RISK ASSESSMENT FOR MISSING DETAIL OF MANUFACTURING AND EXPIRY DATE ON BLISTER

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QUALITY ASSURANCE DEPARTMENT

RISK ASSESSMENT FOR MISSING DETAIL OF MANUFACTURING AND EXPIRY DATE ON BLISTER

1. **OBJECTIVE:** The Objective of this document is to find out the risk associated with missing details of Manufacturing & Expiry date on Blister of tablets.

2. **SCOPE:** The scope of this document is limited to Manufacturing & Expiry date on Blister of tablets manufactured

3. **RESPONSIBILITY:**

Department	Responsibility
Production Team	• Review & Pre Approval of Risk Assessment Protocol cum Report. • Post Approval of Risk Assessment Protocol Cum Report.
Quality Assurance Team	• Preparation, Review, and Compilation of Risk Assessment Protocol cum Report. • Post Approval of Risk Assessment Protocol Cum Report.
Quality Control	• Review & Pre Approval of Risk Assessment Protocol cum Report • Post Approval of Risk Assessment Protocol Cum Report.

4. **REASON FOR RISK ANALYSIS:**
   - To mitigate & monitor the risk of missing of manufacturing & expiry date in blister of tablets.

5. **SITE OF STUDY:……..**

6. **RISK COMMUNICATION & TRAINING:**
   - The Risk analysis team shall be authorized by the Head-QA or his/her designee.
   - Quality Risk Management Team shall be cross functional team comprised of expert from different areas.
   - Training shall be imparted to the concerned team.

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7. RISK IDENTIFICATION, EVALUATION & MITIGATION:

Failure Modes, Effects Analysis (FMEA) is the methodology designed to identify potential failure modes for a product or process, to assess the risk associated with those failure modes, to rank the issues in terms of importance and to identify and carry out corrective actions to address the most serious concerns.

RISK IDENTIFICATION	RISK EVALUATION	RISK MITIGATION
Although Batch detail missing or miss printing does not have any risk related to health, but it is important for product identification in the market. During any complaint (counterfeit products), tracking is done through batch details.	During this pandemic situation people are continuously using sanitizer for their safety. Unknowingly they rub the strips with their wet hands resulting into smudging of printing details. Risk is low until the product is expired or any counterfeit product.	For Risk mitigation, several controls are in place. Verification is done at every stage, trained operators & qualified visual inspectors, Records are maintained at every stage.

8. RISK ASSESSMENT TOOL:

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.
Column 4	Potential Cause
Column 5	Effect of Potential Failure/Cause: Verify that whether risk have GMP impact.
Column 6	Risk Mitigation: Write the risk mitigation strategy as considered in design.
Column 7	References
Column 8/9/10/11	Severity/Occurrence/Detection/Risk level/Risk Acceptance: Risk Priority Number to be calculated by taking Severity, Occurrence & Detection of potential failure into consideration.
Column 12	Recommended action: Recommended actions should be given for controlling failure occurrence.
Column13/14/15/16	Severity/Occurrence/Detection/Risk level/Risk Acceptance: After recommendation implementations, Risk Priority Number to be calculated by taking Severity, Occurrence & Detection of potential failure into consideration.

Table 1: Instruction for each column given above

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Procedure: Risk analysis for evaluation of Manufacturing and Expiry details missing from Blister foil	Quality Risk Assessment Date: QRA No.:

S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
MATERIAL															
1.	Rubber Stereo	Improper size of rubber stereo	Improper impression on blister foil	Smudging & Miss-printing of details over Blister foil	Proper records of Stereo are maintained	• SOP "Manufacturing of Rubber Stereo" • SOP "Batch Coding/ Printing System	1	2	2	4	• Dedicated box to be arrange for placing the ink bottle and thinner in all blister machine • Rejection box shall be made which will consist of lock & key, to keep the rejected strips obtained during the initial machine setting and foil change over • Training to the concerned person shall be provided to remain vigilant towards such observation to avoid such scenario in future. • Requalification of visual inspectors shall be carried out and rotation of visual inspectors be reduced from 4 hr to 2 hr.	NA	NA	NA	NA
		Improper dilution	Solution A & B not equally prepared		Hold time established for Ink (7 days)										
		Improper setting of stereo over drum	Untrained operator		All Operators & their subordinates are qualified & trained		1	2	2	4		NA	NA	NA	NA
			Double sided tape not used				1	2	2	4		NA	NA	NA	NA
		Stereo not used	No impression		Verification of Stereo records		1	1	2	2		NA	NA	NA	NA
2.	Ink	Expired ink used	Impression not printed on Blister foil		Ink purchased from approved vendor		1	1	2	2		NA	NA	NA	NA
3.	Thinner	Spillage of thinner over printed strips	Inks used for printing are organic in nature & easily diluted by thinner or IPA (Solvent)		Dedicated box available for thinner		1	2	2	4		NA	NA	NA	NA
4.	Hand Sanitizer	Hands of operator remain wet after sanitization			Trained Operator		1	2	3	6		NA	NA	NA	NA
5.	Specimen Sample	Not verified	Miss printing missed during verification		Printing detail available in BPR & Stereo log book		1	1	1	1		NA	NA	NA	NA
					Specimen sample jointly verified by QA & production		1	1	1	1		NA	NA	NA	NA
6.	Printed Foil	Vendor not approved	Foil is of bad quality		Approved Vendor		1	1	1	1		NA	NA	NA	NA
7.	Rejection	Rejection box not available	Rejected strips mixed		Rejection box with lock & key available		1	2	3	6		NA	NA	NA	NA
METHOD															
8.	Untrained Operator	Hands after sanitization not properly dried	Wet hands result into smudging of batch coding detail	Smudging & Miss-printing of details over Blister foil	Trained Operators	•SOP "Rejection Handling Management during Packing In-Process"	1	2	3	6		NA	NA	NA	NA
		Spillage of thinner by	Smudging of batch coding details				1	2	3	6		NA	NA	NA	NA

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S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
		mistake		Smudging & Miss-printing of details over Blister foil	Trained Operators	•SOP "Rejection Handling Management during Packing In-Process" •SOP for "Training of Employees" •SOP "Qualification Challenge Test of Visual Inspector" •SOP No.: "Visual Inspector Qualification For Parenteral Products"					• List of visual inspectors shall be displayed in packing area. • During the initial machine setting and foil change over, the window between the primary and secondary area shall be kept close so as to avoid such observation. Training shall be imparted for the same. • Before entering in to primary and secondary packing area, Instruction display shall be holded in change rooms to ensure hand should be dried off completely. Training shall be provided for the same.				
		Rubber Stereo not adequately set	May be displaced				1	2	1	2		NA	NA	NA	NA
		Batch code missed during initial setting	Possibility of less no. of rubber stereos set over printed foil				1	2	1	2		NA	NA	NA	NA
		Specimen sample not collected	Miss printing missed out				1	1	1	1		NA	NA	NA	NA
		Rejected strips not removed after break	Mixed with normal strips				1	2	3	6		NA	NA	NA	NA
		Hopper loaded before verifying printing	Miss printed blister strips packed				1	1	1	1		NA	NA	NA	NA
9.	Untrained Visual Inspector	Missed out defective blister strips	Weak eye sight				1	2	3	6		NA	NA	NA	NA
			Un-attentiveness				1	2	3	6		NA	NA	NA	NA
			Untrained				1	2	3	6		NA	NA	NA	NA
10.	Documentation	SOP not followed	Stereo not manufactured as per SOP		SOP in place		1	1	3	3		NA	NA	NA	NA
			Batch coding not done as per batch detail		BPR in place		1	2	1	2		NA	NA	NA	NA
11.	Batch Coding	Wrong batch detail	Untrained Operator		Verification done at every stage by QA & Production		1	2	2	4		NA	NA	NA	NA
12.	Thinner Spillage	Printing detail got smudged	Printing detail not readable or removed		Separate box available for Ink & Thinner		1	2	1	2		NA	NA	NA	NA
13.	Sanitization	Hand sanitizer used frequently	Ink dilute with hand sanitizer		Persons are well trained and aware about practices		1	2	3	6		NA	NA	NA	NA
14.	Ink & thinner	Unavailability of dedicated boxes for Ink & thinner	Ink & thinner will mix up and used or spill by mistake		Dedicated boxes available for thinner & Ink and as per practice kept separately		1	2	3	6		NA	NA	NA	NA
15.	Rejection Box	Unavailability of rejection box	Rejected Strip further forwarded for Secondary packing		Separate Rejection boxes are available and as per practice rejected strips are kept in rejected box after any break		1	2	3	6		NA	NA	NA	NA
16.	Initial Verification	Initial Verification not done	Missed to do initial verification		Printing detail on plain foils verified before running blister machine	•Verification records	1	1	1	1		NA	NA	NA	NA

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S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
17.	Printing Detail	Wrong printing detail	Wrong stereo prepared	Smudging & Miss-printing of details over Blister foil		•BPR	1	2	1	2		NA	NA	NA	NA
18.	Previous complaint	Same complaint accelerated previously also	Improper CAPA of previous complaints		Till now 95 batches manufactured and no any such complaint received	•SOP "Packing In-process"	1	1	1	1		NA	NA	NA	NA
19.	Current Practices	Hand Sanitization	Frequently hands are sanitized due to covid-19 pandemic		As per instructions, hands are sanitized before going for machine operation activities		1	2	3	6		NA	NA	NA	NA
		Initial machine setting	Stereo drum or stereo not properly set initially		Verification of strips detail done after initial setting		1	2	1	2		NA	NA	NA	NA
		Lunch Break	Defective strips remains in web during lunch break & used in packing		Instructions are given to reject those strips which remains in web after a break		1	2	3	6		NA	NA	NA	NA
		Stage wise verification	Stage wise verification not done		Verification part is documented after every stage		1	1	1	1		NA	NA	NA	NA
		Specimen sample collection	Specimen sample not collected or attached in BPR for reference		Specimen sample is attached with BPR for reference purpose & stereo are returned and their rejection record is maintained for tracking purpose.		1	1	1	1		NA	NA	NA	NA
		Thinner used in area	Too much thinner used		Trained operator		1	2	3	6		NA	NA	NA	NA
		Window/Hatch not closed during break & initial setting	Window/Hatch used for segregation of primary & secondary packing area remains open during lunch break or initial setting resulting into mixing od defected strips with rejected strips		Hatch is closed as a part of practice during any break		1	2	3	6		NA	NA	NA	NA
20.	Terminal Inspection	Terminal Inspection not done	Random terminal inspection not done		Terminal inspection is done for each product and documented		1	1	1	1		NA	NA	NA	NA
MAN															
21.	Training	Persons not trained	Operators, their subordinates and visual inspectors not properly		Training given to all related persons	• SOP "Training of Employees"	1	2	3	6	Low Risk	NA	NA	NA	NA

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S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
			trained												
22.	Practices	Current practices not followed	Current verification practices not followed during different stages		Verification practices are a part of documentation		1	2	3	6		NA	NA	NA	NA
23.	Customer	Customer sanitize the strip	Customer used wet hand during receiving strip from pharmacist resulting into smudging of printed details	Smudging & Miss-printing of details over Blister foil	No control		**1**	**3**	**3**	**9**	**Severity:** Risk level related to severity is low, as it is not related to health **Occurrence:** Possibility of Occurrence is high, as there is no control outside the site **Detectability:** There is no method of failure detection, only controls are available at site level & recommendations can be given	NA	NA	NA	NA
24.	Packing Verification	Strips not verified during packing	Strips missed for detail verification during primary & secondary packing		Verification is a part of documentation		1	2	3	6	Low Risk	NA	NA	NA	NA
25.	Visual Inspectors	Untrained visual inspectors	Didn't aware about the critical aspects of packing		Rotation is done after every 4 hours		1	2	3	6		NA	NA	NA	NA
		Too hectic schedule	Tired of being continuous working resulting into missing of rejected strips				1	2	3	6		NA	NA	NA	NA
26.	Vendor	Ink & foil quality improper	Ink & foil is of low quality resulting into temporary impression		Approved Vendor		1	1	1	1		NA	NA	NA	NA
MEASUREMENT															
27.	Break	Strip kept in web & forwarded for secondary	Rejected strips mixed with proper strips	Smudging & Miss-printing of details over Blister foil	As per the practices, Strips are rejected and kept in rejection box after any break	• SOP "Rejection Handling Management	1	2	3	6	Low Risk	NA	NA	NA	NA

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S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
		packing				During Packing in Process"									
28.	In-Process checks	Strips not verified during in-process	Rejected strips missed by the checkers		In-process checks are part of documentation and are done after every 1 hour.	• SOP "Batch Coding Printing System"	1	2	3	6		NA	NA	NA	NA
29.	Camera System	Camera not verify the printing defects	Camera not verified the printing details		Camera system required for verification of any printing defect		1	2	3	6		NA	NA	NA	NA
30.	Sufficient Number of persons	Sufficient persons not available	Insufficient number of visual inspectors		Complete strips are verified by sufficient checkers		1	2	3	6		NA	NA	NA	NA
31.	Dilution of Ink	Ink not diluted properly	Ink not properly mixed		Trained operators perform the activity of ink preparation		1	2	3	6		NA	NA	NA	NA
32.	Frequency of Qualifying Visual Inspectors	Visual inspectors not qualified as per schedule	Unqualified Visual inspectors missed the rejected strips		Visual inspectors are qualified as per schedule		1	1	1	1		NA	NA	NA	NA
33.	Product Expiry	Expired product may be used	Expiry cannot be identified	Health issue	Expiry date can be tracked through carton		3	2	1	6	Severity is high in case expired product used by patient, but overall risk is low as expiry can be tracked through Carton	NA	NA	NA	NA
MACHINE															
34.	Initial Machine Setting	Improper initial setting of machine	Stereo not properly in lined with drum	Smudging & Miss-printing of details over Blister foil	Strips are verified and documented during initial machine setting	• SOP "Plant Equipment Preventive Maintenance"	1	2	1	2	Low Risk	NA	NA	NA	NA
35.	Stereo Drum	Stereo Drum not properly set	Loose Stereo drum				1	2	1	2		NA	NA	NA	NA
36.	Initial Challenge	Challenge test not performed for printing detail	Initial challenge test not performed				1	2	1	2		NA	NA	NA	NA
37.	Breakdown	Machine run after breakdown	Rejected strips remained in web after a break & mixed with good strips		Separate rejection box is available for strips generated after a break		1	2	3	6		NA	NA	NA	NA
38.	Preventive Maintenance	Scheduled Preventive maintenance not	Machine not working properly due to missing of preventive maintenance		Preventive maintenance done as per schedule and records maintained		1	1	1	1		NA	NA	NA	NA

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S.No.	Item/Function	Potential failure mode	Potential Cause/Mechanism of Failure	Potential Effect of Failure	Current control	Reference	S	O	D	Risk Priority number	Recommended actions (if any)	Post Risk			
												S	O	D	RPN S*O*D
		done													
39.	Qualification	Blister packing machine not qualified	Unqualified Blister machine not work properly		Qualification done as per schedule and records maintained		1	1	1	1		NA	NA	NA	NA
MILEU															
40.	Covid 19 pandemic	Continue hand sanitization	As ink used is organic in nature and got dissolved in solvent	Smudging & Miss-printing of details over Blister foil	Persons are instructed to dry their hands before going for machine operation	• SOP "Rejection Handling Management During Packing in Process"	1	2	3	6	Low Risk	NA	NA	NA	NA
41.	Window/Hatch	Window/Hatch opened during break	Rejected strips mixed with good strips when hatch remain opened during break		Window/Hatch are always closed as per practice in case of any break		1	2	3	6		NA	NA	NA	NA
42.	Material Storage	Foil, Ink or thinner not properly stored	Temperature/RH reaches high in primary packing storage area		Proper area is maintained for storage of foil etc.		1	1	2	2		NA	NA	NA	NA
43.	Light Intensity	Light intensity not proper for online verification	Detail not visible	Missed critical details	Light intensity verified during qualification	•SOP "Monitoring of Light Intensity of Visual Booth"	1	1	2	2		NA	NA	NA	NA

Table 2: The above table shows Potential failure mode, effect of potential failure along with Risk Probable Number, Risk Mitigation & Recommended Actions.

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Assessment of Severity, Occurrence and Detection			
Severity Effect	**Likelihood Occurrence**	**Likelihood of Detection**	**Rating**
No Effect	Unlikely	Always Detected	1
Moderate Effect	Possible	Might Detect Failure	2
Serious Effect	Almost Certain (every time)	Lack of Detection Control	3

Evaluation of RPN	
RPN Rating	**Category**
12 to 27	High
7 to 11	Medium
Upto 6	Low

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9. CONCLUSION: After evaluation, it is concluded that the risk related to missing printing detail is moderate and does not have any impact on persons health (except counterfeit product or expired product), It is the first time, such type of complaint is received, it may be due to current pandemic situation, people are using sanitizers continuously whether outside or inside premises of company and knowingly or unknowingly touch the strips with wet hands resulting into smudging of the printed matter.

10. RECOMMENDATION: On the basis of above conclusion, following are the recommendations for better controls.

- Dedicated box to be arrange for placing the ink bottle and thinner in all blister machine
- Rejection box shall be made which will consist of lock & key, to keep the rejected strips obtained during the initial machine setting and foil change over
- Training to the concerned person shall be provided to remain vigilant towards such observation to avoid such scenario in future.
- Requalification of visual inspectors shall be carried out and rotation of visual inspectors be reduced from 4 hr. to 2 hr.
- List of visual inspectors shall be display in packing area.
- During the initial machine setting and foil change over, the window between the primary and secondary area shall be kept close so as to avoid such observation. Training shall be imparted for the same.
- Before entering in to primary and secondary packing area, Instruction display shall be holded in change rooms to ensure hand should be dried off completely. Training shall be provided for the same.

11. REFERENCES:

- Reference SOP of Risk Assessment.
- Related SOP's.

12. DOCUMENTS TO BE ATTACHED:

- Related documents.

13. DEVIATION FROM PRE DEFINED SPECIFICATION, IF ANY:

Deviations from the pre-defined acceptance criteria observed in accordance with QA SOP **"Handling of Deviations"**, shall be documented in the Risk analysis Protocol cum report.

14. CHANGE CONTROL, IF ANY:

Change control observed in accordance with QA SOP **"Change Management"**, shall be documented in the Risk analysis Protocol cum report.

15. ABBREVIATIONS:

FMEA	: Failure Mode Effect Analysis
RPN	: Risk Priority Number
CAPA	: Corrective action preventive action
WHO	: World health organization

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16. REPORT APPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OPERATING MANAGER (QUALITY ASSURANCE)			
HEAD (PRODUCTION)			

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			