QUALITY RISK ASSESSMENT & MITIGATION PLAN	
FAILURE MODE EFFECT ANALYSIS FOR MIXING OF CARTONS	
Reference Document No.:	**Risk Assessment No.:**

QUALITY RISK ASSESSMENT & MITIGATION PLAN

(FAILURE MODE EFFECT ANALYSIS FOR MIXING OF CARTONS)

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FAILURE MODE EFFECT ANALYSIS FOR MIXING OF CARTONS

Reference Document No.:	Risk Assessment No.:

1. **OBJECTIVE:** To provide the documented evidence that there is low level of risk in case of "Mixing of Cartons".

2. **SCOPE:** The scope of this document is limited to Carton mixing at ……. facility.

3. **RESPONSIBILITY:**

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

4. **REASON FOR RISK ANALYSIS:**

To mitigate & monitor the risk associated with the mixing of cartons.

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:

INTRODUCTION: Carton mix up is the contamination of one product with another product by human Errors, inadequate process or plant design. It depends upon the nature of mixing which decides whether the complaint is Critical, Major or Minor.

CARTON MIXING CAN BE CONSIDERED 04 TYPES:

1. **Carton of same product with different batch nos.:** Change in batch no. does not have any impact on product quality.
2. **Carton of different products with same content & claim:** Same API claim does not impact the product quality,
3. **Carton of different products with different content & claim:** Different content with different claim may have severe impact on health.
4. **Carton of same product with different label claim:** Two type of mixing can be considered i.e. Carton depicting higher claim while inside strips with lower claim & vice versa. In both cases, if by taken by mistake, the medicine will either loose its effectiveness or will overdose.

As …… & …….. tablets are used in the treatment of Overactive bladder (OAB) symptoms. OAB is a collection of urinary symptoms, including frequent urination, urgent need to urinate, and inability to control urination.

……: Dosage: PO qDay means maximum daily dose of 75 mg for ……..& 15 mg for …….

…….: Dosage: PO qDay means maximum daily dose of 150 mg for …… & 15 mg for ……..

Note: *po (per os) means "by mouth" pc (post cibum) means "after meals" prn (pro re nata) means "as needed" q3h (quaque 3 hora) means "every three hours" qd (quaque die) means "every day"*

Hypothetically if incase of carton mixing, if …….. is given thrice a day considering carton claim of …….. then also it will be effective as per the minimum dose per day (…….. maximum daily dose for …… and will not have any severe health impact.

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RISK IDENTIFICATION	RISK EVALUATION	RISK MITIGATION
Carton mixing may be 04 types: 1. Carton of same products with different batch nos. 2. Carton of different products with same content & claim. **3. Carton of different products with different content & claim.** 4. Carton of same product with different label claim.	**Criticality of mixing of cartons depends on type of carton mixing:** 1. Mixing of same Cartons with different batch nos. having same claim & content does not have any impact on product quality. 2. Mixing of cartons of different products with same content & claim have product identity problem. 3. **Mixing of different cartons with different content & claim comes under critical observation& may lead to severe impact on health**. 4. Mixing of carton of same product with different label claim may or may not have impact, it depends on mixing potency.	• Packing materials are stored in separate racks. • Primary & Secondary material are stored separately. • Line clearance procedure is followed before start the overprinting & packing. • Overprinting on Carton/Catch covers/labels is done batch wise, only one product at a time. • Different product are not packed in close proximity unless there is proper physical segregation. • Outdate, obsolete and rejected packaging materials are destroyed and records are maintained. • Persons doing visual inspection are trained to perform their activities. • Proper design of flow of material.

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

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

Name of Facility/Equipment/Utility/System/Activity/Procedure/Unit Operation: Carton mix-up | **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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
1.	Carton mix-up	Carton mixing at vendor end	Mixed Carton reach to receiving area	Mixed cartons received	• Vendor qualification done on dated.	SOP No.: "Receipt Handling and Storage of Packing Materials" SOP No.: "Dispensing of Packing Materials" SOP No.: 'Line Clearance" SOP No.: "Operation and Cleaning of Autocartonator" SOP No.: "Operation and Cleaning of Packing Conveyor"	1	2	2	4 **Severity:** Severity of carton mix up from vendor end is of low category as checks are sufficient in further stages to control the carton mixing. **Occurrence:** Mix up of cartons from vendor side is possible **Detection:**100% verification is not possible	• Dispensed material shall be kept in lock and key. • Vendor audit shall be conducted for this issue of carton mixing. • The overprinting of cartons having same size, colour, shape and layout shall be coded in different area,	NA	NA	NA	NA
2.		Carton mix-up during packing material receipt	Missed cartons may reach to packing storage area.	• Material receipt procedure not available.	• SOP for Receipt, Handling and Storage of Packing Materials (SOP	SOP No.: "Qualificatio	1	2	2	4 **Severity:** Severity of		NA	NA	NA	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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
				• Material receipt through manual procedure. • Material receipt checklist not available.	No. ……..) is in place. • Material receipt procedure done through SAP. • Material receipt checklist is in place, during material receipt following check point verified. ➢ E-way bill of the consignment. ➢ Appropriateness of company address on the delivery documents. ➢ Approved Manufacturer / Supplier address with AVL (Approved Vendor List). ➢ Availability of Vendor Certificate of Analysis copy. ➢ Reference of Purchase Order number on the documents. ➢ Description of the material in purchase order tallies with consignment delivery document etc.	n Challenge Test of Visual Inspector" SOP No.: "Production Process Control"				carton mix up during packing material receipt is of low category as checks are sufficient in further stages to control the carton mixing. **Occurrence:** Mix up of cartons during receipt is possible as 100% cartons are not verified. **Detection:** 100% verification is not possible	machines and in different period to avoid such type mix-up in future batches. SOP No. (Production process and control) shall be enhanced for better control. • Revised the SOP (Production process and control) and				

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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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
3.		Carton mix-up during packing material storage	Carton will be forwarded for Dispensing	• Material storage procedure not available.	• SOP for Receipt, Handling and Storage of Packing Materials (SOP No. HWH-010) is in place. • Warehouse officer/Executive shall take the daily incoming from SAP and shall entered rack No.in work sheet. • Warehouse person shall enter all noted inventory in SAP bin location. • After release in SAP all type approved packaging material transfer to dedicated location and enters details in SAP for Bin Location updating.		1	2	2	4 **Severity:**Severity of carton mix up during packing material storage is of low category as checks are sufficient in further stages to control the carton mixing. **Occurrence:**Mix up of cartons during storage is possible in case separator is not available or not properly arranged. **Detection:** 100% verification is not done during storage	mentioned the clause that the cartons of same colour, size, shape and layout shall be procured from alternate vendor. Freeze the vendor in SAP for similar looking cartons to avoid the mix up and same shall be also mentioned in SOP.	NA	NA	NA	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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
4.		Carton mix-up during dispensing packing material.	• Mixed Carton will reach to coding area	• Line Clearance procedure not available. • Dispensing of packing Material procedure not available. • Dispensing done without "Packing Material Issue Slip". • Procedure for printing of material identification slip not available. • Issuance of additional packing materials through Manual procedure.	• SOP for Dispensing of Packing Materials (SOP No. …….) is in place. • All dispensing activity of packing material done through SAP generated packing material issue slip. There is well defining procedure for generation of packing material issue slip in SOP. • Material identification slip generated through SAP with pre-printed quantity as per batch packing material issue slip. There is well defining procedure for printing of material identification slip in SOP. • Issuance of additional packing materials activity done through SAP generated packing material issue slip. There is well defining procedure for generation of packing material issue slip in SOP		1	2	2	4 **Severity:** Severity of carton mix up during dispensing of packing material storage is of low category as checks are sufficient in further stages to control the carton mixing. **Occurrence:**100% cartons are not verified during dispensing. **Detection:**100 % verification is not done	• The list of the cartons of same color, size, shape and layout with different strength shall be prepared for proper identification and to avoid the carton mix-ups. • 100% inspection shall be done after dispensing and 100%	NA	NA	NA	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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
5.		Carton mix-up during Batch coding.	Mixed carton will reach to Secondary packing area	• Line clearance procedure not available. • Batch Coding done without verification of material. • Reconciliation procedure of dispensed material procedure not available. • Procedure for storage of printed carton not available. • The process of carton over coding is manual process and during the process the person might have missed the carton, mistakenly due to same size, shape and layout and similar color except for difference in brand name as it is a continuous online process and there may be possibility that one such carton could have been missed.	• SOP for Batch Coding / Printing System is in place. • SOP having well defines procedure for line clearance of coding/ printing area. • As per SOP two step verification (Doer and checker) procedure by production and QA is in place. • Production person shall make the request for the overprinted cartons of the required batch as per production plan in log book. • After completion of the coding of the cartons, store in separate rack with status label and make entries in log book. • Reconciliation procedure of dispensed material is part of BPR and after completion of reconciliation product transfer for further stage. • Container color code procedure available for handling of different type of material such as good and reject material in SOP. Blue colure container used for storage of good		1	2	2	4 **Severity:** Severity of carton mix up during batch coding is of low category as checks are sufficient in further stages to control the carton mixing. **Occurrence:** Mix up can be missed During batch coding, if cartons are of same type or design. **Detection:**100 % verification is not possible	inspection shall be done after overprinting of cartons. • Proposal for online carton coding and Camera detection system for improved controls. • Re-qualification of visual inspector shall be done as per SOP (Qualification Challenge Test of Visual	NA	NA	NA	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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
					carton and Red color container used for reject carton.						Inspector) and revise the rejection album accordingly				
6.		Carton mix-up during secondary packing area.	• Market Complaint • If prescribed, may lead to health issue	• Line clearance procedure not available. • After carton packing verification procedure not available. • Handling of similar looking material procedure not available. • Visual Inspectors not trained. • Proper training not available.	• SOP for Line clearance procedure (SOP No. …….) is in place. • SOP for operation & cleaning of auto cartonator (SOP No. ……..) is in place. • SOP for operation & cleaning of packing conveyor (SOP No. ……) is in place. • SOP having well defines procedure for line clearance of secondary packing area and equipment's. • As per SOP two step verification (Doer and checker) procedure by production and QA is in place. • Procedure for online inspection after carton packing is in place. • Packed carton verification done by		3	2	2	12 **Severity:** Severity of carton mix up during secondary packing is of high category as during secondary packing, final check of each carton is done during online visual inspection. In case of online failure (carton mixing not verified) then the severity can be high. Because further only terminal		1	2	2	4 Severity decreases after completion of recommendations

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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	RPN (SxOxD)	Recommended Actions (if any)	Post Risk Evaluation			
												S	O	D	RPN SxOxD
					qualified inspector. • SOP for Qualification and Challenge Test of Visual Inspector (SOP No. ……) is in place. • SOP for Production Process and Control (SOP No. ……..) having procedure for Similar looking products shall not be packed on adjacent secondary packing lines. • Remaining pack stocks of Cartons are reviewed. • Control Samples are reviewed.					inspection is done which does not cover 100% carton inspection. **Occurrence:** Chance of missing the carton mixing during online monitoring is possible incase visual inspectors are not properly trained. **Detection:** 100% verification is possible in case of trained visual inspectors but in case of same designed cartons, chance of error is there.					

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

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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
Up to 6	Low

S.No.	Recommended Action	Responsible Person	Target Date of Completion
1.	The Dispensed material shall be kept in lock & key.		
3.	Vendor audit shall be conducted for this issue of carton mixing.		
4.	The overprinting of cartons having same size, colour, shape and layout shall be coded in different area, machines and in different period to avoid such type mix-up in future batches. SOP (Production process and control) shall be enhanced for better control.		
5.	Revised the SOP (Production process and control) and mentioned the clause that the cartons of same colour, size, shape and layout shall be procured from alternate vendor. Freeze the vendor in SAP for similar looking cartons to avoid the mix up and same shall be also mentioned in SOP**.**		
6.	The list of the cartons of same color, size, shape and layout with different strength shall be prepared for proper identification and to avoid the carton mix-ups.		
7.	100% inspection shall be done after dispensing and 100% inspection shall be done after overprinting of cartons.		
8.	Proposal for online carton coding and Camera detection system for improved controls.		
9.	Re-qualification of visual inspector shall be done as per SOP (Qualification Challenge Test of Visual Inspector) and revise the rejection album accordingly.		

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CAPA (Required/Not Required): Required
If required, mention CAPA 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:

……

……

……

Remarks (if any):

……

……

……

……

……

Verified By
Operating Person QA
(Sign & Date)

Approved By
Head QA
(Sign & Date)

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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
PO qday	: po (per os) means "by mouth" pc (post cibum) means "after meals" prn (pro re nata) means "as needed" q3h (quaque 3 hora) means "every three hours" qd (quaque die) means "every day"

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15. FMEAAPPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OPERATING PERSON (QUALITY ASSURANCE)			

REVIEWED BY:

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

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			