PERFORMANCE QUALIFICATION

PROTOCOL

FOR

RAPID MIXER GRANULATOR

EQUIPMENT ID. No.	
LOCATION	
DATE OF QUALIFICATION	
SUPERSEDE PROTOCOL No.	**NIL**

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

PROTOCOL CONTENTS

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

1.0 PROTOCOL APPROVAL:

INITIATED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (PRODUCTION)			
HEAD (ENGINEERING)			

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

2.0 OBJECTIVE:

- To provide documented evidence that the Equipment is performing consistently, repeatedly and reproducibly within its established operating range and the results of all test parameters meet the pre-defined acceptance criteria

3.0 SCOPE:

- The Protocol covers all aspects of Performance Qualification for the **Rapid Mixer Granulator (Make- Elicon Pharma**, **Capacity- 600 liter)** installed in the …….
- Equipment Transfer from …….
- This Protocol will define the methods and documentation used to qualify the Rapid Mixer Granulator for PQ.

4.0 RESPONSIBILITY:

The Validation Group, comprising of a representative from each of the following departments, shall be responsible for the overall compliance of this Protocol.

DEPARTMENTS	RESPONSIBILITIES
Quality Assurance	• Preparation, Review, Approval and Compilation of the Performance Qualification. • Co-ordination with Quality Control, Production and Engineering to carryout Performance Qualification Activity. • Monitoring of Performance Qualification.
Production	• Review of Performance Qualification Protocol. • To co-ordinate and support Performance Qualification Activity.
Engineering	• Review of Performance Qualification protocol for correctness, completeness and technical excellence. • Responsible for trouble shooting (if occurred during execution). • Maintenance & preventive maintenance as per schedule.

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

5.0 EQUIPMENT DETAILS:

Equipment Name	Rapid Mixer Granulator
Equipment ID.	
Manufacturer's Name	Elicon Pharma
Supplier's Name	Elicon Pharma
Location of Installation	

6.0 SYSTEM DESCRIPTION:

RMG or high sear machine is a very precision machine, performing dry mixing and wet granulation in the same bowl in only 6 to 20 min. the entire Operational is fully dust free and automatic including discharge. All parts coming in contact with mix are of stainless AISI 316 L quality and are highly polished. Drive motors, electrical control station are supplied in flameproof construction as per client's requirement.

Basic machine consist of base frame made from MS angle and channels. Top of the frame is covered by one big MS plate. Complete base frame is cladded by SS sheet. Top plate is cladded by 1.5 mm thick SS embossed sheet for anti- slip property and easy cleaning. Mixing bowl is fixed on top of this plate. There are two impellers inside the bowl. Main impeller run in horizontal plane and chopper granulation impeller run in vertical plane. Top lid is operated pneumatic festo cylinder. Main impeller is support on main shaft, which has its special Z type housing. Z type housing totally eliminates any chance of cross contamination of product mix with bearing lubricants. Z type housing cap contains PTFE and Labyrinth seal along with air purging facility totally eliminates cross contamination. Chopper blades are directly mounted on chopper shaft. Chopper housing is entirely made of AISI 316 L having air purging and special seals. Main impeller is having unique design and blade angle, thus pushing the material radial direction. Machine has a discharge outlet with pneumatic cylinder. Discharge piston has profile exactly matching with the vessel interior, giving a perfect sealing arrangement.

CHARGING AND DRY MIXING

Pre- weighed raw material is charged through the charging port located on the top lid of the RMG bowl. This is achieved through IPC Bin/paste kettle using a material handling device.

Once charged the dust proof charging interface is manually disengaged and the charging hole is sealed shut. All machine safety control is activated.

Main impeller and chopper are operated in slow speeds through PLC and hen in fast speed as per process requirement. Duration of total process time is timer controlled.

WET MIXING/ GRANULATION

Binder thus added into the mass by slow/fast Operational of the main impeller with concurrent Operational of the chopper results in dough formation. This Operational is on a timed cycle basis and is continuously monitored by the operator through the ampere meter reading which is displayed on the operating panel of the RMG.

7.0 REASON FOR QUALIFICATION:

- Equipment Transfer from …….
- After completion of the Operation Qualification of the Equipments, it is imperative to perform the Performance Qualification. The study will establish that the parameters are followed, critical variables are under control and the quality of the output is, as desired.

8.0 SITE OF STUDY:

…….

9.0 FREQUENCY OF QUALIFICATION:

- Once in every two year.
- After any major breakdown or after major modification.
- After Change of Location.

10.0 PRE-QUALIFICATION REQUIREMENTS:

The below mentioned activities should be completed prior to commencing the performance qualification activity:

- Design Qualification.
- Installation Qualification.
- Operational Qualification.
- Preparation of SOP for Operation & Cleaning of Rapid Mixer Granulator.
- Preparation of SOP for Preventive Maintenance Rapid Mixer Granulator.

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

11.0 TESTS AND CHECKS:

11.1 Verification of Documents:

Verification for availability, completeness and approval status of all the required relevant documents shall be done and observations shall be recorded in the performance qualification report.

- Executed and approved Design Qualification document.
- Executed and approved Installation Qualification document.
- Executed and approved Operational Qualification document.
- SOP for Operation & Cleaning of Rapid Mixer Granulator.
- SOP for Preventive Maintenance Rapid Mixer Granulator.

Procedure:

- Verify the above mentioned documents for availability, completeness and approval status.
- If any deviation is observed the same has to be recorded giving reasons for deviation and approved.
- Supporting documents would form a part of the PQ report.

Acceptance Criteria:

All the documents should be available, complete and approved by respective authorities.

PERFORMANCE QUALIFICATION PROTOCOL FOR RAPID MIXER GRANULATOR

11.2 Evaluation of Performance Using Placebo Formulation:

Objective:

- To verify the performance of equipment in the range of operational parameters established in Operational Qualification Activity.
- To establish the performance based range of operating parameters for performance qualification activity using Placebo Formulation.

11.2.1 Checks:

Verification of Power Consumption

- Ampere Load of Impeller with product.
- Ampere Load of Chopper with product.

Dry Mixing

- Appearance of Dry mix at all locations.

Wet Mixing

- Appearance of Wet mix at all locations.
- Uniformity of cohesive wet mass at all locations.
- Granule Formation.
- Presence of Dry Powder Lumps.
- Product Discharge Function.

11.2.2 Method:

- Load the sifted raw materials to the RMG bowl.
- Perform dry mixing by RMG as per the parameters and instructions specified in the BMR of product.
- Perform visual checks for mixing of the powders in Bowl.
- After completion of specific dry mixing time, draw samples from different locations of RMG.
- Perform visual check for uniformity of appearance of all samples.
- Add binder solution to RMG.
- Perform wet mixing for specified time.
- Collect samples from different locations and inspect visually for uniformity of consistency of wet mass at different locations and for the presence of any dry powder lump in the samples of different locations.

11.2.3 Acceptance Criteria:

- Power consumption should be within range as specified in the specifications of equipment.
- Dry and wet mixed mass should be uniform in all the locations of RMG and no dry powder lump should be present in any sample of wet mixed mass.

11.3 Evaluation of Performance Using Drug Product:

11.3.1 Objective:

To evaluate and to provide documented evidences for performance of equipment for mixing of raw materials of different physical & chemical properties to form a homogeneous blend of uniform physical and chemical properties.

11.3.2 Checks:

Dry Mixing

- Appearance of Dry mix at all locations.

Wet Mixing

- Appearance of Wet mix at all locations.
- Uniformity of cohesive wet mass at all locations.
- Granule Formation.
- Presence of Dry Powder Lumps.

Product Discharge Function

11.3.3 Method:

- Load the sifted raw materials to the RMG bowl.
- Perform dry mixing by RMG as per the parameters and instructions specified in the BMR of product.
- Perform visual checks for mixing of the powders in Bowl.
- After completion of specific dry mixing time, draw samples from different locations of RMG.
- Perform visual check for uniformity of appearance of all samples.
- Add binder solution to RMG.
- Perform wet mixing for specified time.
- Collect samples from different locations and inspect visually for uniformity of consistency of mass at different locations and for the presence of any dry powder lump in the samples of different locations.
- Send collected samples to QC for analysis of:

Blend uniformity analysis.

11.3.4 Acceptance Criteria:

- Assay of samples of all locations should be within the limit specified for products.
- RSD of all individual values of Assay should not be more than 5.0%.
- Dry and wet mixed mass should be uniform in all the locations of RMG and no dry powder lump should be present in any sample of wet mixed mass.

11.3.5 Sampling Locations:

- Samples to be taken of Dry Mixing from locations specified as below.

Where,

U1= Upper Left

U2= Upper Center

U3= Upper Right

L1= Lower Left

L2= Lower Center

L3= Lower Right

M1= Middle Left

M2= Middle Center 1

M3= Middle Center 2

M4= Middle Right

Quantity of Sample: Each sample of 3 times average weight.

No. of Samples:

3 - Samples from Upper Layer

4 - Samples from Middle Layer

3 - Samples from Lower Layer

1- Composite Sample

12.0 CHECKLIST OF ALL TESTS & CHECKS:

A checklist shall be provided to ensure that all tests or checks required for this protocol have been executed. After execution observations shall be recorded in Performance Qualification Report.

The list includes:

- Verification of DQ, IQ & OQ & other documents.
- Verification of performance using placebo formulation at dry mixing stage.
- Verification of performance using placebo formulation at wet mixing stage.
- Verification of performance using Drug product at dry mixing stage.
- Verification of performance using Drug product at wet mixing stage.
- Blend Uniformity Analysis of samples collected from different locations at Dry Mixing Stage.

13.0 REFERENCES:

The Principle References are as following:

- Validation Master Plan.
- Schedule - M – "Good Manufacturing Practices and Requirements of Premises, Plant and Equipment for Pharmaceutical Products."
- WHO Essential Drugs and Medicines Policy, QA of Pharmaceuticals, Vol-2. Good Manufacturing Practices and Inspection.

14.0 DOCUMENTS TO BE ATTACHED:

- Operation and Maintenance Manual.
- Raw data of blend uniformity analysis.
- Any other relevant document.

15.0 NON COMPLIANCE:

All the Non-compliances of procedure, specifications, sampling, analysis and documentation activities shall be monitored & recorded.

16.0 DEVIATION FROM PRE-DEFINED SPECIFICATION, IF ANY:

- In case of any deviation observed during PQ, inform to Head QA for necessary action.
- Document the deviation detail in observed deviation section.
- The Head QA will study the impact of deviation. If deviation is acceptable and it does not have an Impact on operation as well as on performance of the machine & prepare final conclusion.

17.0 CHANGE CONTROL, IF ANY:

- If any change control is required during PQ, inform to Head QA for necessary action.
- Document the details observed.
- The Head QA will study the impact of change. If change is acceptable and it does not have an Impact on operation as well as on performance of the machine & prepare final conclusion.

18.0 ABBREVIATIONS:

DQ	:	Design Qualification
GB	:	General Block
ID	:	Inner Diameter
IQ	:	Installation Qualification
NLT	:	Not Less Than
OQ	:	Operational Qualification
PLC	:	Programmable Logical Controller
PQ	:	Performance Qualification
QC	:	Quality Control
RMG	:	Rapid Mixer Granulator
RSD	:	Relative Standard Deviation
SOP	:	Standard Operating Procedure
SS	:	Stainless Steel
WHO	:	World Health Organization