RISK ANALYSIS STUDY PROTOCOL FOR MERGING OF BLOCKS

DATE OF RISK ANALYSIS	
SUPERSEDE PROTOCOL No.	**NIL**

REPORT CONTENTS

RISK ANALYSIS STUDY PROTOCOL FOR MERGING OF BLOCKS

1.0 PROTOCOL APPROVAL:

INITIATED BY:

RISK ANALYSIS STUDY PROTOCOL FOR MERGING OF BLOCKS

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (PRODUCTION)			
HEAD (ENGINEERING)			
HEAD (QUALITY CONTROL)			
HEAD (SAFETY)			

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			

2.0 OBJECTIVE:

- To provide documented evidence that there is no risk in merging of Blocks.
- To confirm and establish that the merging of Blocks will not have any impact on adjacent classified areas integrity.

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3.0 SCOPE:

This risk analysis study Protocol is applicable for performing risk analysis study for merging of Blocks.

4.0 RESPONSIBILITY:

Department	Responsibility
Quality Assurance	• Shall prepare & Review the Risk analysis Protocol. • Execution of the Risk analysis Protocol with Production, Quality Control & Maintenance Department: verification of components

	Calibration Records of Instrument, Collection of samples with QC person and send to QC for Analysis. • Verification of test & Results. • Deficiency (if any) & Corrective Action. • Shall compile the data & Prepare Summary Report • Risk analysis Protocol shall be approved by the QA prior the execution. • Shall review the executed Protocol to check the compliance and corrective action for any discrepancies found. Also shall prepare the summary and conclusion of the Risk analysis Study.
Quality Control	• Reviewing of Risk analysis Protocol for Correctness, Completeness and Technical Excellence. • Take the sample as per Protocol in presence of QA person. • Post approval of Risk analysis Protocol after Execution.
Engineering	• Reviewing of Risk analysis Protocol for Correctness, Completeness and Technical Excellence. • Responsible for Trouble shooting (if occurred during execution).
Production	• Reviewing of Risk analysis Protocol for Correctness, Completeness and Technical Excellence. • To provide support for execution of Risk analysis Study as per Protocol. • Post approval of Risk analysis Protocol after execution.
Safety	• Reviewing of Risk analysis Protocol for Correctness, Completeness and Technical Excellence. • Responsible for Trouble shooting (if occurred during execution).

5.0 REASON FOR RISK ANALYSIS:

To evaluate the risk in merging of Blocks.

6.0 SITE OF STUDY:

Manufacturing area.

7.0 RISK COMMUNICATION & TRAINING:

- The Risk analysis team shall be authorized by Head-QA or his/her designee.

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- Quality Risk Management Team shall be cross functional team comprise of expert from different areas such as QA, QC, Production, Engineering & Safety.
- Training shall be imparted to the team members before execution of Protocol for proper understanding of the procedure. Training shall be recorded in Training attendance Record.

8.0 RISK IDENTIFICATION & EVALUATION:

- In existing facility Block 1 is separated from Block 2 by a brick wall partition.
- Corridor of Block 1 is qualified under Grade D.
- Block 1 corridor (3400 mm) shares its adjacent area with Hardgel corridor (3000 mm), Three Granulation corridors (2400 mm), Compression Corridor (2100 mm) & Coating corridor (2400 mm).
- Differential pressure of Block corridor is more than the adjacent core areas (Hardgel, Granulation, Compression, Coating & Quarantine) ie; Cascade type differential pressure.

	Pressure Differential (Pascal)	Adjacent areas
G-block Corridor (40-45 Pascal)	10-15	Material entry of Hardgel
	10-15	Man entry of Hardgel
	25-30	Material entry of Granulation
	25-30	Man entry of Granulation
	25-30	Material entry of Compression
	25-30	Man entry of Compression
	25-30	Material entry of Coating
	25-30	Man entry of Coating

G-block Corridor	Pressure Differential (Pascal)	Adjacent areas
	25-30	Granules Store
	25-30	Granules Store (Low RH)
	25-30	Solution preparation room
	25-30	Tablet store
	25-30	Tablet Store (Low RH)
	25-30	Material Entry of Hard gel Capsule filling
	25-30	Man Entry of Hard gel Capsule filling

Table 1: Pressure differential of Block 1 corridor with respect to adjacent areas:

- Any change in corridor of Block 1 will have an impact on the integrity of adjacent airlocks having pressure lower than adjacent corridors.

9.0 RISK MITIGATION:

- Expansion in Block 2 should be done in such a manner that there should be no disturbance in Block 1 core areas, for this before merging of the both corridor one week Differential Pressure between both corridor will be monitored by calibrated Magnehelic gauge.
- There should not be no pressure variance in both manufacturing corridor.
- An artificial Alupan wall to be made before merging of corridors to avoid any contamination.
- After that, merging of both corridors should be started.
- Block 2 qualification to be done before removing of Alupan partition sheet.

- **Following are the qualification parameters:**

(i) Viable Particle count
(ii) Non-viable count
(iii) Pressure Differential
(iv) Air velocity
(v) Filter integrity
(vi) Temperature
(vii) RH
(viii) Air flow pattern.

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Grade	Test to be performed	Acceptance Criteria
D	**Viable Particle Count**	NMT 500 cfu/m^3 by Air Sample
		NMT 100 cfu/4 Hours by Settle plate (Diameter 90 mm)
	Non- viable Particle Count	NMT 29300/m^3 Particles of 5.0µ or above at rest condition should be observed
		NMT 3520000/m^3 particles of 0.5µ or above
	Pressure Differential between Block 1 & Block 2 corridors	Block 1 & Block 2 should be same, there should be no process variance.
	Air velocity, Air volume & Air distribution	The Average measured clean air velocity should be 70-250 ft/min at 6 inches downstream from their filter face.
	HEPA Filter Integrity test	The PAO penetration / leak through HEPA filters should not be greater than 0.03% of the upstream PAO concentration.
	Temperature & RH	Should be as per designed area**:** (22±2ºC; RH: 50±5%)
	Air flow pattern	Should be as per design

Table -2: Block 1 & Block 2 corridor shall be qualified as per D-grade requirement ie; as per ISO14644

- After qualification of F-block, the partition between both corridors (Block 1 & Block 2) to be merged.
- As Pressure differential of both corridor is greater than core areas, hence chance of cross contamination will be reduced.
- After removal of Alupan sheet & merging of both blocks, again the area qualification of both block corridors shall be repeated for confirmation.

10.0 RISK ANALYSIS, RE-RISK ANALYSIS CRITERIA:

10.1 Failure Mode, Effect Analysis:

In the following section a table is produced for the risk analysis using FMEA tool. The significance or instruction for each column is described in the following paragraph.

Column 1:	**Serial number** of Risk Analysis item
Column 2:	**Item/Function:** Identify the process step or component associated with the risk.
Column 3:	**Potential Failure Mode:** Identify the type of risk associated with the process or component.

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Column 4:	**Effect of Potential Failure/Cause:** Verify that whether risk have **GMP impact.**
Column 5/6/7/8/9:	**Severity/Occurrence/Detection/Risk level/Risk Acceptance:** Risk Priority Number to be calculated by taking Severity, Occurrence & Detection of potential failure into consideration.
Column 10:	**Risk Mitigation**: Write the risk mitigation strategy as considered in design.
Column 11/12/13/14/15:	**Severity/Occurrence/Detection/Risk level/Risk Acceptance:** Risk Priority Number to be calculated after mitigation by taking Severity, Occurrence & Detection of potential failure into consideration.
Column16:	**Recommended action:** Recommended actions should be given for controlling failure occurrence.

Table 3: Instruction for each column given above

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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FACILITY: MERGING OF BLOCK 1 AND BLOCK 2 CORRIDOR **QRA No.:**	Reference change control……..

S. No.	Item/ Function	Potential Failure Mode	Effect of Potential Failure/ Cause	Severity	Occurrence	Detection	*Risk Priority Number	Risk Acceptance Yes/No	Risk Reduction	Severity	Occurrence	Detection	*Risk Priority Number	Risk Acceptance Yes/No	Recommended Actions (If any)
1.	**Common Corridor between existing Block 1 & New Block 2 to be merged**	AHU Failure	Air will contaminate, due to dust non-viable particle count will get increase	10	4	4	160	Yes	Block 1 core area to be segregated from Block 2 by maintaining pressure differential & Alupan sheet partition.	4	4	4	64	No	1. Partition to be verified by QA before merging of corridors. 2. Regular monitoring of pressure differential to be done for 07 days before merging of corridors. 3. Proper training on gowning to be given to the personnels involved in merging of corridor to avoid contamination & cross-contamination
			Pressure differential will get disturbed leading to increase in Non viable count	7	4	4	112	Yes	Pressure Differential maintained between Block 1 & Block 2	1	4	4	16	No	
		HEPA filters integrity	Filters may got chocked due to dust collection	7	4	4	112	Yes	HEPA Filters adjacent to construction area should be covered properly	4	4	4	64	No	
		Return Risers	Filters may got chocked due to dust collection	4	4	10	160	Yes	Return riser filters adjacent to construction area should be covered properly	4	4	4	64	No	
		Environmental monitoring	Viable particle count will increase which leads MLT failure.	10	4	7	280	Yes	Particle count verification to be done before & after merging of corridor and cleaning & sanitization procedure shall be available.	4	4	4	64	Yes	
			Environmental parameters Temperature leads to failure	4	4	4	64	No	Continuous temperature monitoring to be done before & after merging of corridor	1	4	4	16	No	
			Environmental parameters Humidity leads to failure	4	4	4	64	No	Continuous humidity monitoring to be done before & after merging of corridor	1	4	4	16	No	
		Cross-contamination	Material movement will get disturbed leading to cross-contamination.	10	4	10	400	Yes	As partition of Alupan sheet will be done before merging of wall, hence material movement will not get disturbed leading to contamination.	4	4	4	64	No	
		Personnel	Man movement will increase. Personnel involved in merging of corridors may lead to contamination	4	4	10	160	Yes	As partition of Alupan sheet will be done before merging of wall, hence man movement will not get disturbed leading to contamination.	1	4	4	16	No	

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S. No.	Item/ Function	Potential Failure Mode	Effect of Potential Failure/ Cause	Severity	Occurrence	Detection	*Risk Priority Number	Risk Acceptance Yes/No	Risk Reduction	Severity	Occurrence	Detection	*Risk Priority Number	Risk Acceptance Yes/No	Recommended Actions (If any)
		Gowning	Improper gowning cause contamination	10	4	10	400	Yes	Proper secondary gowning to be done before entering the core area	1	4	4	16	No	
		Air flow pattern change	Return riser may get chocked	4	4	10	160	Yes	Partition during merging of corridors will reduce chances of riser chocking	1	4	4	16	No	
		Power Failure recovery	Environment monitoring get disturbed	10	4	1	40	No	Power failure backup will be given to that particular AHU system to avoid any discrepancy	1	4	1	4	No	

Table 4: The above table shows Potential failure mode, effect of potential failure along with Risk Probable Number, Risk Mitigation & Recommended Actions.

*** The Risk Priority Number (RPN/Overall Risk) changes based upon the risk. The Risk Assessment team shall decide the acceptance criteria. For example the risk priority number is categorized as below:**

Risk Priority Number (RPN)	Risk levels
1-64	**Low**
65-343	**Medium**
344-1000	**High**

RPN = Severity x Occurrence x Detection

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11.0 FREQUENCY OF RISK ANALYSIS:

Yearly

12.0 CONCLUSION:

Risk analysis data shall be written on Risk Analysis Study Report for merging of corridors, clearly stating the achievement or non-compliance of the acceptance criteria, effect of the deviations made during the Risk analysis and in case of failure, investigation carried out and their findings.

13.0 RECOMMENDATION:

Recommendation shall be written on the Risk Analysis Study Report for merging of corridors, clearly stating that there is no impact/adverse impact on the person & environment and corridors can be/Can`t be merged under recommended environmental conditions.

14.0 REFERENCES:

SOP **"Quality Risk Management"**, SOP No.: QAA/055

15.0 DOCUMENTS TO BE ATTACHED:

- Area qualification report
- Layout of G-block corridor
- Layout of F-block corridor

16.0 DEVIATION FROM PRE DEFINED SPECIFICATION, IF ANY:

Deviations from pre defined procedures & specification during merging of G-block & F-block corridor shall be investigated in accordance with CQA SOP **"Handling of Deviations"**, **SOP No. CQA/018** and shall be documented in the Risk analysis report.

17.0 CHANGE CONTROL, IF ANY:

Change control during merging of G-block & F-block corridor shall be authorized in accordance with CQA SOP **"Change Control"**, **SOP No. CQA/017** and shall be documented in the Risk analysis report.

18.0 ABBREVIATIONS:

RH : Relative Humidity
CFU : Colony Forming Unit
ISO : International Organization of Standards
FMEA : Failure Mode Effect Analysis
GMP : Good Manufacturing Practices
AHU : Air Handling Unit
HEPA : High Efficiency Particulate Air Filter
MLT : Microbial Limit Test
RPN : Risk Priority Number

19.0 Annexure:

Annexure-I

CHANGES TO BE DONE IN BLOCK 1 & BLOCK 2

S.No.	Existing Facility	Proposed Changes
Block 1 existing facility and proposed changes		
Compression		
1.	Compression Cubicle no. 15 exist (51 station)	Convert to Coating Cubicle no. 14
2.	Compression Cubicle no. 16 exist (45 station)	Convert to Coating Cubicle no. 15
3.	Compression Cubicle no. 17 exist (45 station)	Convert to Coating Cubicle no. 16
4.	Compression Cubicle no. 18 exist (20 station)	Convert to Coating Cubicle no. 17
Block 2 proposed changes		
Granulation		
1.	New Granulation Cubicle no. 12	Facility to be made (Granulation Cubicle no. 12)
2.	New Granulation Cubicle no. 13	Facility to be made (Granulation Cubicle no. 13)
3.	New Granulation Cubicle no. 14	Facility to be made (Granulation Cubicle no. 14)
Compression		
4.	New Compression Cubicle no. 15 (51 station)	Facility to be made (Compression Cubicle no. 15)
5.	New Compression Cubicle no. 16 (45 station)	Facility to be made (Compression Cubicle no. 16)
6.	New Compression Cubicle no. 17 (45 station)	Facility to be made (Compression Cubicle no. 17)
7.	New Compression Cubicle no. 18 (20 station)	Facility to be made (Compression Cubicle no. 18)