HOLD TIME STUDY PROTOCOL

FOR

HARDGEL CAPSULES

PROTOCOL NO.	
SUPERCEDES	Nil
PROTOCOL EFFECTIVE DATE	
REPORT EFFECTIVE DATE	

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

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HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

1.0 PROTOCOL PREAPPROVAL

PROTOCOL PREPARED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
QUALITY ASSURANCE				

PROTOCOL REVIEWED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
PRODUCTION				
QUALITY CONTROL				

PROTOCOL APPROVED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
QUALITY ASSURANCE				

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

1.0 Objective:

The objective of this protocol is to study the effect of "Hold Time" on the bulk of **……..** to verify that during the hold period, the Product shall meet predetermined quality specifications. The protocol also details the responsibilities and activities associated with this Hold Time Study.

2.0 Introduction:

The Samples of **……** subjected to Hold Time Study shall be stored under simulated conditions and shall be analyzed as per the established specifications at different time points of study as specified.

Analytical methods for testing of bulk of ……. have been satisfactorily adopted into the QC laboratory.

On completion of the study, a report shall be prepared and final conclusion shall be drawn in the same. It shall be implemented in routine manufacturing. This document shall form the basis of the production scale batches. Any variation to the established Hold Time shall be explained and justified, in accordance with the change control procedure.

3.0 RESPONSIBILITIES:

S.No.	Department	Responsibilities
1.	Production	Review of Hold time study protocol and Report
2.	Quality Control	Review of Hold time study protocol & report Analysis of samples and reporting the results
3.	Quality Assurance	Preparation, Review & Approval of Hold time study protocol & report, Sampling and compilation of results

4.0 PROCEDURE:

4.1 Bulk hold time study:

Test the sample from the bulk from the three batches at Zero (0) time point. Store sample from three batches for a period of specific time period given different process stage under simulated conditions at Temp. NMT 27°C and Relative humidity NMT 50 %.

S.No.	Name of stage	Sample Qty. Required for hold time study
1	Dry Mixing stage	200 gm
2	Binder Solution	100 gm
3	Pre-Lubrication	200 gm
4	After Lubrication	200 gm
5	Filled Capsule	400 Capsule for Chemical + 100 gm Capsule for micro test

Section 5.0 (Matrix for Hold Time Study).

Acceptance criteria:

Bulk sampled at different time points shall meet the acceptance criteria as mentioned in Table No. 1.

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5.0 Matrix for hold time study

5.1.1 Matrix for hold time study of Dry mixing stage

Storage Time	Sample Quantity for testing	Tests to be performed
a) Type of Sample: Dry mixing		
Initial	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
07 Day	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
15 Days	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
30 Days	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
45 Days	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
60 Days	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing

5.1.2: specifications for Dry Mixing stage

S.No.	Tests	Limits
01	Description	
02	LOD	
03	Assay	
Additional Test		
04	Microbial limit test	
	A. Total viable aerobic count	
	Aerobic bacteria	NMT 10^2 cfu/gm
	Fungi	NMT 10^1 cfu/gm
	B. Pathogens	
	1. *E. coli*	Absent

5.2.1 Matrix for hold time study of Binder solution

Storage Time	Sample Quantity for testing	Tests to be performed
Type of Sample: Binder Solution		
Initial	2 gm +10 gm (Chemical + microbiological sample)	Description, & Microbiological testing
12 Hours	2 gm + 10 gm (Chemical + microbiological sample)	Description, & Microbiological testing
24 Hours	2 gm + 10 gm (Chemical + microbiological sample)	Description, & Microbiological testing
36 Hours	2 gm + 10 gm (Chemical + microbiological sample)	Description, & Microbiological testing
48 Hours	2 gm + 10 gm (Chemical + microbiological sample)	Description, & Microbiological testing
72 Hours	2 gm + 10 gm (Chemical + microbiological sample)	Description, & Microbiological testing

5.2.2: Specifications for Binder Solution

S.No.	Tests	Limits
01	Description	
Additional Test		
02	Microbial limit test	
	A. Total viable aerobic count	
	Aerobic bacteria	NMT 10^2 cfu/gm
	Fungi	NMT 10^1 cfu/gm
	B. Pathogens	
	1. *E. coli*	Absent

5.3.1 Matrix for hold time study of Pre Lubrication granules:

Storage Time	Sample Quantity for testing	Tests to be performed
Type of Sample: Pre Lubrication granules		
Initial	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
7 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
15 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
30 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
45 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
60 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing

5.3.2 : specifications for Pre Lubrication granules

S.No.	Tests	Limits
01	Description	
02	LOD	
03	Assay	
Additional Test		
04	Microbial limit test	
	A. Total viable aerobic count	
	Aerobic bacteria	NMT 10^2 cfu/gm
	Fungi	NMT 10^1 cfu/gm
	B. Pathogens	
	1. *E. coli*	Absent

5.4.1 Matrix for hold time study of After Lubrication granules

Storage Time	Sample Quantity for testing	Tests to be performed
Type of Sample: After Lubrication granules		
Initial	20 gm +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
7 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
15 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
30 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
45 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing
60 Days	20 gm + 10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Microbiological testing

5.4.2: specifications for After Lubrication granules

S.No.	Tests	Limits
01	Description	
02	LOD	
03	Assay	
Additional Test		
04	Microbial limit test	
	A. Total viable aerobic count	
	Aerobic bacteria	NMT 10^2 cfu/gm
	Fungi	NMT 10^1 cfu/gm
	B. Pathogens	
	1. *E. coli*	Absent

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5.5.1 Matrix for hold time study of Filled Capsules

Storage Time	Sample Quantity for testing	Tests to be performed
Type of Sample: Filled Capsules		
Initial	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing
7 Days	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing
15 Days	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing
30 Days	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing
45 Days	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing
60 Days	60 Capsules +10 gm (Chemical + microbiological sample)	Description, LOD, Assay & Dissolution Microbiological testing

5.5.2: specifications for Filled Capsules

S.No.	Tests	Limits
01	Description	
02	LOD	
03	Assay	
04	Dissolution	
Additional Test		
05	Microbial limit test	
	A. Total viable aerobic count	
	Aerobic bacteria	NMT 10^2 cfu/gm
	Fungi	NMT 10^1 cfu/gm
	B. Pathogens	
	1. *E. coli*	Absent

6.0 DEVIATION AND CHANGE CONTROL:

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7.0 SUMMARY AND CONCLUSION:

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8.0 REFERENCE:

ICH, FDA, EMEA and Annexure IV WHO TRS 992

9.0 ABBREVIATION:.

S.No	Abbreviation	Extended Form
01	SOP	Standard Operating Procedure
02	HTSP	HOLD Time Study Protocol
03	LOD	Loss on Drying

10.0 REPORT POSTAPPROVAL:

COMPILED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
QUALITY ASSURANCE				

REVIEWED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
PRODUCTION				
QUALITY CONTROL				

APPROVED BY:

DEPARTMENT	NAME	DESIGNATION	SIGNATURE	DATE
QUALITY ASSURANCE				

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

Annexure I

RESULTS OF DRY MIXING STAGE

BATCH NO.		**MFG. DATE**	
BATCH SIZE		**EXP. DATE**	

S.No.	Tests	Limits	0 hours (Initial)	07 Days	15 Days	30 Days	45 Days	60 Days
01	Description							
02	LOD							
03	Assay							
Additional Test								
04	Microbial limit test							
	A. Total viable aerobic count							
	Aerobic bacteria	NMT 10^2 cfu/g						
	Fungi	NMT 10^1 cfu/g						
	B. Pathogens							
	1. E. coli	Absent						

Compiled By_____ **Reviewed By**_____

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

Annexure II

RESULTS OF BINDER SOLUTION

BATCH NO.		**MFG. DATE**	
BATCH SIZE		**EXP. DATE**	

S.No.	**Tests**	**Limits**	**0 hours (Initial)**	**12 Hours**	**24 Hours**	**36 Hours**	**48 Hours**	**72 Hours**
01	Description							
Additional Test								
02	Microbial limit test							
	A. Total viable aerobic count							
	Aerobic bacteria	NMT 10^2 cfu/g						
	Fungi	NMT 10^1 cfu/g						
	B. Pathogens							
	1. E. coli	Absent						

Compiled By_____ **Reviewed By**_____

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Annexure III

RESULTS OF PRE-LUBRICATION GRANULES

BATCH NO.		**MFG. DATE**	
BATCH SIZE		**EXP. DATE**	

S.No.	Tests	Limits	0 hours (Initial)	07 Days	15 Days	30 Days	45 Days	60Days
01	Description							
02	LOD							
03	Assay							
Additional Test								
04	Microbial limit test							
	A. Total viable aerobic count							
	Aerobic bacteria	NMT 10^2 cfu/g						
	Fungi	NMT 10^1 cfu/g						
	B. Pathogens							
	1. E. coli	Absent						

Compiled By_____ **Reviewed By**_____

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

Annexure IV

RESULTS OF AFTER LUBRICATION GRANULES

BATCH NO.		**MFG. DATE**	
BATCH SIZE		**EXP. DATE**	

S.No.	**Tests**	**Limits**	**0 hours (Initial)**	**07 Days**	**15 Days**	**30 Days**	**45 Days**	**60Days**
01	Description							
02	LOD							
03	Assay							
Additional Test								
04	Microbial limit test							
	A. Total viable aerobic count							
	Aerobic bacteria	NMT 10^2 cfu/g						
	Fungi	NMT 10^1 cfu/g						
	B. Pathogens							
	1. E. coli	Absent						

Compiled By_____ **Reviewed By**_____

HOLD TIME STUDY PROTOCOL CUM REPORT FOR HARDGEL CAPSULE

Annexure V

RESULTS OF FILLED CAPSULE

BATCH NO.		**MFG. DATE**	
BATCH SIZE		**EXP. DATE**	

S.No.	Tests	Limits	0 hours (Initial)	07 Days	15 Days	30 Days	45 Days	60Days
01	Description							
02	LOD							
03	Assay							
04	Dissolution							
Additional Test								
03	Microbial limit test							
	A. Total viable aerobic count							
	Aerobic bacteria	NMT 10^2 cfu/g						
	Fungi	NMT 10^1 cfu/g						
	B. Pathogens							
	1. E. coli	Absent						

Compiled By_____ **Reviewed By**_____