair</li> </ul> |          |        |
| <b>6.3.2 Equipment</b>                               | <ul style="list-style-type: none"> <li>• Commissioning</li> <li>• Maintenance</li> <li>• Outdoor equipment</li> </ul>  |          |        |
| <b>6.3.2.1 Equipment Construction</b>                | <ul style="list-style-type: none"> <li>• Contact surfaces</li> <li>• Lubricants, coolants, etc.</li> <li>• Design to minimize contamination</li> </ul>   |          |        |
| <b>6.3.2.2 Equipment Maintenance</b>                 | <ul style="list-style-type: none"> <li>• Procedures</li> <li>• Records</li> <li>• Hand over/hand back</li> </ul>   |          |        |
| <b>6.3.2.3 Computer Systems</b>                      | <ul style="list-style-type: none"> <li>• Access controls</li> <li>• Change controls</li> <li>• Consistent function</li> <li>• Back up, disaster recovery</li> </ul>  |          |        |
| <b>6.3.3 Utilities</b>                               | <ul style="list-style-type: none"> <li>• Risk of contamination</li> </ul>  |          |        |
| <b>6.3.4 Water</b>                                   | <ul style="list-style-type: none"> <li>• Specification</li> <li>• Treatment and monitoring</li> <li>• Positive pressure/back flow</li> </ul>   |          |        |
| <b>6.4 Work Environment</b>                          |  |          |        |
| <b>6.4.1 Air Handling</b>                            | <ul style="list-style-type: none"> <li>• Effectiveness</li> <li>• Recirculation</li> </ul>   |          |        |
| <b>6.4.2 Controlled Environment</b>                  | <ul style="list-style-type: none"> <li>• Required</li> <li>• Monitoring</li> <li>• Deviations</li> </ul>   |          |        |
| <b>6.4.3 Cleaning and Sanitary Conditions</b>        | <ul style="list-style-type: none"> <li>• Appropriately clean</li> <li>• Procedures, schedules</li> <li>• Waste control</li> </ul>  |          |        |
| <b>6.4.4 Pest Control</b>                            | <ul style="list-style-type: none"> <li>• Free of infestation</li> <li>• Contractor controls</li> <li>• Records, review of effectiveness</li> </ul>   |          |        |
| <b>6.4.5 Lighting</b>                                | <ul style="list-style-type: none"> <li>• Adequate</li> </ul>   |          |        |

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| 6.4.6 Drainage   | <ul style="list-style-type: none"> <li>• Adequate</li> <li>• Air break</li> </ul>  |          |        |
| 6.4.7 Washing and Toilet Facilities                        | <ul style="list-style-type: none"> <li>• Adequate facilities</li> <li>• Clean</li> </ul>   |          |        |
| <b>7. PRODUCT REALIZATION</b>                              |  |          |        |
| 7.1 Planning of Product Realization                        | <ul style="list-style-type: none"> <li>• Process flow diagram</li> <li>• Critical parameters</li> <li>• Batch or continuous</li> <li>• Multi purpose</li> <li>• Equipment &amp; lines ID</li> </ul>  |          |        |
| <b>7.2 Customer-related Processes</b>                      |  |          |        |
| 7.2.1 Determination of Requirements Related to the Product | <ul style="list-style-type: none"> <li>• Customer requirements</li> <li>• Agreed additional requirements</li> </ul>  |          |        |
| 7.2.2 Review of Requirements Related to the Product        | <ul style="list-style-type: none"> <li>• Mutually agreed specifications</li> <li>• Contract review</li> </ul>  |          |        |
| 7.2.3 Customer Communication                               | <ul style="list-style-type: none"> <li>• Implementation of customer requirements</li> <li>• Notification to customers of significant changes</li> </ul>  |          |        |
| <b>7.3 Design and Development</b>                          |  |          |        |
| <b>7.4 Purchasing</b>                                      |  |          |        |
| 7.4.1 Purchasing Process                                   | <ul style="list-style-type: none"> <li>• Qualification and control of suppliers</li> <li>• Approved supplier list</li> <li>• Audit of key suppliers</li> <li>• Selection and control of subcontractors</li> <li>• Follow-up of audit corrective actions</li> <li>• Material specifications</li> <li>• BSE/TSE, etc. risks</li> </ul> |          |        |
| 7.4.2 Purchasing Information                               | <ul style="list-style-type: none"> <li>• Purchasing agreement</li> <li>• Supplier review of specifications</li> <li>• Supplier notification of significant change</li> </ul>   |          |        |
| 7.4.3 Verification of Purchased Product                    | <ul style="list-style-type: none"> <li>• Procedure for approval and release</li> <li>• Quarantine</li> <li>• Sampling procedures and conditions</li> <li>• Testing/verification</li> <li>• Bulk deliveries</li> </ul>  |          |        |

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| <b>7.5 Production and Service Provision</b>                               |   |          |        |
| <b>7.5.1 Control of Production and Service Provision</b>                  |   |          |        |
| <b>7.5.1.1 Production Instructions and Records</b>                        | <ul style="list-style-type: none"> <li>• Controlled master batch instructions</li> <li>• Retrievable batch records</li> <li>• Suitable details</li> </ul>   |          |        |
| <b>7.5.1.2 Equipment Cleaning</b>   | <ul style="list-style-type: none"> <li>• Dedicated or controls for cross-contamination</li> <li>• Cleaning effectiveness and justification</li> <li>• Documentation of cleaning</li> <li>• Storage of utensils and sampling devices</li> <li>• Continuous processes, frequency of cleaning</li> </ul> |          |        |
| <b>7.5.1.3 Recovery of Solvents...</b>                                    | <ul style="list-style-type: none"> <li>• Controls in place</li> <li>• Traceability</li> </ul>   |          |        |
| <b>7.5.1.4 In-Process Blending /Mixing</b>                                | <ul style="list-style-type: none"> <li>• Blending procedures</li> <li>• Defined blending parameters</li> <li>• Part containers/tails</li> </ul>   |          |        |
| <b>7.5.1.5 In-Process Control</b>   | <ul style="list-style-type: none"> <li>• Program</li> <li>• Sampling procedures</li> <li>• Results recorded</li> <li>• Control actions</li> </ul>   |          |        |
| <b>7.5.1.6 Packaging and Labeling</b>                                     | <ul style="list-style-type: none"> <li>• Procedures</li> <li>• Label control</li> <li>• Mix-up prevention</li> </ul>  |          |        |
| <b>7.5.1.7 Records of Equipment Use</b>                                   | <ul style="list-style-type: none"> <li>• Sequence of activities</li> </ul>  |          |        |
| <b>7.5.2 Validation of Processes for Production and Service Provision</b> | <ul style="list-style-type: none"> <li>• Process consistency</li> </ul>   |          |        |
| <b>7.5.3 Identification and Traceability</b>                              |   |          |        |

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| 7.5.3.1 Traceability                        | <ul style="list-style-type: none"> <li>• Material to their manufacturer</li> <li>• Material through production</li> <li>• Unique batch numbering</li> <li>• Batch definition for continuous processing</li> <li>• Traceability of reprocessed material</li> <li>• Origin of manufacturing site</li> </ul>   |          |        |
| 7.5.3.2 Inspection & Test Status            | <ul style="list-style-type: none"> <li>• Approval of materials &amp; packaging</li> <li>• Controls for unapproved materials</li> <li>• Identification of containers and equipment</li> <li>• Status identification</li> <li>• Identification of unlabeled container</li> <li>• Evaluation of raw materials beyond expiration or use date</li> <li>• Quarantine control</li> </ul> |          |        |
| 7.5.3.3 Labeling                            | <ul style="list-style-type: none"> <li>• Excipient labeling content</li> <li>• Special storage condition labeling</li> </ul>  |          |        |
| 7.5.4 Customer Property                     | <ul style="list-style-type: none"> <li>• Procedures</li> <li>• Agreements for confidential information</li> </ul>   |          |        |
| 7.5.5 Preservation of Product               |   |          |        |
| 7.5.5.1 Handling, Storage, and Preservation | <ul style="list-style-type: none"> <li>• Appropriate conditions and record</li> <li>• Outdoor storage</li> <li>• Bulk storage dispensing</li> <li>• Stock rotation</li> </ul>   |          |        |
| 7.5.5.2 Packaging Systems                   | <ul style="list-style-type: none"> <li>• Adequate protection to excipient</li> <li>• Storage of packaging components</li> <li>• Reusable packaging</li> <li>• Bulk container cleanliness</li> <li>• Bulk container seals</li> <li>• Tamper evident seals</li> </ul>   |          |        |
| 7.5.5.3 Delivery and Distribution           | <ul style="list-style-type: none"> <li>• Distribution records</li> <li>• Traceable to consignee</li> <li>• Retrieval or market withdrawal procedure</li> </ul>  |          |        |

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| 7.6 Control of Measuring and Monitoring Devices | <ul style="list-style-type: none"> <li>• Calibration procedures, records, and status</li> <li>• Standards-handling and storage</li> <li>• Frequency and limits</li> <li>• Out-of-calibration actions</li> </ul>       |          |        |
| <b>8. MEASUREMENT, ANALYSIS AND IMPROVEMENT</b> |   |          |        |
| 8.1 General                                     | <ul style="list-style-type: none"> <li>• Quality management processes</li> </ul>  |          |        |
| 8.2 Measurement and Monitoring                  |   |          |        |
| 8.2.1 Customer Satisfaction                     | <ul style="list-style-type: none"> <li>• Measurements (e.g. complaints, returns, feedback)</li> </ul>   |          |        |
| 8.2.2 Internal Audit                            | <ul style="list-style-type: none"> <li>• Program, conducted; frequency</li> <li>• Audit documentation</li> <li>• Corrective measures</li> <li>• Verification of corrective actions</li> </ul>                         |          |        |
| 8.2.3 Measurement and Monitoring of Processes   | <ul style="list-style-type: none"> <li>• Measurement of critical process control points</li> <li>• Use of appropriate techniques</li> <li>• Periodic review and actions</li> </ul>                                    |          |        |
| 8.2.4 Measurement and Monitoring of Product     | <ul style="list-style-type: none"> <li>• Documented test methods</li> <li>• Fit for purpose</li> <li>• Compendial methods used</li> <li>• Compendia changes</li> <li>• Periodic reviews of product quality</li> </ul> |          |        |
| 8.2.4.1 Laboratory Controls                     | <ul style="list-style-type: none"> <li>• Procedures and records</li> <li>• Reagent and standards</li> </ul>   |          |        |
| 8.2.4.2 Finished Excipient Testing & Release    | <ul style="list-style-type: none"> <li>• Quality Unit responsibility</li> <li>• Testing instructions</li> <li>• Release criteria</li> <li>• Continuous processes</li> </ul>   |          |        |
| 8.2.4.3 Out-of-Specification Test Results       | <ul style="list-style-type: none"> <li>• Procedures, records and actions</li> </ul>   |          |        |
| 8.2.4.4 Retained Sample                         | <ul style="list-style-type: none"> <li>• Kept, size, and storage</li> <li>• Retention period</li> </ul>   |          |        |
| 8.2.4.5 Certificates of Analysis                | <ul style="list-style-type: none"> <li>• Format and content</li> <li>• Alignment to specification</li> <li>• Skip lot testing</li> </ul>  |          |        |
| 8.2.4.8 Impurities                              | <ul style="list-style-type: none"> <li>• Defined and controlled</li> <li>• Residual solvents</li> </ul>   |          |        |

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| 8.2.4.7 Stability                    | <ul style="list-style-type: none"> <li>• Data to support storage conditions</li> <li>• Determination of expiry/re-evaluation period</li> <li>• Stability program</li> <li>• Container type</li> <li>• Stability indicating method and parameters</li> <li>• Results review and actions</li> </ul> |          |        |
| 8.2.4.8 Expiry/Retest periods        | <ul style="list-style-type: none"> <li>• Defined and communicated</li> </ul>  |          |        |
| 8.3 Control of Nonconforming Product | <ul style="list-style-type: none"> <li>• Procedure and records</li> <li>• Process to retrieval</li> <li>• Quarantine</li> <li>• Destruction records</li> </ul>  |          |        |
| 8.3.1 Reprocessing                   | <ul style="list-style-type: none"> <li>• Reprocessing instructions</li> </ul>   |          |        |
| 8.3.2 Reworking                      | <ul style="list-style-type: none"> <li>• Rework instructions</li> <li>• Excipient quality impact assessment</li> </ul>  |          |        |
| 8.3.3 Returned Excipient Product     | <ul style="list-style-type: none"> <li>• Procedures and records</li> <li>• Identified and quarantined</li> </ul>  |          |        |
| 8.4 Analysis of Data                 | <ul style="list-style-type: none"> <li>• Measures of Quality Management System effectiveness</li> <li>• Types of data</li> <li>• Periodic reviews</li> </ul>  |          |        |
| 8.5 Improvement                      |   |          |        |
| 8.5.1 Continual Improvement          | <ul style="list-style-type: none"> <li>• Inputs that identify continual improvement opportunities</li> </ul>  |          |        |
| 8.5.2 Corrective Action              | <ul style="list-style-type: none"> <li>• Root cause analysis</li> <li>• Complaints</li> </ul>   |          |        |
| 8.5.3 Preventive Action              | <ul style="list-style-type: none"> <li>• Risk assessment</li> </ul>   |          |        |