PROTOCOL

FOR

DIRTY EQUIPMENT HOLD TIME (DEHT) STUDY

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

PROTOCOL FOR DIRTY EQUIPMENT HOLD TIME STUDY (DEHT)

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1.0 PRE-APPROVAL:

The Author signature indicates that this document has been prepared in accordance with existing cGMP standards and adequately reflects the tasks and deliverables necessary for validation of dirty equipment hold time.

Prepared By/Function	Designation	Signature	Date

The reviewer's signature indicates that, this document has been reviewed and it accurately and completely reflects the tasks and deliverables necessary for validation of dirty equipment hold time and that the documentation and information included complies with 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 DIRTY EQUIPMENT HOLD TIME STUDY (DEHT)

2.0 OVERVIEW:

2.1 Objective:

The objective of this Protocol is to provide an outline for performing DEHT study, after type A cleaning by estimating the microbial load and by estimating the chemical residue after performing type B cleaning.

The DEHT study shall be initiated after completion of a defined campaign of selected product & shall be completed after 7 days (including weekends or holidays if any) from the study initiation date.

2.2 Scope:

This protocol shall cover responsibilities of different departments, reference documents and standard operating procedures, validation study plan, selection criteria, procedure for validation study/approach, acceptance criteria, incident report, revalidation criteria and documentation for conducting a DEHT study.

3.0 RESPONSIBILITIES:

Responsibilities of departments for execution of a DEHT study are as follow:

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 the 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 DOCUMENT:

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"	

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5.0 VALIDATION STUDY PLAN:

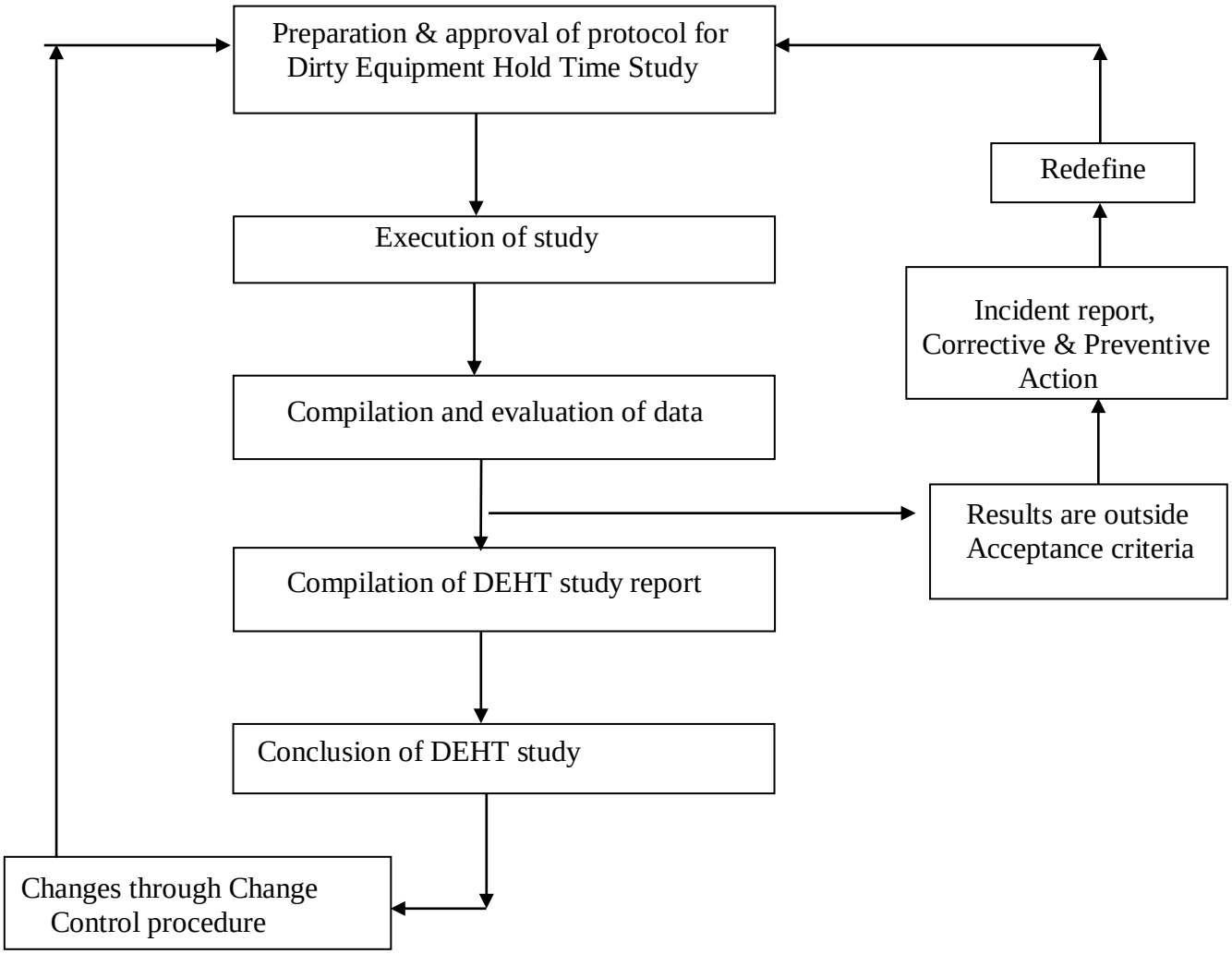
5.1 Plan for Study:

Following is the plan for the study;

5.1.1 The DEHT study shall be initiated after completion of a defined Campaign or Batch of the selected product

5.1.2 Evaluation of microbial load after holding equipment for a storage period of seven days, after Type 'A' cleaning.

5.2 Activity flow / details:



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6.0 SELECTION CRITERIA AND SAMPLING DETAILS:

6.1 Product Selection Criteria

The first campaign or Batch of product shall be selected for the study. On the basis of solubility of the active ingredients, the chemical residue shall be determined.

6.2 Equipment selection criteria:

The study shall be performed on the equipment used for the packaging of the selected product.

6.3 Sampling Technique:

Following are the details of sampling techniques selected for DEHT study.

Swab sampling; Texwipe PP swab sticks shall be used for collecting chemical residue and Sterile HiMedia cotton swabs shall be used for collecting Microbial Samples.

6.4 Sampling method:

Swab sampling is the sampling method selected for the study.

6.5 Rationale for selection of sampling methods:-

Direct surface sampling method which can focus on worst case locations. The quantified results of the sample can be extrapolated to the whole equipment

6.6 Selection of Sampling locations:

Difficult to clean locations of equipment for swab sampling shall be selected.
Refer current approved swab location sheet for the particular equipment.

6.7 Sampling area:

6.7.1 Swab sampling shall be performed for area 25 cm^2 (5 cm X 5 cm) for microbial analysis. For the sampling locations having curved surfaces, blade surfaces, or other non-planar surfaces, approximate area of more than 25 cm^2 shall be considered

6.7.2 Swab sampling shall be performed for approximately 100 cm^2 (10 cm X 10 cm) for chemical analysis. For the sampling locations having curved surfaces, blade surfaces, other non-planar surfaces, approximate area of more than 100 cm^2 shall be considered

6.8 Sampling Procedure:

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

6.9 Test Required:

6.9.1 Bioburden - Sampled over a period of 7 days
Total bacterial count
Total fungal count (Yeast & Molds)

6.9.2 Chemical residue

Residue of worst case molecule after Type 'B'

6.10 Analytical Methodology:

For microbial analysis:

6.10.1 Pour the content of swab device onto sterile Petri dish, add to it 15 to 20 ml of sterile Soyabean Casein Digest Agar Medium which has been previously melted and cooled to 45°C.

6.10.2 Allow it to solidify at room temperature.

6.10.3 Incubate the inverted plates at 20°C to 25°C for 72 hrs and then transfer the plates at 30°C to 35°C for 48 hrs.

6.10.4 Observe the plates after completion of incubation and report the results.

6.10.5 A. R. No. for analytical reports shall be allotted as per SOP.

For Chemical Residue analysis:

6.10.6 Analysis for estimation of residue shall be done as per current version of the standard testing procedure for selected product.

6.10.7 A.R. No. for analytical reports shall be allotted as per SOP for Assigning Analytical Report Number SOP.

7.0 PROCEDURE FOR VALIDATION STUDY:

7.1 Execution procedure:

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

7.1.1 After completion of packaging of the defined campaign for the selected product, the Dirty equipment hold time (DEHT) study shall be initiated.

7.1.2 Type A' cleaning shall be performed after completion of packaging of selected product as per the respective equipment specific cleaning SOP.

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

7.1.4 The equipment shall be stored as per the SOP for 'Procedure for storage and usage of equipment and accessories before and after cleaning'.

7.1.5 This DEHT shall be performed for a storage period of 7 days.

7.1.6 Dirty equipment/ accessories under storage shall be sampled for microbial analysis on Day-1, Day-2, Day-3, Day-5 and Day-7.

7.1.7 After sampling of 7^{th} day, Type 'B' cleaning of the equipment shall be performed and sampled for microbial and chemical analysis.

7.1.8 If the scheduled day of sampling falls on any holiday or weekly off then the sampling shall be done on the next working day. Sampling shall be done as per predefined sampling plan as per the SOP for 'Swab Sampling'.

7.1.9 The locations of sampling for particular equipment are the most contact Surface areas and shall be performed as per the current approved 'Swab Location Sheet' for the particular equipment.

7.1.10 Analysis of the samples, review and release of results shall be done as per respective

testing Procedures for chemical analysis. For microbial analysis follow the procedure mentioned above.

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

7.1.12 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 equipment in dirty state shall be established

7.2 Sampling plan:

7.2.1 Samples shall be withdrawn from the equipments for microbial analysis during the DEHT study. At Day 7, after 'Type B' cleaning, samples shall be withdrawn for the chemical residue according to the following sampling plan:

7.2.2 Day 'zero' sampling shall be done as per the 'swab location sheet' and all subsequent sampling shall be done from the adjacent area of previous sampling location.

7.2.3 Following are the sampling schedule/ frequency:

From each location- Total 7 times

i. Day-0 (before storage),
ii. Day-1 (during storage after 24 Hrs),
iii. Day-2 (during storage 48 Hrs),
iv. Day-3 (during storage 72 Hrs),
v. Day-5 (during storage 120 Hrs),
vi. Day-7 (during storage 168 Hrs),
vii. Day-7 (After Type 'B').

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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.

8.3.1 Acceptance limits for microbial Study are:

Day-0 to Day-7:

Total Bacterial Count: **Not More than 100 cfu/swab**

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

Day-7 after 'Type B' cleaning:

Total Bacterial Count: **Not More than 25 cfu/swab**

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

8.3.2 Acceptance limit for chemical residue after 'Type B' cleaning is a predefined limit of Not More Than 10 ppm. If the previous product is evaluated for limit of the chemical residue, acceptance limit is assigned by calculating residue limit through MACO formula

A study report, which comprises of the conclusion and recommendations of the validation study, shall be prepared

8.4 Deficiency 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

Dirty Equipment Hold Time study shall be revalidated in the cases when there is Change in acceptance criteria for microbial analysis

9.0 FINAL REPORT:

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Summarized By: _____ Date: _____

Reviewed By : _____ Date: _____

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10.0 ABBREVIATIONS:

S.No.	Abbreviations	Description
1.	DEHT	Dirty Equipment Hold Time
2.	SOP	Standard Test Procedure
3.	CAPA	Corrective Action Preventive Action
4.	ppm	Parts per million
5.	CFU	Colony Forming Units

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11.0 ATTACHMENTS:

S.No.	Description

Reviewed By: _____ Date: _____

12.0 REVISION HISTORY:

Version	Description of Change	Effective Date
00	New	--