1.0 REPORT APPROVAL:

Signing of this approval page of Protocol indicates agreement with the qualification approach described in this document. If modification to the qualification approach becomes necessary, an addendum shall be prepared and approved .The protocol cannot be used for execution unless approved by the following authorities.

This performance qualification protocol of Water phase vessel, Wax phase vessel, Main manufacturing vessel and storage vessel has been reviewed and approved by the following persons:

FUNCTION	NAME	DESIGNATION	DEPARTMENT	SIGNATURE	DATE
PREPARED BY			QUALITY ASSURANCE		
REVIEWED BY			QUALITY ASSURANCE		
			ENGINEERING		
			QUALITY CONTROL		
APPROVED BY			HEAD OPERATION		
			QUALITY ASSURANCE		

2.0 OVERVIEW:

2.1 OBJECTIVE:

The objective of developing and executing this protocol is to

- Document the verification of all aspects of the equipments that can affect product quality.
- To establish, check and document the performance of equipments in the established/ predetermined operating ranges.

2.2 PURPOSE:

The purpose of this report is to provide the documented evidence that the functions of the Water Phase Vessel, Wax Phase Vessel, Main Manufacturing Vessel and Holding Vessel which affect the product quality, equipment integrity, and safety of operating and maintenance personnel is taken into consideration.

2.3 SCOPE:

The scope of this report shall define the test procedures, documentation and acceptance criteria to establish that the operational parameters of water phase vessel, wax phase vessel, main manufacturing vessel and holding vessel is as per the requirement of manufacturing facility at …….

Once the performance qualification has been completed successfully, the equipments shall be released for the production purposes.

2.4 RESPONSIBILITY:

In accordance with protocol, following functions shall be responsible for the qualification of system.

Execution Team (Comprising members from Production, Quality control, Engineering and Quality Assurance) and their responsibilities are following:

- Prepares the performance qualification protocol.
- Ensures that the protocol is in compliance with current policies and procedures on system Qualification.
- Distributes the finalized protocol for review and approval signatures.
- Execution of Qualification protocol.
- Review of protocol, the completed qualification data package, and the final report.
- The analysis of sample shall be carried out by quality control department.
- Engineering department shall support for execution.
- The production operator/supervisor shall carry out the cleaning and operation of machine.

Head – Quality control/Production/Engineering:

- Review of protocol, the completed qualification data package, and the final report.
- Assist in the resolution of validation deficiencies.

Head – Operation and Quality Assurance:

- Review and approval of protocol, the completed qualification data package, and the final report.

2.5 EXECUTION TEAM:

The satisfactory operation of the equipments shall be verified by executing the performance qualification studies described in this protocol. The successfully executed protocol documents that the equipments is operational and is satisfactorily working.

Execution team is responsible for the execution of performance qualification of the equipments. Execution team comprises of:

NAME	DESIGNATION	DEPARTMENT	SIGNATURE	DATE

3.0 PREREQUISITE

3.1 Approved Standard operating procedure of the equipment shall be available.

3.2 The maximum capacity of the equipment shall be verified by taking the batch/lot to suit the requirement.

3.3 The installation and operational qualification of the equipment shall be successfully completed before the execution of the performance qualification.

3.4 All the deficiencies and discrepancies related to the equipment which affect the product quality and corrective action taken shall be recorded in the appropriate section of the protocol.

3.5 After completion of PQ activities, equipment shall be cleaned as per respective cleaning SOP's and released for manufacturing.

4.0 REVALIDATION CRITERIA:

The machine shall be revalidated if

- There are any major changes, which affect the performance of the equipment.
- Batch/lot size taken out of the range on which performance is done
- As per revalidation date and schedule

5.0 PERFORMANCE QUALIFICATION PROCEDURE

5.1

- EQUIPMENT DESCRIPTION:

Water Phase Vessel:

- The Water Phase Vessel consists of following Components:
- Water Phase vessel comprises of top lid and bottom torispherical dished end welded with central cylindrical shell.
- Water Phase Vessel is provided with jacket for steam supply and temperature sensor for monitoring temperature of the phase.
- Water Phase vessel is provided with manhole for addition of the materials , top mounted nozzles for vacuum, and liquid material suction.
- Stirrer entry at the bottom of the vessel with the motor of the stirrer is fixed on a side angular bottom of the vessel. It is provided with a VFD for speed variation.
- Entire vessel is mounted on 4 Nos. leg supports which are fixed.

Wax Phase Vessel:

- The Wax Phase Vessel consists of following Components:
- Wax Phase vessel comprises of top lid and bottom torispherical dished end welded with central cylindrical shell.
- Wax Phase Vessel is provided with jacket for heating with steam supply and temperature sensor for monitoring temperature of the phase.
- Wax Phase vessel is provided with manhole for addition of the materials , top mounted nozzles for vacuum and liquid material suction.
- Stirrer entry at the bottom of the vessel with the motor of the stirrer is fixed on a side angular bottom of the vessel. It is provided with a VFD for speed variation.
- Entire vessel is mounted on 4 Nos. leg supports which are fixed.

Main Manufacturing Vessel:

The Main Manufacturing Vessel consists of following components:

- Manufacturing Vessel comprises of top dish end and bottom dish end welded with

central cylindrical shell.

- Manufacturing Vessel is provided with jacket and glass wool insulation at shell and bottom dish end for heating of vessel. Steam is the heating medium of the vessel.
- The manufacturing vessel is provided with temperature sensor for monitoring of temperature of the product.
- Top entry agitator of anchor type with scrapper is provided inside the vessel for mixing. It is provided with a VFD for speed variation.
- There is provision of recirculation line for recirculation of the product from the bottom of the vessel to top.
- The top dish end is provided with nozzles as per the service requirement and this top dish end is lifted with the help of hydraulic cylinder lifting.
- Manufacturing vessel is mounted on load cells that are used to measure the load on vessel.

Holding Vessel:

- Jacketed vessel comprises of top lid with top mounted stirrer.
- Jacketed Vessel is provided with jacket for heating with steam.
- Stirrer entry at the top with the drive for the stirrer is mounted on a hinged plate at the top edge of the vessel. It will be provided with a VFD for speed variation.
- Jacketed vessel is designed for steam circulation.
- Entire vessel is mounted on 4 Nos. legs.

5.2 RISK ANALYSIS:

- Pressure Gauge
- Safety Valve
- Temperature sensor

S.No.	Risk identified	Control measures
1.	Vessel Pressure	• Should be between 0 – 6 Kg/cm^2.
2.	Safety Valve	• Should be set at 3.2 Kg/cm^2.
3.	Temperature	• Should not be more than 100

5.3

- Read all procedure for each stage before beginning the test steps. Verify and record the verification of all critical operation functions. Challenge each of the control system and each sub system.
- Any function, system or subsystem that fails a particular challenge should be identified and proceeding to the next section of the testing criteria.
- Any modification to the equipment to enable the compliance with the operation protocol must be documented and approved prior to completion of the challenged section. Any modification that has an effect to the operation of the equipment must be challenged. Each challenge will be generated and approved by each department.
- In the jacketed storage vessel, API and excipient is mixed and transferred to wax phase vessel.
- In wax phase vessel, API mixes by taking the required quantity of excipient at specified RPM and temperature for a specified time period and same process is continued in Water phase vessel where API mixes in aqueous phase in required quantity of excipient at specified RPM and temperature for a specified time period.
- Both Wax phase and water phase is transferred to manufacturing vessel by vacuum where both phase are mixed and pH is adjusted. Finally sample is withdrawn.
- PQ batch of maximum batch size shall be manufactured to evaluate the performance of the vessels.

- The medicament shall be manufactured as per BMR No._____ for maximum batch size.
- Batch No. of maximum batch sizes shall be _____
- Detail of the PQ batches shall be mentioned under the heading of "Product Details".
- Start the manufacturing procedure as per the BMR.
- Samples shall be sending to the QC Department for analysis.
- Note: In manufacturing area maintain temperature 22°± 3°C, Relative Humidity between 50 ± 5 % is to be maintained.

5.4 PRODUCT PROFILE:

Product details of the performance qualification batch shall be verified from the BMR of the product and record in the following section

5.4.1 Product Name : _____

Generic Name : _____

Product Code : _____

Batch Number : _____

Batch Size : _____

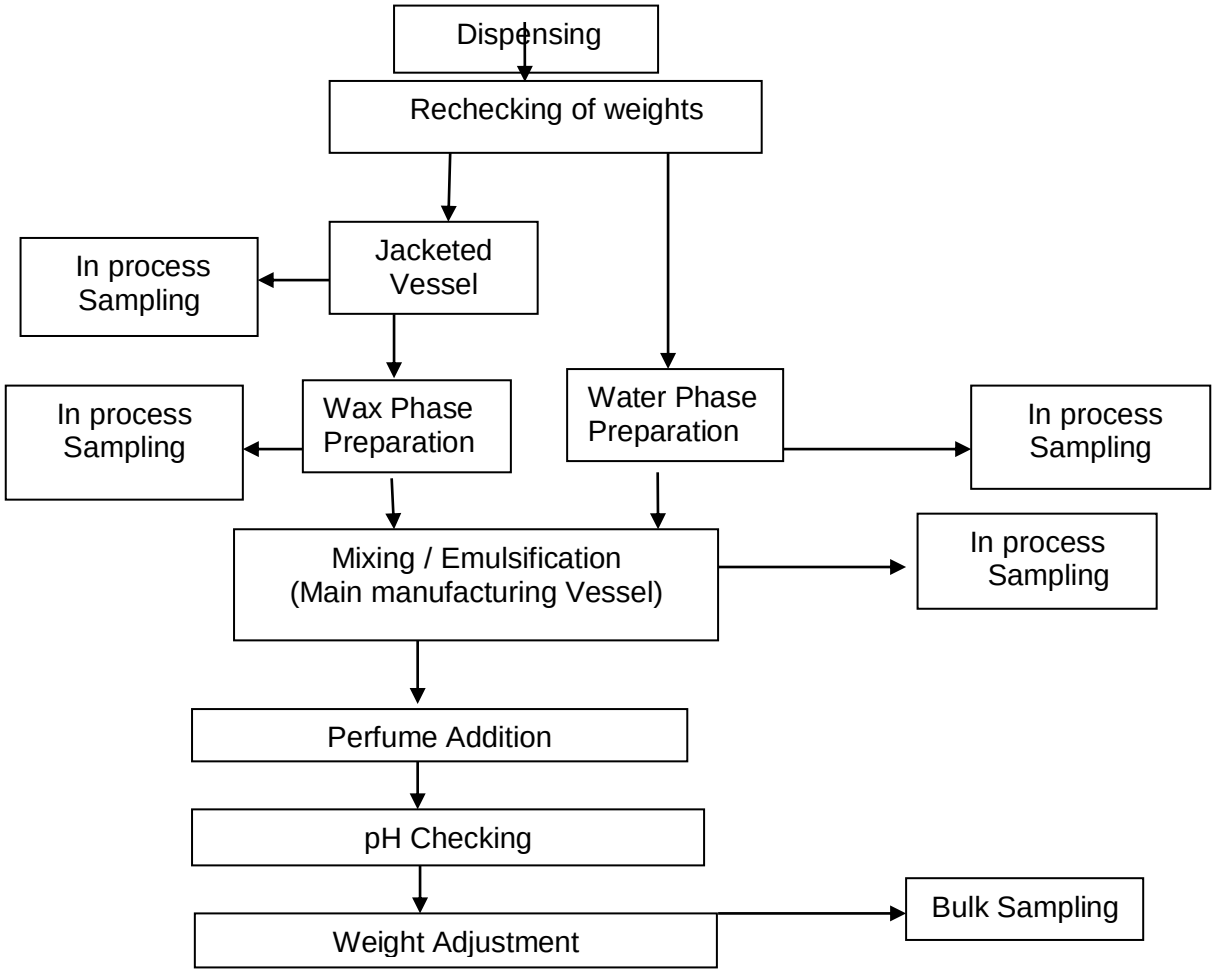
Mfg. Date : _____

Exp. Date : _____

BMR Number : _____

5.5 PROCESS FLOW DIAGRAM WITH QUALIFCATION PARAMETERS OF WATER PHASE VESSEL, WAX PHASE VESSEL, MANUFACTURING VESSEL:

Process flow diagram of water phase vessel, wax phase vessel, manufacturing vessel is mentioned below:



5.6 SAMPLING MATRIX:

The qualification matrix is as following, the challenge run shall be performed for each machine individually:

5.6.1 HOLDING VESSEL:

S.No.	Process Parameter	Method of verification	Acceptance Criteria
1	Uniformity of temperature throughout the vessel.	Note temperature every 15 minutes with calibrated thermometer and correlate with the system.	Monitor and establish same for efficiency of equipment for temperature uniformity throughout the vessel should be as per BMR.
2	Temperature achieved for conversion.	Note down the temperature of system display & actual temperature of oil phase using calibrated thermometer.	Should be monitored and established.
3	Time required for conversion.	Time required for complete conversion from Wax to oil phase.	Monitor and establish time of melting.
4	Conversion of Wax phase to oil.	Remove approx 50 gm sample from vessel (Check clarity of oil phase for complete conversion)	Should be clear as oil phase.
5	Time required to achieve temperature	Note temperature with calibrated thermometer & correlate with system	Temperature should be as per BMR.
6	Dissolution of API in melted oil.	Remove approx 50 gm from each point (check for the clarity of phase for complete dissolution of the API)	Should be clear without any un-dissolved API particles.
7	Transfer Capability	Check at different interval	Should be transferred smoothly.

5.6.2 WAX PHASE VESSEL:

S.No.	Process Parameter	Method of verification	Acceptance Criteria
1	Uniformity of temperature throughout the vessel.	Note temperature every 15 minutes with calibrated thermometer and correlate with the system).	Monitor and establish same for efficiency of equipment for temperature uniformity throughout the vessel should be as per BMR.
2	Temperature achieved for conversion.	Note down the temperature of system display & actual temperature of oil phase using calibrated thermometer.	Should be monitored and established.
3	Time required for conversion.	Time required for complete conversion from Wax to oil phase.	Monitor and establish time.
4	Conversion of Wax phase to oil.	Remove approx 50 gm sample from vessel (Check clarity of oil phase for complete conversion)	Should be clear as oil phase.
5	Time required to achieve temperature	Note temperature with calibrated thermometer & correlate with system	Temperature should be as per BMR.
6.	Dissolution of parabens and API.	Remove sufficient sample from the vessel to check the clarity.	Should be clear without any un-dissolved particles.
7	Transfer Capability	Check at different interval	Should be transferred smoothly.

5.6.3 Water Phase Vessel:

S.No.	Process Parameter	Sampling criteria	Acceptance Criteria
1	Uniformity of temperature throughout the vessel.	To check the uniformity of temperature from the in built system.	Monitor and establish same for efficiency of equipment for temperature uniformity throughout the vessel should be as per BMR.
2	Time required to achieve temperature	(Note temperature with calibrated thermometer & correlate with system)	Monitor and establish time.
3.	Dissolution of parabens and API .	Remove sufficient sample from the vessel to check the clarity.	Should be clear without any un-dissolved particles .
3.	Transfer Capability	Check at different interval	Should be transferred smoothly.

5.6.4 Manufacturing Vessel:

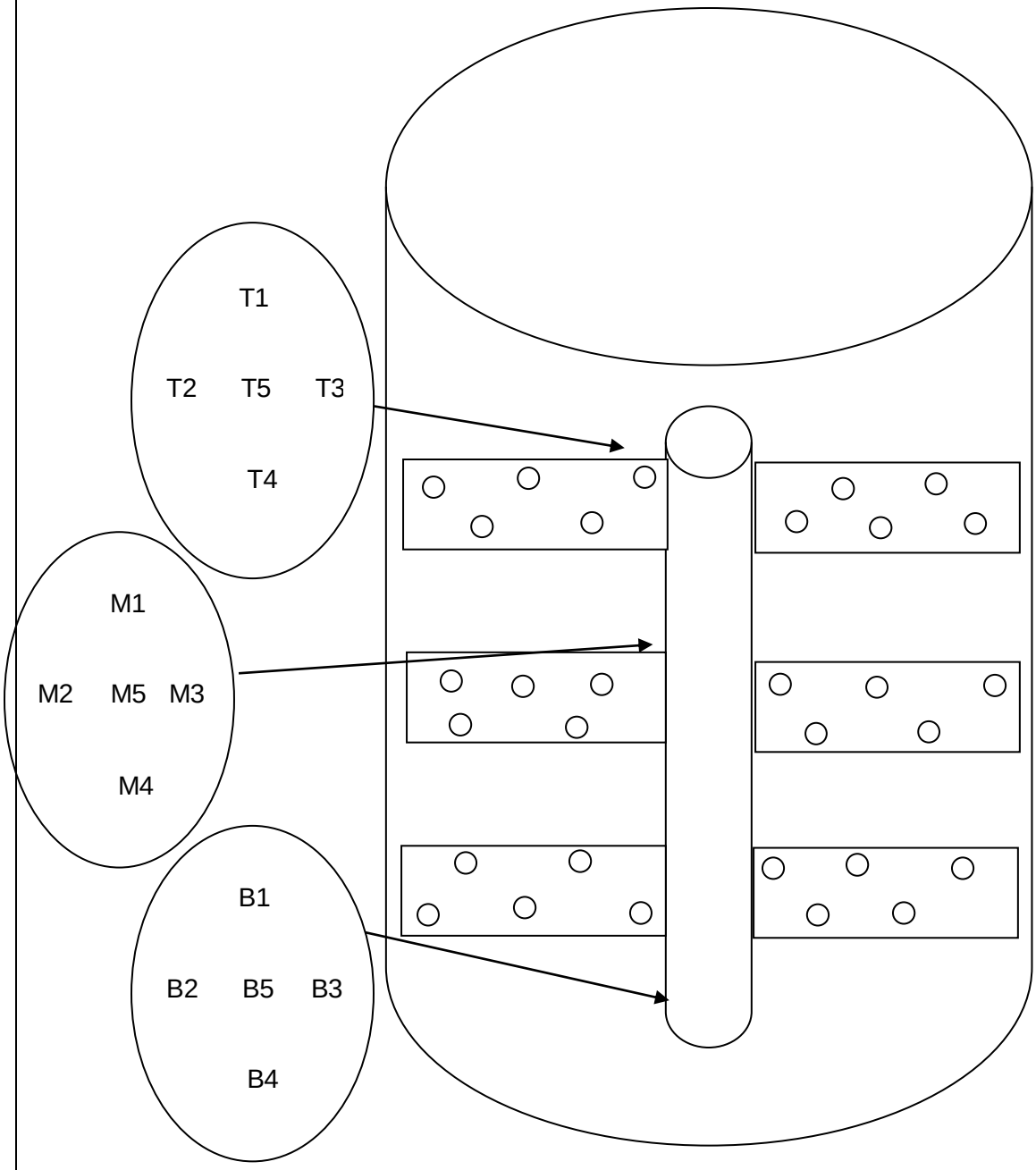
S. No.	Process Parameter	Sampling criteria	Acceptance Criteria
1	Temperature of both Aqueous & oil Phase	Not down temperature of both aqueous and oil phase	Temperature should be as per BMR.
2	Stirring speed of anchor stirrer	Note RPM of the stirrer with calibrated Tachometer and correlate the rpm with system.	RPM should be as per BMR.
3	Homogenization time and temperature	Note temperature and homogenization time.	Monitor and establish homogenization time.
4	Vacuum Efficiency	Note the vacuum during process with calibrated compound gauge .	The product should be free from air entrapment.

S.No.	Process Parameter	Sampling criteria	Acceptance Criteria
5	Cooling Efficiency	Note temperature with calibrated thermometer & correlate with system.	Monitor and establish cooling time.
6	Transfer Capability	Check at different interval	Should be transferred smoothly.

5.6.5 SAMPLING PLAN:

S.No.	Batch Size	Mixing Time	Anchor RPM	Sampling Criteria	Test Parameter
1.	1500 kg	As per BMR	As per BMR	Top, Middle & Bottom (5 Points from each location). 20-30 gm approximate from each point.	Assay of ……..
				1 Composite sample * 100 – 120 gm approx. (Collect approximately 40 gm sample from each location i.e. top, middle and bottom and make composite sample).	Assay of……., Appearance, and pH.

Figure - 1



5.6.6 Sampling Locations:

Top: T1: Rear side of tank.
T2: Left side of tank.
T3: Right side of tank.
T4: Front side of tank.
T5: Center of tank.

Middle: M1: Rear side of tank.
M2: Left side of tank.
M3: Right side of tank.

M4: Front side of tank.

M5: Center of tank.

Bottom: B1: Rear side of tank.

B2: Left side of tank.

B3: Right side of tank.

B4: Front side of tank.

B5: Center of tank.

5.7 SET PARAMETERS:

5.7.1 SET PARAMETERS FOR JACKETED VESSEL:

S.No.	Test	Specification
1.	Product Temperature	75°C - 85°C
2.	Stirrer speed	60 RPM

5.7.2 SET PARAMETERS FOR WATER PHASE VESSEL.

S.No.	Test	Specification
1.	Product Temperature	73°C - 77°C
2.	Stirrer speed	900 RPM

5.7.3 SET PARAMETERS FOR WAX PHASE VESSEL.

S.No.	Test	Specification
1.	Product Temperature	73°C - 77°C
2.	Stirrer speed	900 RPM

5.7.4 SET PARAMETERS FOR MANUFACTURING PHASE VESSEL.

S.No.	Test	Specification
1.	Product Temperature	As per BMR
2.	Anchor RPM	20-25 RPM

5.8 ACCEPTANCE CRITERIA:

The test will be considered failed if the actual test results do not correspond to the expected results as following:

- pH – As per specification
- Appearance – As per specification
- Assay – As per specification

5.9 RECORDING OF SAMPLING:

DATE	BATCH NUMBER	SAMPLING POINT	QUANTITY	SAMPLED BY (SIGN. & DATE)

Remark: ----------

Reviewed by (Sign/Date)

5.10 OBSERVATIONS AND RESULTS OF CHALLENGE TESTS:

Product Name				Batch No.	
Batch Size		RPM		Final Mixing Time	

Top Sample (Assay)					
Content	T1	T2	T3	T4	T5

Middle Sample (Assay)					
Content	M1	M2	M3	M4	M5

Bottom Sample (Assay)					
Content	B1	B2	B3	B4	B5

Test	Result (Composite Sample)
Appearance	
pH	
Assay:	

Remark: ----------

Reviewed by (Sign/Date)

5.11 IN PROCESS CHECKS DURING MANUFACTURING PROCESS:

5.11.1 JACKETED VESSEL

Batch No._____ **Frequency:_____**

Test Parameter	Sampling Time	Temp. (System)	Top Temp. (Thermometer)	Bottom Temp. (Thermometer)	Remarks
Uniformity of temperature					

S.No.	Test Parameter	Start Temperature in system	Temperature of oil phase in system	Temperature of oil phase. (Thermometer)	Remarks
1.	Temperature achieved for conversion				

S.No.	Test Parameter	Addition of wax		Conversion of wax to oil		Conversion Time	Remarks
		From	To	From	To		
1.	Time required for conversion						

S.No.	Test Parameter	Top Sample	Bottom Sample	Remarks
1.	Conversion of wax phase to oil			

Test Parameter	Initial Stage of system		Desired Temp.		Top Temp.	Bottom Temp.	Total Time Required to achieve temperature
	Time	Temp.	Time	Temp.			
Time required to achieve temperature							

Test Parameter	Initial	Middle	End	Remark
Transfer Capability				

Batch No._____ **Frequency: _____**

Date/ Time	Product Temperature	Stirrer (RPM)	Remark

Remark: ----------

Reviewed by (Sign/Date)

5.11.2 WAX PHASE VESSEL

Batch No._____ **Frequency: _____**

Test Parameter	Sampling Time	Temp. (System)	Top Temp. (Thermometer)	Bottom Temp. (Thermometer)	Remarks
Uniformity of temperature					

PHARMA DEVILS	PERFORMANCE QUALIFICATION PROTOCOL FOR WATER PHASE VESSEL 1000 LTRS, WAX PHASE VESSEL 1000 LTRS, MAIN MANUFACTURING VESSEL 1765 LTRS, HOLDING VESSEL 50 LTRS	PROTOCOL No.:

S.No.	Test Parameter	Start Temperature in system	Temperature of oil phase in system	Temperature of oil phase. (Thermometer)	Remarks
1.	Temperature achieved for conversion				

S.No.	Test Parameter	Addition of wax		Conversion of wax to oil		Conversion Time	Remarks
		From	To	From	To		
1.	Time required for conversion						

S.No.	Test Parameter	Top Sample	Bottom Sample	Remarks
1.	Conversion of wax phase to oil			

Test Parameter	Initial Stage of system		Desired Temp.		Top Temp.	Bottom Temp.	Total Time Required to achieve temperature
	Time	Temp.	Time	Temp.			
Time required to achieve temperature							

Test Parameter	Initial	Middle	End	Remark
Transfer Capability				

Batch No._____ **Frequency: _____**

Date/Time	Product Temperature	Stirrer (RPM)	Remark

Remark: ----------

Reviewed by (Sign/Date)

5.11.3 WATER PHASE VESSEL

Batch No._____ **Frequency: _____**

Test Parameter	Sampling Time	Temp. (System)	Top Temp. (Thermometer)	Bottom Temp. (Thermometer)	Remarks
Uniformity of temperature					

Test Parameter	Initial Stage of system		Desired Temp.		Top Temp.	Bottom Temp.	Total Time Required to achieve temperature
	Time	Temp.	Time	Temp.			
Time required to achieve temperature							

Test Parameter	Initial	Middle	End	Remark
Transfer Capability				

PHARMA DEVILS	PERFORMANCE QUALIFICATION PROTOCOL FOR WATER PHASE VESSEL 1000 LTRS, WAX PHASE VESSEL 1000 LTRS, MAIN MANUFACTURING VESSEL 1765 LTRS, HOLDING VESSEL 50 LTRS	PROTOCOL No.:

Batch No._____ **Frequency: _____**

Date/ Time	Product Temperature	Stirrer (RPM)	Remark

Remark: ----------

Reviewed by (Sign/Date)

5.11.4 MANUFACTURING VESEL:

S.No.	Test Parameter	Top	Bottom	Remark
1.	Temperature of both Aqueous & Oil Phase			

S.No.	Test Parameter	Time		Top Temperature	Bottom Temperature	Remark
		From	To			
2.	Homogenization time for emulsification					

S.No.	Test Parameter	Temperature before cooling		Cooling Time		Temperature after cooling		Remark
				From	To	Top	Bottom	
		Top	Bottom					
3.	Cooling efficiency							

Sr. No.	Test Parameter	Initial	Middle	End	Remark
4.	Transfer Capability				

Batch No._____ **Frequency: _____**

Date/ Time	Product Temperature	Anchor RPM	Remark

Remark: ----------

Reviewed by (Sign/Date)

5.12 Environmental Monitoring During Process:

Environmental monitoring shall be done and record in the following table during manufacturing process run:

Limit: Temperature (°C) : ____ ± ____°C

Relative Humidity (%) : ____ ± ____% (**Frequency**: Every 1 Hour)

Date	Time	Temperature		Difference (a-b)	Relative humidity	Remarks
		Dry Bulb Reading (˚C) (a)	Wet Bulb Reading (˚C) (b)			

Remark: ----------

Reviewed by (Sign/Date)

6.0 DEFICIENCY AND CORRECTIVE ACTION(S) REPORT(S):

Following deficiency was verified and corrective actions taken in consultation with the validation team.

Description of deficiency:

Corrective action(s) taken:

Deviation accepted by
(Sign/Date)

Deviation Approved by
(Sign/Date)

7.0 PERFORMANCE QUALIFICATION FINAL REPORT:

7.1 SUMMARY:

7.2 CONCLUSION:

Prepared By
Sign/Date

Checked By
Sign/Date

7.3 FINAL REPORT APPROVAL:

It has been verified that all tests required by this report are completed, reconciled and attached to this protocol or included in the performance qualification summary report. All amendments and discrepancies are documented, approved and attached to this protocol. (If applicable) Signature in the block below indicate that all items in this qualification report of Water phase Vessel, Wax phase vessel, Main Manufacturing Vessel, and Storage vessel have been reviewed and found to be acceptable and that all variations or discrepancies have been satisfactorily resolved.

FUNCTION	NAME	DESIGNATION	DEPARTMENT	SIGNATURE	DATE
REVIEWED BY			QUALITY ASSURANCE		
			ENGINEERING		
			QUALITY CONTROL		
			PRODUCTION		
APPROVED BY			HEAD OPERATION		
			QUALITY ASSURANCE		