HOLD TIME STUDY PROTOCOL

FOR

CLEANED EQUIPMENTS

Protocol No.	
Supersedes	Nil
Protocol Effective Date	
Report Effective Date	

CLEANED EQUIPMENT HOLD TIME STUDY PROTOCOL CUM REPORT

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1.0 PRE-APPROVAL:

PREPARED BY :				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
QUALITY ASSURANCE				
CHECKED BY :				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
MICROBIOLOGIST				
QUALITY CONTROL				
PRODUCTION				
APPROVED BY:				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
QUALITY ASSURANCE				

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2.0 OBJECTIVE:

The objective of this document is to lay down a procedure for carrying clean Equipment Hold time study and to establish the hold time for Cleaned equipment or vessel in solid oral facility.

3.0 SCOPE:

This document is applicable to the cleaned equipments which are used to manufacture various products in Solid facility after establishment of effective cleaning procedure by cleaning validation; this document shall also define the responsibility, equipment details, sampling method, sampling plan and acceptance criteria for equipment hold time study.

4.0 PURPOSE OF STUDY:

The purpose of this protocol shall be extended to establish hold time for a Type A & Type B cleaning.

A. Studying the microbial load after holding it un-cleaned for specified time period. This Study is applicable to manufacturing equipments which are Type A cleaned.

B. Type B cleaning shall be carried out immediately after the completion of specified hold time period and microbial analysis data shall be recorded for the same. Evaluate result of above study for both chemical and microbial contamination against cleaned (Type B cleaning) equipment to understand level of contamination to decide effective cleaning methodology.

5.0 RESPONSIBILITIES

To conduct the Equipment Hold Time Study, a team shall be formed. The team consists of members from the Production, QC, and QA Engineering department.

Departments	Responsibilities
Quality Assurance	• Monitoring of protocol completeness, accuracy, technical excellence and applicability. • Preparation of Protocol. • Review of Protocol. • Approval of Protocol. • To review analytical reports & Compilation.
Production	• To review the Protocol & report. • Cleaning of equipment & control on equipment during hold time study • To provide details of equipments.
Quality Control	• To review the Protocol & Report. • Microbial sampling • Analyzing the samples withdrawn during the execution of the protocol • Preparation of raw data of analysis. • Submission of data to QA and review of final report.
Engineering	• Engineering department is responsible for the appropriateness of the qualification reports and to ensure that the preventive maintenance program is performed as per schedule.

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6.0 METHOD OF CLEANING

There are 2 types of cleaning performed:

Type A Cleaning: Cleaning done between batches of same product. This is less time consuming using vacuum or dry mop.

Type B Cleaning: Cleaning done between batches of different products at the time of changeover. This is more time consuming involving potable water and purified water.

7.0 CRITERIA FOR THE SELECTION OF EQUIPMENT

The equipments which are selected on the basis of their critical design is given below for Hold Time Study.

S.No.	EQUIPMENTS NAME	EQUIPMENTS ID
01	Mass Mixer	
02	FBD Bowl	
03	Paste Kettle with Binding Scoops	
04	Sieves	
05	Coating Solution Tank (SS)	
06	Coating Pan	
07	Compression Machine	
08	De-Duster	
19	Colloidal Mill	
10	Multi-Mill	

8.0 SAMPLING PLAN WITH SAMPLING LOCATIONS:

8.1 Sampling Plan

The study for “Hold time study of type A cleaned equipment” shall be extended for 24hrs**.** Study shall be conducted for microbiological analysis as per plan (**Table-1**)

After holding equipment unclean for 0hrs,12 hrs, 24 hrs,48 hrs.

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8.1.1 Table-1: Hold Time for Cleaned Equipment after Type A Cleaning

SAMPLING PLAN (Type A cleaned Equipment)				
S.No.	**Hold time Study**	**Sampling Time**	**Test to be performed**	**Acceptance Criteria**
1.	0 Hrs	Sample to be done immediately after of A type cleaning	Microbial	To monitor and Establish limit for microbial Count
2.	12 Hrs	Sample to be done immediately after 12 hrs of A type cleaning	Microbial	
3.	24 Hrs	Sample to be done immediately after 24 hrs of A type cleaning	Microbial	
4.	48 Hrs	Sample to be done immediately after 48 hrs of A type cleaning	Microbial	
7.	After B Type Cleaning	Sampling to be done immediately after Type B cleaning for chemical	Chemical	

8.1.2 Table-2: Hold Time for Cleaned equipment After Type B Cleaning

The study for " Hold time study of cleaned equipment" shall be extended for 24 hrs. Study shall be conducted for microbiological analysis as per plan (Table-2) after holding equipment Cleaned (Type B) for 1st day,(immediate after B cleaning), 2nd day 3rd day,5th day,7th day every interval of 24 hours.

SAMPLING PLAN (Type B cleaned Equipment)				
S.No.	**Hold time Study**	**Sampling Time**	**Test to be performed**	**Acceptance Criteria**
1.	1st day	Sampling to be done immediately after Type B cleaning.	Microbial & Chemical	Microbiological- NMT 25 cfu/ Swab (4inch^2) Total fungal count (Yeast & molds) shall be Nil per swab. (4 inch^2)
2.	2nd day	Sample to be done immediately after24 hrs of holding	Microbial	
3.	3rd day	Sample to be done immediately after 48hrs of holding	Microbial	
4.	5th day	Sample to be done immediately after 96 hrs of holding	Microbial	Chemically NMT 10 (ppm /4 inch^2)
5.	7th day	Sample to be done immediately after 144 hrs of holding	Microbial	

8.2 Sampling Location

The following sampling location are describe in as **Annexure-I.**

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9.0 STORAGE:

The cleaned equipment shall be stored properly in the area dedicated for the storage of Type A cleaned equipment.

10.0 SWAB SAMPLING:

Swab sample shall be taken as per the standard operating procedure, after the final cleaning of equipment qualifies the visual inspection test.

Collect swab sample shall be transfer to QC for further microbial & chemical analysis.

10.1 Swab sampling for chemical analysis: swab sample shall be taken as per the standard operating procedure and should be analyzed within 4 hrs of sampling.

11.0 STUDY PROCEDURE:

12.1 Type A Cleaning

- Select most critical equipments of solid section.
- Manufacture product as per BMR.
- Clean the equipment sufficient to take next batch of same product.
- Withdraw samples for microbial analysis from locations as shown & record the result as per the **Annexure-II.**

12.2 Type B Cleaning

- Manufacture product as per BMR in equipment to be hold.
- Clean the equipments thoroughly sufficient to take next batch of different product.
- Withdraw samples for microbial analysis from defined location for 7 days period.
- Record the result and perform statistical analysis as per **Annexure-III.**

12.0 ACCEPTANCE CRITERIA:

During specified holding period, the Total Bacterial Count and total fungal count shall be monitored.

13.1 Microbial Determination: During specified holding period, the total Bacterial count shall be monitor & establish per swab and total fungal count (Yeast & moulds shall be Nil per swab).

13.2 Chemical determination: The residue content detected in each swab collected shall be below the acceptance limit derived, for type B cleaning.

13.3 Acceptance Limit for chemical determination: Not more than 100cfu/Swab and 10 ppm / swab.

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13.0 DEVIATION AND CHANGE CONTROL:

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15.0 DATA RECORDING:

Annexure I: Sampling Plan for Cleaned Equipment

Annexure II: Data Recording for Microbes, Fungus and Pathogen count for Type A Cleaned Equipments.

Annexure III: Data Recording for Microbes, Fungus and Pathogen count for Type B Cleaned Equipments.

16.0 SUMMARY AND CONCLUSION:

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17.0 POST APPROVAL:

COMPLIED BY :				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
QUALITY ASSURANCE				
REVIEWED & CHECKED BY :				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
QUALITY ASSURANCE				
QUALITY CONTROL				
PRODUCTION				
APPROVED BY:				
DEPARTMENT	**NAME**	**DESIGNATION**	**SIGNATURE**	**DATE**
QUALITY ASSURANCE				

18.0 REVISION HISTORY:

S. No.	Effective Date	Revision No.	Reason for Revision
1.		00	New

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ANNEXURE I

SAMPLING PLAN FOR CLEANED EQUIPMENTS

Microbial Swab Sampling				
S.No.	**Name of the Equipment**	**Location**	**Sample Name**	**No. of Swab Location**
1.	**Mass Mixer**	Blades	S1	3
		Bowel Inner side	S2	
		Lid	S3	
2.	**FBD Bowl**	Inner wall	G1	3
		Cone wall	G2	
		Sieves	G3	
3.	**Paste Kettle with Binder Scoop**	Inner wall	P1	3
		Bottom wall	P2	
		Scoop Surface	P3	
4.	**Sieves**	Upper Surface	F1	2
		Lower Surface	F2	
5.	**Coating Solution Tank (SS**	Inner wall	C1	3
		Lid	C2	
		Bottom wall	C3	
6.	**Coating Pan**	Inner wall	V1	2
		Spray Gun	V2	
7.	**Compression Machine**	Hopper	T1	3
		Discharge Chute	T2	
		Turret	T3	
8.	**De-Duster**	Discharge Chute	D1	2
		Perforated Plate	D2	

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Microbial Swab Sampling				
S.No.	**Name of the Equipment**	**Location**	**Sample Name**	**No. of Swab Location**
9.	**Colloidal Mill**	Hopper inner wall	M1	3
		Outlet Point	M2	
		Turbo Homonizer	M3	
10.	**Multi-Mill**	Inlet Wall	Q1	3
		Middle Cabinet	Q2	
		Blades	Q3	

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ANNEXURE II

Data Recording for Microbes, Fungus and Pathogen count for Type A Cleaned Equipments

Product Name …… Batch No. ……

Equipment Name……. Equipment ID No. …….

S.No.	Tests	Limits	Initial	12 hours	24 hours	48 hours
01						
	Aerobic bacteria	NMT 10^2 cfu/ml				
	Fungi	NMT 10^1 cfu/ml				
	1. *E. coli*	Absent				
	2. *Salmonellae*	Absent				
	3. *Staphylococcus aureus*	Absent				
	4. *Pseudomonas aeruginosa*	Absent				

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ANNEXURE III

Data Recording for Microbes, Fungus and Pathogen count for Type B Cleaned Equipments

Product Name ……. **Batch No. ……**

Equipment Name……. **Equipment ID No. …….**

S.No.	Tests	Limits	Initial	24 hours	48 hours	72 hours	96 hours	120 hours	144 hours
01	Microbial limit test								
	A. Total viable aerobic count								
	Aerobic bacteria	NMT 10^2 cfu/ml							
	Fungi	NMT 10^1 cfu/ml							
	B. Pathogens								
	1. *E. coli*	Absent							
	2. *Salmonellae*	Absent							
	3. *Staphylococcus aureus*	Absent							
	4. *Pseudomonas aeruginosa*	Absent							