PROTOCOL

FOR

CLEAN EQUIPMENT HOLD TIME (CEHT)

STUDY

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

PROTOCOL FOR CLEAN EQUIPMENT HOLD TIME STUDY (CEHT)

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1.0 PRE APPROVAL:

The author signature indicates that this document has been prepared in accordance with existing cGMP standard and adequately reflects the tasks and deliverables necessary for validation of CEHT.

Prepared By/ Function	Designation	Signature	Date

The reviewer's signature indicates that this document has been verified and it accurately and completely reflects the tasks and deliverables necessary for CEHT study and that the document and information complies with applicable regulatory, corporate/ departmental requirements and current Good Manufacturing Practices.

Reviewed By/ Function	Designation	Signature	Date

The approver's signature indicates that this documentation and information contained herein complies with applicable regulatory, corporate, divisional/departmental requirements and current Good Manufacturing Practices.

Approved By/ Function	Designation	Signature	Date

PROTOCOL FOR CLEAN EQUIPMENT HOLD TIME STUDY (CEHT)

2.0 OVERVIEW:

2.1 Objective:

The objective of this protocol is to establish Clean Equipment & Accessories Hold Time by estimating the bio burden proliferation on the clean processing equipment over a period of storage i.e. time from end of Type B to beginning of Packaging. The study shall be performed to evaluate the established Clean Equipment Hold Time period. It shall be performed over a period of seven days (weekends and adjoining holidays if any).

2.2 Scope:

This protocol shall cover responsibilities of different departments, execution team, reference documents and standard operating procedures, validation study/ approach, acceptance criteria, deviation report, revalidation criteria and documentation for Clean Equipment Hold time Study.

3.0 RESPONSIBILITIES

The responsibilities of the different personnel from different departments for the Clean Equipment Hold Time Study shall be defined as follows:

Quality Assurance

To prepare protocol in consultation with execution team
To compile data and prepare report
To coordinate study activity and ensure compliance
To review and approve execution data and protocol report
To review and take CAPA for incidents observed

IPQA

To perform sampling during execution as per protocol
To report analytical results

Production

To execute validation activity and allot necessary manpower
To report incidence and deviation observed

4.0 REFERENCE OF RELATED DOCUMENTS:

S.No.	DOCUMENT NAME	DOCUMENT No.
1.	CLEANING VALIDATION MASTER PLAN	
2.	SOP FOR "CLEANING VALIDATION"	
3.	SOP FOR "INCIDENCE AND DEVIATION HANDLING"	
4.	SOP FOR "SWAB SAMPLING"	
5.	SOP FOR "STORAGE AND USAGE OF EQUIPMENT AND ACCESSORIES BEFORE AND AFTER CLEANING"	

5.0 VALIDATION STUDY PLAN:

5.1 Selection of Study Period:

Plan for study shall be as per the following procedure.

5.1.1 Study for equipment during storage after 'Type B' cleaning shall be conducted.

5.1.2 This exercise shall be conducted for a storage period of 7 days for study of selected equipment.

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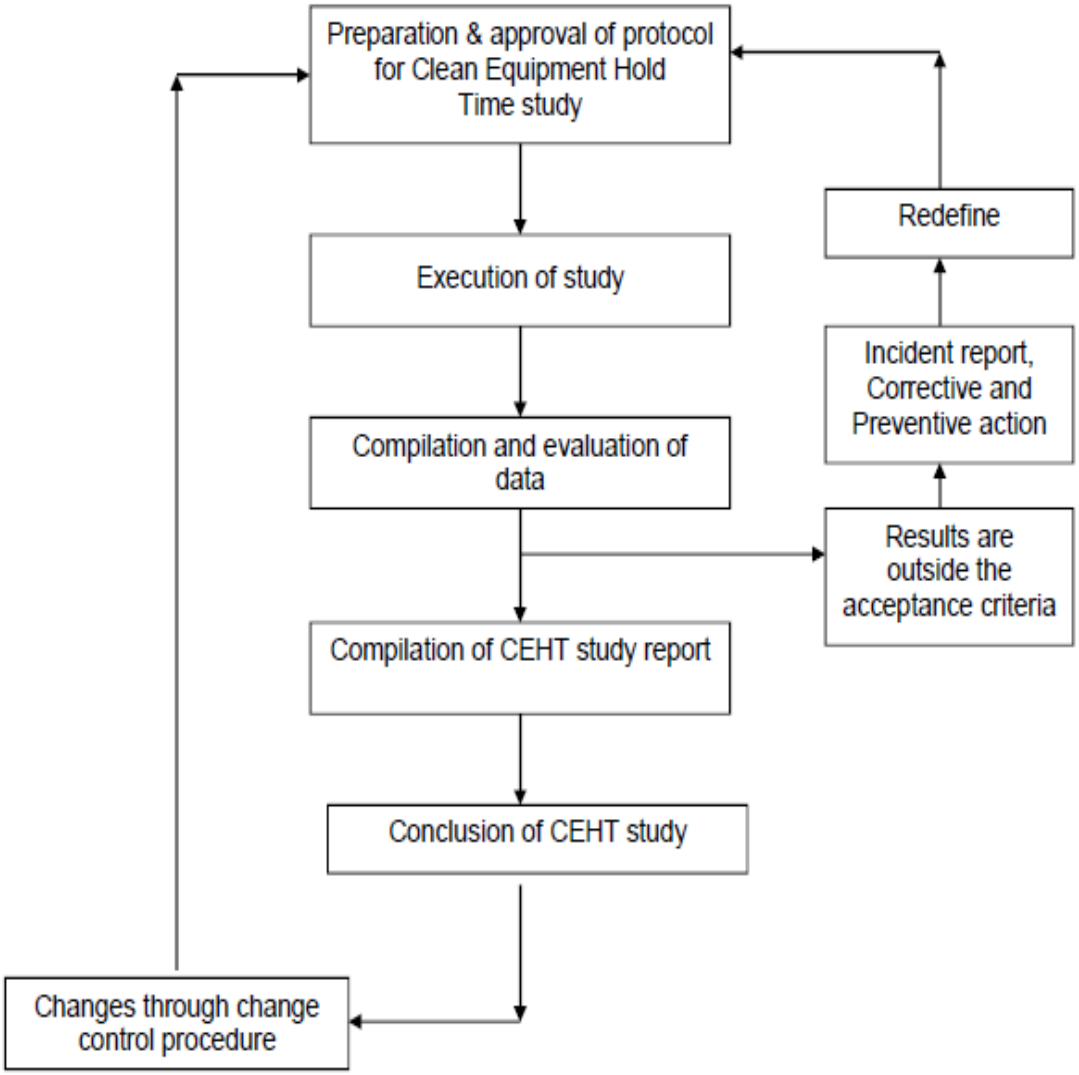
5.2 Activity flow/ details:



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6.0 SELECTION CRITERIA AND SAMPLING DETAILS:

The criteria for selection of different components & parameters for the study shall be as follows.

6.1 Cleaning verification and validation study

Initially one run of study shall be performed after completion of commercial campaign

Equipment and accessories that are involved in the manufacturing of each product shall be defined during the study.

6.2 Selection of target residue:

Bioburden-

i. Total bacterial count

ii. Total fungal count (Yeast & Molds)

6.3 Rationale for Selection of the Process:

Presence of various excipients which are part of drug products prone for the microbial growth shall be considered for the CEHT study.

6.4 Equipment selection criteria: The study shall be performed on the equipment used for the packaging of the selected product.

6.5 Selection of Sampling Technique:

Following are the details of sampling techniques selected for CEHT study:

6.5.1 **Sampling methods:**

Swab sampling is the sampling method selected for the study.

6.5.2 **Sampling locations*:***

6.5.2.1 The Difficult to clean locations of equipment for swab sampling shall be selected based on following criterion,

6.5.2.1.1 Shape of Equipment.

6.5.2.1.2 Cleaning procedure followed.

6.5.2.1.3 Accessibility of each component during cleaning.

6.5.2.1.4 Feasibility of visual check during cleaning.

6.5.3 **Type of swab used*:***

A sterile high culture collecting swab manufactured by High Media for Microbial test shall be used.

6.5.4 **Sampling area:**

6.5.4.1 Swab sampling shall be approximately 25cm^2 for microbial analysis.

6.5.4.2 Preferably adjacent area of the specified sampling locations shall be considered for sampling at different intervals in order to avoid overlapping of sampling area due to re-sampling.

6.5.5 **Sampling Procedure*:***

Swab sampling shall be done as per the current version of SOP for “Swab Sampling” bearing SOP.

6.6 Selection of Acceptance limits:

Acceptance limits for CEHT study shall be same as the microbial limits in the Cleaning Validation protocol.

- **Total Bacterial Count:** Not More Than 25cfu/ swab
- **Fungal count (Yield & Moulds):** Shall be absent

6.7 Selection of Analytical method:

Add 1 ml 0.9 % NaCl solution/Buffered sodium chloride peptone solution to the swab, vortex and pour the content in the Petri dish. Add to it 15 to 20 ml of sterile soya bean casein digest Agar medium which has been previously melted and cooled to 45 °C.

Allow it to solidify at room temperature. Streaking method can be followed.

Incubate the inverted plate at 20 to 25 °C for 48 to 72 hrs and then transfer the plate to conditions of 30 to 35 °C for 24 to 48 hrs.

Observe the plated sample after completion of incubation and report the results.

7.0 PROCEDURE FOR VALIDATION STUDY:

7.1 Execution procedure:

Execution of study shall be done as per the following procedure.

7.1.1 This exercise shall be carried out in a phase wise manner and conducted for a storage period of 7 days.

7.1.2 Equipment shall be sampled on Day-0 (after Type-B cleaning) for microbial analysis and this result shall be the baseline for study.

7.1.3 Clean equipment which is in storage condition shall be sampled on Day-1, Day-2, Day-3, Day-5 and Day-7, to generate microbiological test data. If the scheduled day of sampling falls on any holiday or weekly off, then the sampling shall be done on the next working day.

7.1.4 Sampling shall be done as per the predefined sampling plan. Analysis of the samples shall be done as per respective testing procedures and results shall be reviewed and released as per respective procedures.

7.1.5 The locations of sampling for particular equipment are those with the most contact surface areas and shall be as per the sampling plan.

7.1.6 Record deviation/s, if any, that is observed during the study and review and report with corrective and preventive actions.

7.1.7 Based on the results of study, a report shall be prepared by summarizing the results of validation study with deviation report, conclusion and recommendations and the hold time of the individual equipment in clean state shall be established.

7.2 Sampling plan:

7.2.1 Samples shall be withdrawn from the equipment after it is found to be satisfactorily clean through visual inspection. Follow the below sampling schedule for microbial analysis during the CEHT study.

7.3 Day zero sampling shall be done as per the Sampling locations defined in approved swab location sheet and all subsequent sampling shall be done in such a way that it covers preferably the entire area of the equipment throughout the study.

7.4 Following is the sampling schedule/ frequency.

7.4.1 For the first campaign study, sampling shall be performed on the first and last day of study and control over the Bioburden shall be evaluated.

From each location- Total 6 times

Day-0 (before storage),
Day-1 (during storage),
Day-2 (during storage),
Day-3 (during storage),
Day-5 (during storage),
Day-7 (during storage),

8.0 ACCEPTANCE CRITERIA:

8.1 Study shall be conducted as per the procedure described in the protocol.

8.2 Execution data shall be recorded, reviewed and reported as per the procedure described in the protocol.

8.3 Acceptance criteria shall be as below:

Total Bacterial Count : Not More Than 25 cfu/ swab

Total Fungal count (Yeast &moulds): Must be absent

8.4 Deviation and Corrective Action Report

8.4.1 Deviations observed during the study shall be reported as per SOP for 'Incidence and Deviation Handling'.

8.5 Revalidation Criteria

CEHT study shall be revalidated in the case of a change in cleaning procedure/ Equipment.

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9.0 FINAL REPORT:

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Summarized By: _____ Date: _____

Reviewed By : _____ Date: _____

10.0 ABBREVIATIONS:

S.No.	Abbreviations	Description
1.	Sr.	Serial
2.	No.	Number
3.	CEHT	Clean Equipment Hold Time
4.	CFU	Colony Forming Unit
5.	QA	Quality Assurance
6.	QC	Quality Control
7.	IPQA	In Process Quality Assurance
8.	NA	Not Applicable

11.0 ATTACHMENTS:

S.No.	Description

12.0 REVISION HISTORY:

Version	Description of Change	Effective Date
00	New	--

Reviewed By : _____ Date: _____