RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

PROTOCOL CUM REPORT CONTENTS

S.No.	TITLE	PAGE No.
1.0	Protocol cum Report approval	3
2.0	Objective	4
3.0	Scope	4
4.0	Responsibility	4
5.0	Reason for Risk analysis	4
6.0	Site of Study	4
7.0	Risk communication & training	5
8.0	Risk Identification and Evaluation & Mitigation	5
9.0	Risk analysis tools, Re-Risk analysis Criteria	8
10.0	Conclusion	20
11.0	Recommendation	20
12.0	Reference	21
13.0	Document To be Attached	21
14.0	Deviation	21
15.0	Change Control (If any)	21
16.0	Abbreviation	21
17.0	Protocol cum Report post approval	22

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

1.0 PROTOCOL CUM REPORT APPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

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

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

2.0 OBJECTIVE:

- The objective of this Protocol Cum Report is to evaluate the impact of extraneous material in finished products.

3.0 SCOPE:

- Risk analysis study Protocol cum Report is applicable for ……

4.0 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.

5.0 REASON FOR RISK ANALYSIS:

- To mitigate & monitor the risk of extraneous material on finished products.

6.0 SITE OF STUDY:……..

7.0 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.

8.0 RISK IDENTIFICATION, EVALUATION & MITIGATION:

INTRODUCTION: Extraneous materials are any foreign matter in product associated with objectionable conditions or practices in production, storage or distribution. The contaminant or extraneous material may be related to the active ingredient, excipient materials or colorant. Particles may be generated from the product container or packaging material. These types of particles include glass, rubber, aluminum, plastics and paper. Contamination can also result from the manufacture of the product; examples of these include charred product, detergents and lubricant oils. Metal and metal corrosion, Teflon, graphite and rubber particles are indications of tank, filter or equipment failure. Environmental contaminants such as fibers and skin cells are also found. The most common contaminants in pharmaceuticals are cellulose (cotton and paper) fibers, synthetic fibers, silicone, plastics, rubber, metal particles and corrosion products, glass particles, skin flakes and char particles.

Contaminants can gain entry into a production process stream from several sources such as, Personnel, Poor facility design, Incoming ventilation air, Machinery and other equipment for production, Raw material and semi-finished material, Packaging material, Utilities, Different media used in the production process as well as for cleaning and Clean room clothing.

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

EXTRANEOUS MATERIALS

Fig. 1: Fungal contamination

Fig. 2: Metal piece

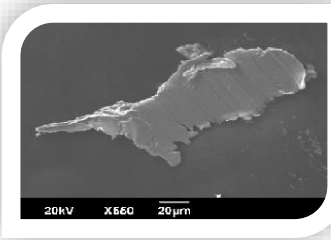


Fig. 3: SEM Imaging of Polymeric

Fig. 4: Hair Follicle

Fig. 5: Black Specks

EXTRANEOUS MATERIAL

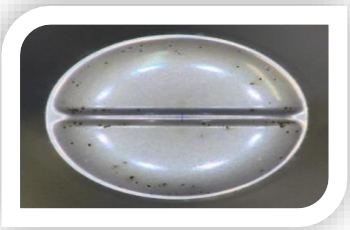


Fig. 6: Punch Corrosion

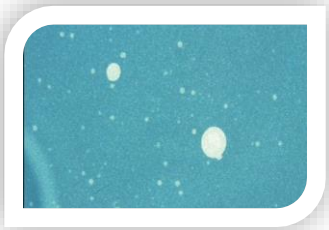


Fig. 7: Silicone particles

Fig. 8: Fibers

Fig. 9: Oil Spot

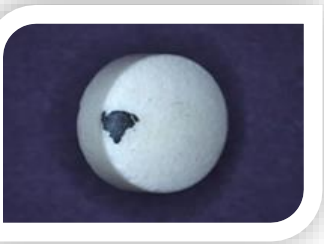


Fig.: 10: Polythene Piece

Fig. 11: Silicone gaskets

Fig. 12: Teflon parts

Fig. 13: Nylon brushes

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

1. **Black specks or particles:** Visual appearance of pharmaceuticals is important in determining how closely patients comply with their dosage requirements. One problem that is often seen in tablets is black specks (Fig. 5), on the surface. These specks can form because of contaminants in raw materials or from the tablet manufacturing process, and various interactions that may occur during storage.

2. **Metal Pieces:** Metal particles (Fig. 2) are common contaminants in the drug manufacturing process, a problem that should be addressed before the product goes to market. However, the recent recalls of several Rx and OTC medications due to metal contamination show that more needs to be done to prevent contaminants from reaching the public. Though small in size, repeated ingestion of metal-contaminated pharmaceuticals can lead to metal poisoning -lead and chromium particles being the most dangerous.

3. **Metal corrosion:** A common problem during the fabrication of stainless steel equipment is the embedding of iron in the stainless steel surface. The iron corrodes when exposed to moist air or when wetted, leaving rust streaks. It is a natural process that creates a gradual destruction of materials due to a chemical reaction. In terms of tablet compaction, this reaction is usually between the granulate and the tooling. Common issues associated with corrosion include:
   - Damage to the tooling (Fig. 6)
   - Transfer to tablets
   - Damage to tablet press parts

4. **Hair follicles:** Human hair (Fig. 4) is one of the most common particulate contaminants that occur in pharmaceutical raw material. The hair and, where relevant, beard and moustache should be covered. Although hair follicle contamination is not hazardous but it gives unpleasant look & the patient avoid of taking such product.

5. **Fibers:** Fibers (Fig. 8) have typically diameter of less than or equal to 40 microns (size is based on experience), and a length: diameter ratio larger than 3:14. Examples are fibers from FBD bags, filters, Lint free cloth etc.

6. **Cable Tie:** Cable ties are used in pharma sector for tying knots in double polybags containing API, Excipients, Bulk, Uncoated tablets, Coated tablets etc. Sometimes by mistake broken cable tie pieces got mixed up with the product.

7. **Polythene pieces:** Polybag pieces are commonly found in API's & Excipients, all materials in pharma sectors are packed in double polybags, low quality poly bags shred their pieces which further mixed in bulk resulting into cross contamination & product failure. These polybag pieces are detected & controlled through sifting & sieving.

8. **Rubber pieces:** Rubber hand gloves are used as a protective gear in pharma sector. Low quality gloves may shred their fibers & pieces which while processing mixed up with product. Gloves shall be verified for its intactness on regular basis during manufacturing activity.

9. **Silicones pieces:** All gaskets (Fig. 11) & transfer tubes used in pharma are of food grade Silicones. It comes in direct contact of product during processing. Long term use of these parts result into shredding of particles, although is of food grade but its contamination shall be avoided. Continuous verification shall be done before usage.

10. **Teflon pieces:** Many contact parts are made of Teflon (Fig. 12), continuous ruggedness of Teflon with product & during cleaning sometimes result into Teflon fiber release which further result into product contamination.

11. **Oil Spots:** Oil is used for lubrication of equipment parts & for punch polishing, hence if not controlled, the oil (Fig. 9) of the machine parts may transferred to product resulting in contamination. Although oil used in pharma is of

food grade, but contamination shall be avoided, hence for the same dummy tablets shall be run after preventive maintenance.

12. **Fungal contamination on tablet surface:** Fungal contamination (Fig. 1) in pharmaceutical products represents a potential hazard for two reasons. First, it may cause product spoilage; second, product contamination represents a health hazard to the patient, It has been estimated that around half of the fungi found in the environment could cause infections in people (mycosis). With pharmaceutical products, the two major hazards are air and the skin. Fungal growth takes place where the environment is not controlled. Hence temperature, RH & ACPH of the environment shall be maintained.

13. **Water/Moisture:** Water plays important role in manufacturing process, but that water is purified water with controlled Pharmacopoeial parameters. If some water from the outside source mixed with the product then that raw water shall be considered as extraneous material for that process like coating. Coating process is controlled by compressed air, any malfunctioning in compressed line results into water leakage may contaminate the whole batch. Monitoring of such process is difficult and care must be taken while coating.

14. **Pest:** Pests (Insects, Rodents, Birds) can cause large economic losses in the pharmaceutical industry through contamination of raw materials, storerooms, laboratories, production areas, packaging and finished products. Pest control program shall be there to avoid such contamination.

15. **Detergents:** Detergents used for cleaning can lead to contamination, if not cleaned properly. Dirty equipments can lead to stains over tablet surfaces. Proper cleaning shall be done after usage. Validation shall be there for the cleaning agent.

16. **Nylon Brush fibers:** Nylon brushes are used in pharma for cleaning of surfaces & used in blisters for removing powder. Low quality brushes can shred their fibers & resulting into contamination of bulk & finished products.

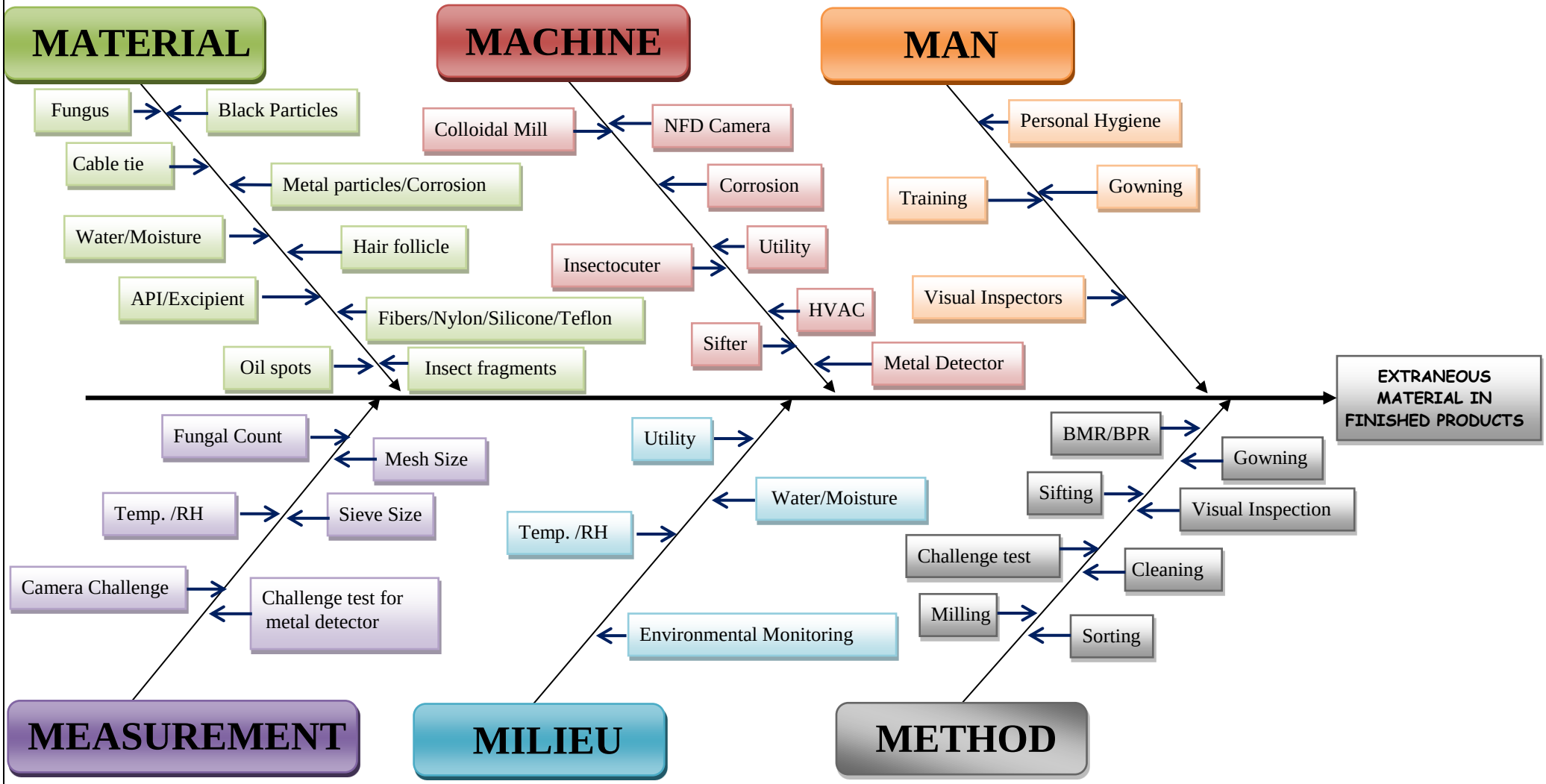
RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

S.No.	RISK IDENTIFICATION	RISK EVALUATION	RISK MITIGATION
1.	Risk associated with extraneous material is from minor to critical. It depends on the type of foreign material observed. Sometimes it is in-built from the system or process (black particles, metal pieces, fibers, silicon pieces, Teflon pieces, Oil spots, detergents, nylon fibers), and sometimes it is from the outside environment (Hair follicle, cable tie, Polythene) pieces, Rubber pieces, Fungus, Water & Pest). Risk associated with the products shall be identified for its criticality.	After risk identification, evaluation shall be done for each component of the factor associated with it. Risk probable number shall be allotted to each factor on the basis of its criticality. Recommendations shall be given against each critical factor.	After Risk evaluation, risk mitigation shall be given to slow down the criticality of the associated risks. More than one control can be allotted for each risk. After the control measures, if risk is still high then recommendations shall be given & the risk is again re-evaluated.

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

9.0 RISK ANALYSIS TOOLS, RE-RISK ANALYSIS CRITERIA:

9.1 Fish bone/6M/Ishikawa diagram:



RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

SUMMARY OF THE 6 M/FISH BONE DIAGRAM/ISHIKAWA DIAGRAM: It is used for the evaluation of Impact of extraneous material on finished products; following are the areas of concern considered for investigation. Man, Material, Measurement, Method, Milieu & Machine. It has been evaluated that all of the 6 M may contribute in defects related to extraneous material.

MAN: Personnel who are supervising or performing drug manufacturing or control can be a potential source of microbiological contamination and a vector for other contaminants. The main reasons for contamination from the personnel include:

- Lack of training.
- Direct contact between the operator's hands and starting materials, primary packaging materials and intermediate or bulk product
- Inadequate personnel cleanliness.
- Access of unauthorized personnel into production, storage, and product control areas.
- Inadequate gowning and personnel protective equipment, and
- Malpractices like eating food, drinking beverages, or using tobacco in the storage and processing areas.

MATERIAL: The raw materials used for production can be a potential source of contamination. The main reasons for contamination from the raw materials include:

- Storage and handling mistakes causing mix-ups or selection errors.
- Contamination with microorganisms or other chemicals.
- Degradation from exposure to excessive environmental conditions such as heat, cold, sunlight, moisture, etc.
- Improper labeling.
- Improper sampling and testing, and Use of materials that fails to meet acceptance specifications.
- Material from unapproved vendor.

MILIEU: The buildings and manufacturing facilities may also contribute to the contamination. The main reasons of contamination due to facility issues include:

- Insufficient size and inadequate organization of the space leading to selection errors like mix-ups or cross contamination between consumables, raw materials, in-process materials, and finished products.
- Inadequate filth and pest controls.
- Rough floors, walls, and ceilings.
- Lack of air filtration systems.
- Improper lighting and ventilation.
- Poorly located vents, ledges, and drains, and Inadequate washing, cleaning, toilet, and locker facilities to allow for sanitary operation, cleaning of facilities, equipment, and utensils; and personal cleanliness.

A poor HVAC system can be a potential source of microbes growth and a transportation mode for dispersing contaminants throughout the manufacturing facility.

The main reasons of contamination due to HVAC issues include:

- Accumulations of organic material in or near HVAC air intakes
- Ineffective filtration of the supply air
- Insufficient magnitude of pressure differentials causing flow of reversal
- Erroneous ratio of fresh air to re-circulated air
- Inability to access ventilation dampers and filters from outside the manufacturing areas, and
- Non-directional airflow within production or primary packing areas.

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

MACHINE: The equipment and utensils used in processing, holding, transferring and packaging are the common source of pharmaceutical contamination. The main reasons for contamination from the equipment include:

- Inappropriate design, size, material leading to corrosion and accumulation of static material and/or adulteration with lubricants, coolants, dirt, and sanitizing agents
- Improper cleaning and sanitization
- Design preventing proper cleaning and maintenance
- Improper calibration and irregular service, and deliberate use of defective equipment.
- Challenge test not performed before the start.
- Machine not qualified.
- Inappropriate preventive maintenance.

METHOD: There are various opportunities for contamination of raw material, intermediates or packaging materials throughout the manufacturing process. The main reasons for contamination during manufacturing process include:

- Inappropriate cleaning in-between batches to minimize the amount of product changeovers.
- Use of an open manufacturing system exposing the product to the immediate room environment.
- Absence of an area line clearance according to approved procedures following each cleaning process and between each batch.
- Lack of cleaning status labeling on all equipment and materials used within the manufacturing facility.
- Sorting not done properly.
- Improper visual inspection.

MEASUREMENT: Measurement itself plays important role in evaluation of extraneous material impact on product quality. There are many factors which shall be regularly monitored & recorded such as:

- Temperature& RH of the area not under control & recording time too exhaustive
- Camera challenge sensitivity is too low to detect any particle or foreign substance
- Metal detector sensitivity too high to detect any metal piece.
- Sieve size & mesh size are inappropriate to capture any extraneous material.

9.2 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.
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 1: Instruction for each column given above

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

Procedure: Risk analysis for Evaluation of impact of extraneous material on finished product quality	**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
EXTRANEOUS MATERIAL															
1.	Hair Follicle	• Tablet fail in description • Unpleasant appearance.	• Improper visual inspection. • Contaminated API/Excipient. • Vendor not qualified. • Improper gowning. • Operator working without goggle.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Procedure for vendor qualification is in place. • Gowning procedure is in place.	• SOP No. • SOP No. • SOP No. • SOP No. • SOP No. • SOP No.	4	3	3	36	Following are the recommendation: • Guide track will be covered with acrylic cover. • Vacuum suction shall be made available on blister packing machine. • Brush shall be made available on blister packing machine for cleaning of PVC & PVDC film during the packing process. • Training shall be imparted to all the concerns regarding gowning & de-gowning.	4	2	3	24
2.	Metal pieces	• Tablet fail in description	• Improper visual inspection. • Contaminated API/Excipient • Vendor not qualified. • Metal detector not available. • Challenged test not performed before the start.	• Market complaint • Product recall • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for vendor qualification is in place. • Procedure for Visual Inspectors qualification is in place. • All tablets are passed through metal	• SOP No. • SOP No. • SOP No. • SOP No. • SOP No. • SOP No.	5	2	1	10	Risk is low hence no action plan is required	NA	NA	NA	NA

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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
					detector										
3.	Metal Corrosion	• Tablet fail in description	• Improper visual inspection. • Equipment not dried properly. • Line clearance procedure not followed.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Line clearance Procedure is in place.	• SOP No. • SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
4.	Fibers	• Tablet fail in description	• Improper visual inspection. • Garments not verified for loose threads. • Lint free cloth not used for type A cleaning.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Use of lint free cloth procedure is in place.in respective equipment SOPs.	• SOP No. • SOP No. • SOP No. • SOP No. • SOP No.:	4	2	2	16	Risk is low hence no action plan is required	NA	NA	NA	NA
5.	Cable tie	• Tablet fail in description	• Improper visual inspection. • Broken tie mixed with granules.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
6.	Polythene pieces	• Tablet fail in description	• Improper visual inspection. • Shredded polythene mixed with granules.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
7.	Rubber pieces	• Tablet fail in description	• Improper visual inspection. • Shredded rubber of gloves mixed with granules.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt.	• SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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
					• Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No.									
8.	Silicones pieces	• Tablet fail in description	• Improper visual inspection. • Old gaskets made of silicones may shred their particles. • Silicone tubes shred their particles which may mix with coating material.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	N A	N A	N A	NA
9.	Teflon Pieces	• Tablet fail in description	• Improper visual inspection. • Contact parts made of Teflon may shred their particles	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	N A	N A	N A	NA
10.	Black particles	• Tablet fail in description	• Improper visual inspection. • Improper sifting. • Improper milling during coating. • API & Excipient from unapproved vendor.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Shifting procedure is well defined in respective products BMR. • Procedure for vendor qualification is in place. • AQL procedure is in place	• SOP No. • SOP No. • SOP No. • SOP No.	3	3	2	18	Risk is low hence no action plan is required	N A	N A	N A	NA
11.	Oil Spots	• Tablet fail in description	• Improper visual inspection. • Equipment not cleaned properly after preventive maintenance.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods	• SOP No. • SOP No. • SOP No. • SOP No. • SOP No. QAH/073	3	3	2	18	Risk is low hence no action plan is required	N A	N A	N A	NA

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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
					• Procedure for Visual Inspectors qualification is in place. • Preventive maintenance procedure is in place • AQL procedure is in place										
12.	Water/Moisture	• Tablet fail in description	• Improper visual inspection. • Water or moisture from compressed air during coating	• Market complaint • Tablet fail in description. • Microbial count failed. • Tablet defects	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • In process checked by both production QA in fix frequency as related BMR.	• SOP No. • SOP No. • SOP No. • SOP No. • Related BMR	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
13.	Fungal on tablet surface	• Tablet fail in description.	• Improper visual inspection. • Temperature and RH not controlled. • Product hold time exceeds	• Market complaint • Tablet fail in description. • Microbial count failed. • Patient safety	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • AQL procedure is in place	• SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
14.	Insect fragments	• Unpleasant appearance.	• Improper visual inspection. • Insectocuter not installed at the entry. • Pesticide program not available.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Insectocuter installed at every entry and procedure for operation and cleaning is in place • Procedure for Pest and rodent control is in place.	• SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
15.	Detergent Stains	• Stains over	• Improper visual inspection.	• Market complaint	• There is well defining procedure of	• SOP No.	4	2	1	8	Risk is low hence no action plan is	NA	NA	NA	NA

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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
		tablet observed.	• Line clearance procedure	• Tablet fail in description.	tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place. • Line clearance procedure is in place.						required				
16.	Nylon brush fibers	• Tablet fail in description	• Improper visual inspection.	• Market complaint • Tablet fail in description.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• SOP No.	4	2	1	8	Risk is low hence no action plan is required	N A	N A	N A	NA
METHOD															
17.	Sifting not performed	• Black Particles. • Insect fragments. • Hair follicle may pass, if sifting not done. • Fibers mix up with granules. • Nylon fibers mix up with granules. • Cable tie may mix up. • Polythene pieces mix ups.	• Improper sieve. • API/Excipient used from unapproved vendor.	• Market complaint • Tablet fail in description. • Product recall. • Health Hazard.	• BMR in place for selection of sieve. • Process validation in place. • Procedure for vendor qualification is in place. • There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods • Procedure for Visual Inspectors qualification is in place.	• Related BMR • Related PV report • SOP No. • SOP No. • SOP No. • SOP No.	4	2	2	16	Risk is low hence no action plan is required	N A	N A	N A	NA
18.	Milling of coating material	• Gun choking. • Coating solution particle suspended. • Shade variation.	• Colloidal mill not used. • Coating material used from unapproved vendor.	• Market complaint • Tablet fail in description. • Product recall.	• Procedure for milling of material through Colloidal mill was mentioned in BMR and monitoring by both production and QA. • Procedure for vendor qualification is in place.	• Related BMR • SOP No.	4	2	1	8	Risk is low hence no action plan is required	N A	N A	N A	NA
19.	Metal detector	• Metal part mix	• Metal detector not	• Market complaint	• Procedure for operation & cleaning of	• SOP No.	4	2	1	8	Risk is low hence no	N	N	N	NA

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

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
		up with tablets	available. • Challenged test not performed before the start.	• Product recall • Tablet fail in description.	metal detector is in place. All tablets are passed through metal detector.						action plan is required	A	A	A	
20.	Cleaning of equipments	• Tablet with stains. • Contamination. • Cross contamination • Product mix-up	• Remaining of detergent contaminate the next product.	• Market complaint • Health hazard. • Toxicity.	• Cleaning SOP for each equipment & process in place. • Cleaning agent qualified for its residues.	• Cleaning validation • Respective SOP's of equipments.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
21.	Improper Gowning	• Hair follicles in tablets. • Skin flakes in tablets • Unpleasant appearance of tablet.	• Gowning improper. • Some body part exposed. • Unhygienic practices.	• Market complaint • Product recall.	• Procedure for primary and secondary gowning is in place. • Working persons are trained. Procedure for training of personal is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	1	8	Risk is low hence no action plan is required	NA	NA	NA	NA
22.	Sorting & Visual Inspection	• Tablets with black particles. • Tablets with foreign particles.	• Improper visual inspection. • Visual inspection not done. • Visual inspector not qualified.	• Market complaint. • Batch hold. • Re-sorting or re-inspection.	• There is well defining procedure of tablets sorting. We have both procedures for sorting, manual and inspection belt. • Terminal Inspection & Transfer of Finished Goods. • Procedure for Visual Inspectors qualification is in place.	• SOP No. • SOP No. • SOP No. • SOP No.	4	2	2	16	Risk is low hence no action plan is required	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.

Rating Scale – Severity
1= No Effect
2= Minor Effect
3= Moderate Effect
4= Serious Effect
5= Hazardous Effect

Rating Scale - Occurrence
1= Unlikely
2= Very Rare
3= Possible
4= Likely
5= Almost Certain (every time)

Rating Scale - Detection
1= Always Detected
2= Will Detect Failure
3= Might Detect Failure
4= Almost certain not to Detect Failure
5= Lack of Detection Control

Acceptance Criteria
51 to ≤ 125 = High Categories
26 to 50 = Medium Categories
Upto25 = Low Categories

PHARMA DEVILS

QUALITY ASSURANCE DEPARTMENT

RISK ANALYSIS STUDY PROTOCOL CUM REPORT FOR EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

Remark if any:

……

……

……

……

……

……

……

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

QUALITY RISK ASSESSEMENT AND MITIGATION SUMMARY REPORT

Name of Facility			
S.No.	Recommended Action	Responsible Person	Target Date of Completion

Verification of Action Plan:

All the above agreed actions completed, Not Completed.

(*In-case any recommendations Not completed, to be tracked through CAPA System)

Remark if any:

……

……

……

……

……

……

……

Verified By
(QA)
Sign & Date……..

Reviewed By:
(Manager QA)
Sign & Date……..

RISK ANALYSIS STUDY PROTOCOL CUM REPORT
FOR
EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

10.0 CONCLUSION:

Risk of Extraneous material on finished product Quality at……..

……

……

……

……

……

……

……

……

……

……

……

……

……

11.0 RECOMMENDATION:

Recommendation shall be written on the Risk Analysis Study Protocol cum Report for evaluation of Defected coated tablets, clearly stating that there is no impact/adverse impact on the product quality.

……

……

……

……

……

……

……

……

……

……

……

……

RISK ANALYSIS STUDY PROTOCOL CUM REPORT
FOR
EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

12.0 REFERENCES:

- Reference SOP of Risk Assessment.
- https://www.mccrone.com/mm/contaminant-identification-pharmaceutical-products/.
- https://tablettingscience.com/solving-problems/.
- https://www.europeanpharmaceuticalreview.com/article/24118/fungal-contamination-pharmaceutical-products-growing-menace/.
- Related SOP's.

13.0 DOCUMENTS TO BE ATTACHED:

- Related documents.

14.0 DEVIATION FROM PRE DEFINED SPECIFICATION, IF ANY:

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

15.0 CHANGE CONTROL, IF ANY:

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

16.0 ABBREVIATIONS:

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

RISK ANALYSIS STUDY PROTOCOL CUM REPORT
FOR
EVALUATION OF EXTRANEOUS MATERIAL IN FINISHED PRODUCTS

17.0 PROTOCOL CUM REPORT POST APPROVAL:

PREPARED BY:

DESIGNATION	NAME	SIGNATURE	DATE
OFFICER/EXECUTIVE (QUALITY ASSURANCE)			

REVIEWED BY:

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

APPROVED BY:

DESIGNATION	NAME	SIGNATURE	DATE
HEAD (QUALITY ASSURANCE)			