PROTOCOL FOR

DIRTY EQUIPMENT HOLD TIME STUDY VALIDATION

FORMULATION BLOCK

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1. OVERVIEW:

1.1 Objective:

The objective of this protocol is to generate back up data to demonstrate the dirty equipment hold time before cleaning and effectiveness of established cleaning procedures after completion of hold time.

1.2 Scope:

This protocol is applicable to perform to establish the dirty equipment hold time (hold time of the equipment between manufacturing process end & cleaning) and evaluate the effectiveness of established cleaning procedures after completion of hold time in production formulation department.

1.3 Responsibility:

To conduct the dirty equipment hold time study team shall be formed. The team shall contain the members from the Quality Control, Production and Quality Assurance Departments. The Validation team is described through the following responsibility:

Department/ Function	Responsibility
Validation group	Preparation of study protocol and review of study report.
Quality Control	Review of the protocol, and sampling as per the sampling plan provided in the protocol and analysis of the samples collected and sharing of analytical results to QA for report compilation.
Production	Review the protocol/ report.
QA	Review & Approval of study protocol/ report and execution of the study protocol, by collecting the samples as per the protocol.

2. EXECUTION TEAM:

Following personnel shall be responsible for the execution of qualification study:

Production	:	To conduct the validation study as per protocol.
Quality Assurance	:	To collect the sample as per protocol.
Quality Control	:	To conduct the microbiology monitoring, analysis of samples and reporting of results.

3. TRAINING RECORD:

3.1 Purpose:

The purpose of the training is to familiarize the trainees with the purpose and procedure of dirty equipment hold time study.

3.2 Scope:

This training is applicable to the protocol for dirty equipment hold time study.

3.3 Topics:

The following topics shall be covered during training: Identifying the responsibility of involved person.

3.3.1 Purpose & procedure of dirty equipment hold time study.

3.3.2 Documentation practices to be followed.

3.3.3 General precautions / guidelines to be followed during validation.

4. DIRTY EQUIPMENT HOLD TIME STRATEGY:

Following are the lines to be performed for dirty hold time study

S.No.	Line	Type of presentation	Rationale
1.	1	Vial	As the process equipments are similar for all the products

5. VALIDATION REQUIREMENTS & OBSERVATIONS:

- After completion of the batch processing hold the equipment as in situ condition for 60 hrs.
- Take the swab sample at the interval of 0, 24, 48, 60th hours for microbial Bio burden before cleaning.
- After completion of hold time of 60 hours the cleaning of equipments shall be carried out as per the standard cleaning procedures (SOPs).
- The samples shall be collected after the cleaning, from manufacturing vessel, filtration vessel, buffer tank, filling manifold, filling pump & nozzle.
- After completion of cleaning process of respective equipment, the cleaned equipment shall be visually verified for cleanliness and shall be rinsed with defined quantities.
- The rinse samples shall be collected from all the identified equipments used in the manufacturing process.
- The rinse samples shall be tested for Conductivity, pH, BET & Bio burden.
- The swab sample shall be tested for Bio burden.
- A summary & conclusion shall be drawn based on the outcome of the study.

5.1 **Sampling procedure for rinse sample:**

- Perform visual inspection of the cleaned equipments and ensure that the equipment is visually clean before sample collection.

Equipment	Volume of WFI for rinsing
Manufacturing Vessel	5 % of vessel working capacity
Filtration Vessel	5 % of vessel working capacity
Buffer Tank	1.0 L
Filling Pump	1.0 L
Filling manifold	1.0 L
Nozzle	1.0 L

- Collect the rinse samples and send it for testing pH, conductivity, bio burden & BET

Test	Sample quantity
pH	100mL
Conductivity	50mL
Bio burden	100 mL
BET	20mL

5.2 **Sampling Locations & Require Test for rinse sample:**

S.No.	Name of Equipment	Rinse Quantity	Sampling location	Sample ID No.	Test
1	Manufacturing Vessel	*	Outlet of the vessel		pH
					Conductivity
					Bio burden
					BET
2	Filtration Vessel	*	Outlet of the vessel		pH
					Conductivity
					Bio burden
					BET
3	Filling Nozzles	1 L	Outlet of the nozzle		pH
					Conductivity
					Bio burden
					BET
4	Buffer Tank	1 L	Outlet of the buffer tank		pH
					Conductivity
					Bio burden
					BET
5	Filling pump	1 L	Outlet of the pump		pH
					Conductivity
					Bio burden
					BET

* - 5 % of vessel working capacity

NOTE: *pH & conductivity is only for information purpose.*

5.3 **Sampling procedure for swab sample:**

- This method allows collection of the samples directly from the uncleaned equipment/system surfaces.
- Immediately after wetting the swab stick, swab the specific equipment surface area as per Figure.1 The surface area to be swabbed is 25 cm^2 (5cm X 5cm) as per Figure.2 and if the area is less than the specified surface whole surface to be swabbed.

Figure – 1[A template for surface sampling]

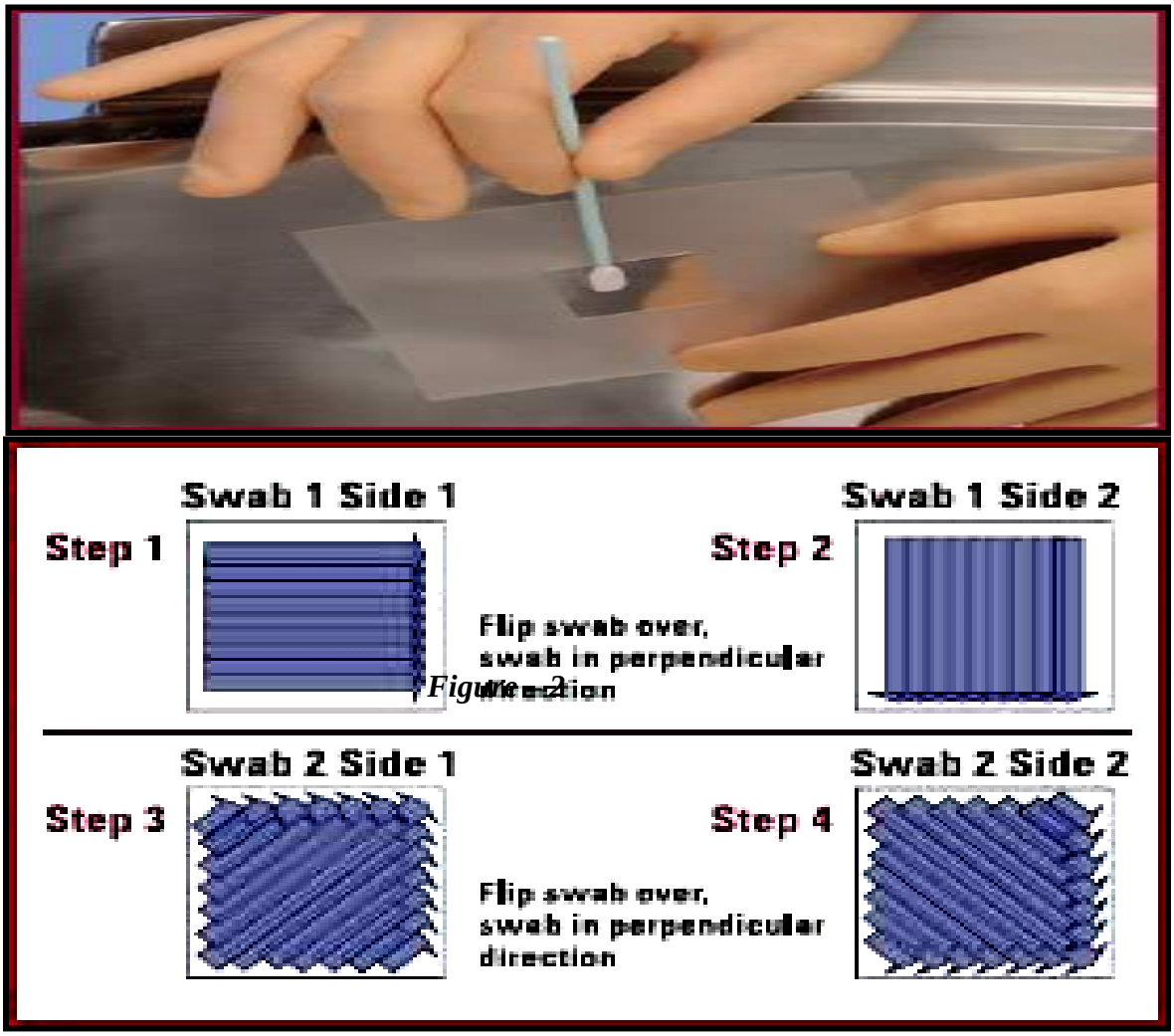

Figure – 2

- In case of surface area where swab sampling for 25 cm2 is not possible following approach shall be followed; Swab the surface such that it will cover the maximum possible accessible area.
- Test the swab sample for the bio-burden as per respective SOP.

5.4 **Sampling Locations for swab sample:**

S.No.	Name of Equipment	Sampling Location	Sample ID No.	Snap No
1	Manufacturing Vessel	Inner surface of vessel		01
		Inside walls of material adding port		02
		Inside of Sampling valve		03
		Outlet of the vessel		04
2	Filtration Vessel	Inner surface of vessel		05
		Inside walls of material adding port		06
		Inside of Sampling valve		07
		Outlet of the vessel		08
3	Buffer Tank	Inner surface of the buffer tank		09
		Outlet of the buffer tank		10
4	Filling Pumps	Inner surface of pump		11
5	Filling Nozzles	Outlet of the Nozzle		12

5.5 **Snapshot of the above locations is listed below for reference:**

6. ACCEPTANCE CRITERIA:

- After respective cleaning procedure, all the product contact parts should be visually clean.
- The limits for rinse and swab sample tested for following tests are mentioned in the below table:

Test		Acceptance criteria
pH		5.0-7.0
Conductivity		NMT 1.3µs/cm^2
Bio burden	Rinse Sample	10 CFU / 100mL
	Swab Sample	10 CFU / Swab
BET		NMT 0.125 EU / mL

7. DEVIATION AND CORRECTIVE ACTION REPORT:

Record the deviations occurred during the execution of program and their justifications, corrective & preventive actions taken shall be recorded.

8. SUMMARY & CONCLUSION:

- Results shall be documented in the test data sheets provided as Annexure -1 to the protocol.
- Based on the observations recorded, evaluation of the results shall be carried out.
- After completion of the test, a detailed summary report (Annexure-2) shall be prepared insisting on the process performed and results obtained.
- On the basis of the results and evaluation, a summary report shall be prepared. The summary report shall signify a conclusion to confirm the successful qualification of the procedure.
- Any modification in the method required before initiating revalidation shall be included in the report.
- The summary report shall be attached with the protocol along with the test data reports.
- Refer Annexure-03 for sampling plan.