QUALITY RISK ASSESSMENT & MITIGATION PLAN

(FAILURE MODE EFFECT ANALYSIS FOR WRONG BATCH CODING ON AMPOULE LABELS

QUALITY RISK ASSESSMENT & MITIGATION PLAN

FAILURE MODE EFFECT ANALYSIS FOR WRONG BATCH CODING ON AMPOULE LABELS

Reference Document No.:	Risk Assessment No.:

1. **OBJECTIVE:** To provide the documented evidence that there is low level of risk in batch coding of Ampoule labels.

2. **SCOPE:** The scope of this document is limited to batch coding of Ampoule labels at ……..facility.

3. **RESPONSIBILITY:**

Department	Responsibility
Quality Assurance	• Preparation, Review, and Compilation of FMEA • Post Approval of FMEA
Production	• Review of FMEA
Engineering	• Review of FMEA

4. **REASON FOR RISK ANALYSIS:**
To mitigate & monitor the risk associated with the batch coding of Ampoules.

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.

7. **RISK IDENTIFICATION, EVALUATION & MITIGATION:** In Pharmaceuticals, Batch coding is the process of adding an identifying code i.e. Batch number, typically made up of a selection of letters and numbers, Date of manufacturing, Date of Expiry and MRP on product Cartons and Container closure systems (Blisters, Ampoules, Three Pieces, FFS & LVP).
   The addition of batch numbers to pharmaceutical products enable companies to quickly trace their products wherever they are in the world in the event of a recall; and help to protect supply chain integrity by quickly identifying whether a product is a counterfeit.
   Further Manufacturing & Expiry Drug expiration dates reflect the time period during which the product is known to remain stable, which means it retains its strength, quality, and purity when it is stored according to its labeled storage conditions.
   In case of failure of any batch coding detail (Batch No., Mfg. Date, Expiry Date and Maximum Retail Price) in a product may leads to failure of its identity (in case of wrong batch number), stability (in case of wrong manufacturing & wrong expiry), customer dissatisfaction & legal action (in case of wrong MRP).
   To avoid such type of issues in future, a quantitative risk assessment (Objective)is performed by using FMEA tool.A risk probable number is being evaluated along with the mitigation plan and recommendations.

   Product Detail: …… Ampoules
   Batch No.: ……..
   Manufacturing Date: 01/2024
   Expiry Date: 12/2026
   Observation: Wrong Expiry Date 01/2024 instead of 21/2026

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RISK IDENTIFICATION	RISK EVALUATION	RISK MITIGATION
Wrong Expiry date may result into wrong usage interpretation. As per the above observation, the product expires one month before its manufacturing, which is not possible, this shows lack of mitigation plans at packing site during batch coding of labels.	There is no risk seems related to patient health, but if interpreted with the given batch detail, the product is already expired before manufacturing. Although the blister packing gives right information about the expiry date i.e. 01/2026. Manufacturing and Expiry gives the shelf life of product itself and such type of misleading details leads to market complaints and customer dissatisfaction.	Although written procedures are available& batch coding details are verified manually, but seems not effective, hence automizations required to avoid manual interference. PLC validation is required to avoid any unwanted access without QA approval & Camera shall be installed so that each and every batch coding detail shall be verified.

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	Effect of Potential Failure/Cause: Verify that whether risk have GMP impact.
Column 5	Potential Cause
Column 6	Risk Mitigation as a Current Control: 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

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

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Reference Document No.:	**Risk Assessment No.:**

QRA No.: ……..

Name of Facility / Equipment / Utility / System / Activity / Procedure / Unit Operation: Risk Assessment for Wrong Batch Coding on Ampoule labels	**Quality Risk Assessment Date: ……**

S.No.	Item / Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference Document No.	S	O	D	Risk Priority Number (S*O*D)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN S*O*D
1.	Man	• Untrained person • Unauthorized access to the machine	• Wrong coded / without coding labels • Malfunctioning of coding machine.	• Improper / wrong coding verifications by untrained / Unauthorized employee • User levels of machine not mapped. • Unauthorized access to machine settings	• SOP Trainings provided to persons. • List of authorized persons available with user privilege rights. Only listed persons can access the coding machine. • 2 user levels are protected in machine. i.e. setting level & service level. • Recipe addition and deletion done by Production supervisor and specimen label verified jointly by production and QA	• SOP No.: "Training of Employees" • SOP No.: "Access Control & Password policy for Automated systems/equipment"	**3**	**2**	**2**	**12** **Severity:** High severity in case of wrong manufacturing or expiry as it does gives wrong information about the shelf life of product. **Occurrence:** Possible as unauthorized access is given to the untrained persons & there is no control of QA during recipe feeding. **Detectability:** Might detect failure, as detection failure is possible in case of change in label roll in between the Ampoule coding.	SOP No.: "Operation and Cleaning of Label Printing and Rewinding" has been revised and the passwords of batch printing machine (Setting/ service) has been implemented, final approval shall be taken by QA &further List has been updated.	**3**	**1**	**1**	**3** **Severity:** Severity of failure remains high **Occurrence:** SOP No.: HPI/023 has been revised and role of QA implemented
2.	Material	• Inappropriate/	• Wrong or	• Coding not possible due	• Labels procured from	SOP No.:	**3**	**1**	**2**	**6**	Low risk hence	N	N	N	NA

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S.No.	Item / Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference Document No.	S	O	D	Risk Priority Number (S*O*D)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN S*O*D
		Unapproved label • Labels of low quality or coding details not readable	incomplete information on coded labels • Wrong interpretation about coding details	to inadequate space for coding on labels • Ink used not compatible with label • Improper coding with low visibility	approved vendors. Procedures available at site that only labels approved from QC are issued to production department • Ink is compatible with labels, no complaint received related to ink diffusion of diffused details	"Handling & Storage of printed labels"				**Severity:** Miss printed labels may be miss interpreted resulting into wrong information **Occurrence:** Till now no any complaint received related to diffused printing **Detectability:** Might detect failure in case the incident of ink diffusion happens in between the coding activity.	no recommendation	A	A	A	
3.	Method	• Poor printing quality • Damaged labels • Power failure during machine operation • Wrong coding on label	• Market complaint • Wrong coding detail	• Procedure not available for machine operation. • Procedure not available for handling of power failure in label coding machine. • Procedure for in process check for label over printing is not available or inadequate procedure for specimen verification of label at	• Procedure available at site for operation and cleaning of Label Printing and Rewinding Machine • Uninterrupted power supply available with label Printing and Rewinding Machine • As per BPR, the frequency for in-process check for label over printing is initially & after every one hour by Production & QA	SOP No.: "Operation and Cleaning of Label Printing and Rewinding"	**3**	**2**	**2**	**12** **Severity:** Severity is high in case of wrong label coding done & missed after change over, resulting into market complaint **Occurrence:** Chance of Occurrence is possible during product change over, as recipe of	SOP No.: "Product Packing Operation in Parenteral blocks" shall be revised to include action items w.r.t verification of message in case of change over & shall be addressed by deviation.	**3**	**1**	**1**	**3** **Severity:** Severity of label coding remains high in case of any failure **Occurrence:** Chance of failure reduced to low, as verification of label roll implemented at

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S.No.	Item / Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference Document No.	S	O	D	Risk Priority Number (S*O*D)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN S*O*D
		• Improper handling of rejected labels • Unscheduled and sudden batch Change overs.		initial, middle & end of label roll. • Procedure for Lock & Key arrangement for rejected labels not in place. • No defined Procedure for handling of Unscheduled and sudden batch Change overs.	alternatively.	• SOP No.: "Operation and Cleaning of Label Printing and Rewinding" • SOP No.: "Operation and Cleaning of External Ampoule Washing"				batch detail is again feed for previous product **Detectability:** There might be the chance that the wrong coding detail missed during verification	SOP No.: "Operation and Cleaning of Label Printing and Rewinding" Shall be revised to incorporate recipe details entered by production and jointly verified by QA during initial, machine stoppage and power failure or any breakdown. During ampoule label coding, Crate shall be provided with lock and key provision in label printing room for handling of rejections of label printing. SOP No.: "Product Packing Operation in Parenteral blocks" shall be revised to include				the initial, middle & at the end of the label coding, further recipe verification to be done after every change over or breakdown along with lock & key provision for rejected labels. **Detection:** Possibility of detection of any failure during coding activity has been increased by implementing related SOP's and related controls

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Reference Document No.: | **Risk Assessment No.:**

S.No.	Item / Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference Document No.	S	O	D	Risk Priority Number (S*O*D)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN S*O*D
											the same. In case, if there is need of change over in between the running batch, same shall be addressed through deviation.				
4.	Machine	• Machine is not qualified. • Machine Breakdown • Ampoule labelling machine does not have 100 % inspection system for coding defects causes miscoding, wrong coding, overlapping of coding & smudging.	• Ampoule printing machine is not able to give consistent and reproducible results • Market complaint	• Procedure for Machine qualification/ requalification is not in place. • Procedure for Preventive maintenance is not in place • Labels without coding/ misprinting/wrong coding can be passed.	• Procedure of requalification is in place • Procedure of Preventive maintenance is available at site. • During coding, Labels checked manually for overprinted details.	• SOP No.: "Operation and Cleaning of Label Printing and Rewinding" • SOP No.: "Preventive Maintenance of Equipment machines"	**3**	**2**	**3**	**18** **Severity:** Smudged or miscoding coding may result into market complaint & wrong coding detail interpretation **Occurrence:** Failure chance is possible as 100% label inspection is not possible by machine **Detectability:** No any detection system is available in machine to check wrong coding	Password protection rights shall be given to QA PLC validation shall be done Camera inspection system is recommended to check 100% of the over coded labels.	**3**	**1**	**2**	**6** **Severity:** Severity remains high until PLC validation & camera installation done **Occurrence:** Chance of failure reduced related SOP's revised and controls (Password protection along with coding of roll verification) implemented **Detectability:** After

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Reference Document No.: | **Risk Assessment No.:**

S.No.	Item / Function	Potential Failure Mode (Failure Mode)	Potential Effect of Failure	Potential Cause/ Mechanism of Failure	Current Control	Reference Document No.	S	O	D	Risk Priority Number (S*O*D)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN S*O*D
															installation of camera & PLC validation, the detectability of coding failure will be increased, till then there might be the chance of failure.

Where: S=Severity; O=Occurrence Probability; D=Detection

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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S.No.	Recommended Action	Responsible Person	Target Date of Completion
1.	The passwords i.e. Setting and Services of batch printing machine shall be with QA department only. Setting Section In-charge QA/Executive QA/Officer QA. Services - Head QA/ Designee The Admin password shall remain with equipment manufacturer. QA person will login the system and after login by QA, initial recipe setting shall be done by Production. The set recipe details shall be cross verified by QA Executive / designee and also during breakdowns and machine stoppage during lunch/tea breaks. The SOP titled "Operation and Cleaning of Label Printing and Rewinding Machine" shall be revised to include the same.		
2.	PLC Validation & Camera Inspection System installation shall be implemented in Ampoule labelling machine to ensure 100% verification of batch coding details towards automization.		
3.	The SOP titled "Product Packing Operation in Parenteral blocks" shall be revised to include the instruction to proceed continuously without any change over to other batch. In case, if there is need of change over in between the running batch, same shall be addressed through deviation.		
4.	The SOP titled "Operation and Cleaning of Label Printing and Rewinding Machine" and SOP titled "Operation and Cleaning of External Ampoule Washing, Drying & Labeling Machine" shall be revised to include verification of label specimen from initial, middle and end stage of each label roll during label coding and during ampoule labelling which shall be affixed in BPR.		
5.	During ampoule label coding, Crate shall be provided with lock and key provision in label printing room for handling of rejections of label printing.		

CAPA (Required/Not Required): Required
If required, mention CAPA No.: ……..

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Reference Document No.:	Risk Assessment No.:

Quality Risk Management Team			Reviewed By Head Operations (Sign & Date)	Approved By Head QA (Sign & Date)
Name	Department	Sign & Date		

Verification of Recommended Action:

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Remarks (if any):

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Verified By
Operating Person QA
(Sign & Date)

Approved By
Head QA
(Sign & Date)

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Reference Document No.:	**Risk Assessment No.:**

9. CONCLUSION:

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10. REFERENCES:

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

11. DOCUMENTS TO BE ATTACHED:

- Not Applicable

12. DEVIATION FROM PRE DEFINED SPECIFICATION, IF ANY:

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13. CHANGE CONTROL, IF ANY:

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14. ABBREVIATIONS:

FMEA	: Failure Mode Effect Analysis
RPN	: Risk Priority Number
CAPA	: Corrective action preventive action
SOP	: Standard Operating Procedure
QRM	: Quality Risk Management
QA	: Quality Assurance
ID	: Identification
MRP	: Maximum Retail Price
FFS	: Filling Forming Sealing
LVP	: Large Volume Parenteral
PLC	: Programmable Logic Controller
GMP	: Good Manufacturing Practices

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15. FMEA APPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OPERATING PERSON (QUALITY ASSURANCE)			

REVIEWED BY:

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

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			