RISK MANAGEMENT REPORT FOR ASCERTAINING THE APPROPRIATE GOOD MANUFACTURING PRACTICE (GMP) FOR POTATO STARCH (GMO FREE STARCH)

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1.0 SCOPE:

This report is applicable for risk management for ascertaining the appropriate Good manufacturing practice (GMP) of excipient Potato Starch (GMO free Starch).

2.0 OBJECTIVE:

The objective of this report is to ascertaining the appropriate GMP elements for excipient "Potato Starch (GMO free Starch)" manufactured by …….. used in manufacturing of the drug product manufactured.

3.0 RISK ASSESSMENT FOR EXCIPIENT:

Section 1: Excipient Source and Product Information	
CRITERIA	**DETAILS**
Name of the site	
Excipient Part Code/Item Number	
Excipient Trade Name	Potato Starch (GMO free Starch)
Excipient Compendial Name	Potato Starch
Status	Approved
Excipient Supplier Name	
Excipient Supplier Address	
Excipient Manufacturer Name	
Excipient Manufacturer Address	
Finished Dosage Form Registered Product Name& Strength(s)	➢ Desogestrel 150 mcg and Ethinylestradiol 20 mcg tablets ➢ Desogestrel tablets 75 mcg ➢ Desogestrel 150 mcg and Ethinylestradiol 30 mcg tablets
Region Finished Dosage Form is Marketed in	

Section 2: Risks presented to the quality and safety of each excipient (A)

CRITERIA	SCORE	REASON FOR SCORE	REFERENCE
Transmissible spongiform encephalopathy/bovine spongiform encephalopathy (TSE/BSE).	1	Potato Starch has been produced from vegetable derivatives.	BSE-Statement
Potential for viral contamination	0	No risk for viral contamination	Potato Starch has been produced from vegetable derivatives.
Potential for microbiological or endotoxin/pyrogen contamination	2	Potential risk however microbiological analysis is carried out at site	Vendor COA and Specification
Potential, in general, for any impurity originating from the raw materials, e.g. aflatoxins or pesticides, or generated as part of the process and carried over, e.g. residual solvents and catalysts.	0	No risk	Residual solvent statement
Sterility assurance for excipients claimed to be sterile	0	Not used in sterilized finished dosage form	Page 4 of report indicating finish dosage of excipient use
Potential for any impurities carried over from other processes, in absence of dedicated equipment and/or facilities	2	Dedicated line for most of steps but common workshop cleaning validation in place	Manufacturer Assessment Questionnaire Supplier Questionnaire
Environmental control and storage/transportation conditions including cold chain management, if appropriate	0	No environment control during storage/transport required, However temperature and Humidity is monitored during storage	Manufacturer Assessment Questionnaire and Supplier Questionnaire

CRITERIA	SCORE	REASON FOR SCORE	REFERENCE
Supply chain complexity	1	Supply from distributor without any third party operations (e.g. packaging, labeling, milling, testing) in intact original manufacturer container	Approved Vendor list
Stability of excipient	1	Expiry is more than 2 years assigned by manufacturer	Manufacturer COA
Packaging integrity evidence	0	Integrity proven (As per site SOP pack integrity is checked upon receipt and seal also checked procedures require packaging inspection upon receipt, tamper sealing in place, etc.)	NA

Section 3: Use and function of the excipient (B)			
CRITERIA	**SCORE**	**REASON FOR SCORE**	**REFERENCE**
Source of the excipient (e.g. animal, mineral, vegetable, synthetic, etc.)	2	Potato Starch has been produced from vegetable derivatives.	BSE-Statement
The pharmaceutical form and use of the medicinal product containing the excipient	2	Excipients used in OSD	Page 4 of report indicating finish dosage of excipient use
The function of the excipient in the formulation, e.g. lubricant in a tablet product or preservative material in a liquid formulation, etc.	2	Used as a Disintegrant in tablet formulation*	Process validation protocols
The proportion of the excipient in the medicinal product composition	1	Maximum Proportion of the excipient in the medicinal product composition is 7.7% **	Bill of material
Daily patient intake of the excipient	1	Maximum daily patient intake of the excipients is 5.0 mg***	Bill of material
Any known quality defect/fraudulent adulterations, both globally and at a local company level related to the excipient	0	No OOS reported in Potato Starch	NA
Whether the excipient is a composite	0	Excipient is pure	Product Questionnaire page 8/ 8
Known or potential impact on the critical quality attributes of the medicinal product	3	Impact on finished dosage form performance and critical Quality Attributes	NA
Other factors as identified or known to be relevant to assuring patient safety	0	No additional factors identified	NA

*** The function of the excipient in the formulation**

1) Desogestrel 150 mcg and Ethinylestradiol 20 mcg tablets - Disintegrant
2) Desogestrel tablets 75 mcg- Disintegrant
3) Desogestrel 150 mcg and Ethinylestradiol 30 mcg tablets - Disintegrant

****Composition of excipient in individual product:**

1) Desogestrel 150 mcg and Ethinylestradiol 20 mcg tablets – **7.7%**
2) Desogestrel tablets 75 mcg – 3.9%
3) Desogestrel 150 mcg and Ethinylestradiol 30 mcg tablets **- 7.7%**

***** Daily patient intake of the excipient in individual product:**

1) Desogestrel 150 mcg and Ethinylestradiol 20 mcg tablets – **5 mg**
2) Desogestrel tablets 75 mcg – 2.5 mg
3) Desogestrel 150 mcg and Ethinylestradiol 30 mcg tablets – **5 mg**

Section 4: Determination of the risk profile and worst-case scenario for excipient			
Overall score (A+B = C)	**Worst case scenario (highest score, when applicable) (A + Worst case B = D)**	**Excipient Risk Profile**	**Reference**
18	NA	Low Potential Risk	NA

- **Low potential risk:** $0 \leq$ score ≤ 19
- **Medium potential risk:** $20 \leq$ score ≤ 38
- **High potential risk:** $39 \leq$ score ≤ 57

4.0 RISK ASSESSMENT FOR EXCIPIENT MANUFACTURER:

Section 5: Excipient Manufacturer High Level GMP Elements: (A1)

CRITERIA	SCORE	REASON FOR SCORE	REFERENCE
Establishment and implementation of an effective pharmaceutical quality system.	1	Availability Quality Policy and Quality Manual	Manufacturer Assessment Questionnaire and Supplier Questionnaire.
Sufficient competent and appropriately qualified personnel.	1	Adequate number of educated and trained personnel at different levels with sufficient qualification is available.	Supplier Questionnaire
Defined job descriptions for managerial and supervisory staff responsible for manufacturing and quality activities.	1	Job descriptions available	Manufacturer Assessment Questionnaire
Training programs for all staff involved in manufacturing and quality activities.	1	Training Program for new/existing staff available	Manufacturer Assessment Questionnaire
Training programs related to health, hygiene and clothing as identified as necessary to the intended operations.	1	Health and Hygienic requirement for areas and personnel available	Manufacturer Assessment Questionnaire and Supplier Questionnaire.
Provision and maintenance of premises and equipment appropriate to the intended operations.	1	Preventive maintainace of equipment programme available.	Manufacturer Assessment Questionnaire
Documentation system(s) covering all processes and specifications for the various manufacturing and quality operations.	1	Documentation of result of analysis and batch documentation for all process and in process checks being recorded including yield at different stages.	Manufacturer Assessment Questionnaire
Systems for coding and identifying starting materials, intermediates and excipients to allow full traceability.	1	Yes, traceability system is in place.	Supplier Questionnaire

CRITERIA	SCORE	REASON FOR SCORE	REFERENCE
Qualification program of suppliers.	1	Perform regular Quality Impacting materials supplier inspection and audits.	Supplier Questionnaire
System for quality control of the excipient and a responsible person independent from production to release the batches.	1	A system is in place to ensure that materials are not released or used before completion of evaluation by quality management.	Manufacturer Assessment Questionnaire
Retention of records for incoming materials and excipients and retention of samples of excipients for the periods required by EudraLex Volume 4, Part II.	1	QC records kept for 6 years and retained samples for finished products one year for bulk delivery, two years for packed deliveries.	Supplier Questionnaire
Systems to ensure that any activity contracted out is subject to a written contract.	1	Contract manufacturer are only used after contract is concluded.	Supplier Questionnaire
Maintenance of an effective system whereby complaints are reviewed and excipients may be recalled.	1	Having procedure for handling of product complaints and product recall.	Manufacturer Assessment Questionnaire and Supplier Questionnaire
Self-inspection program.	1	Self inspection program available	Manufacturer Assessment Questionnaire and Supplier Questionnaire
Environmental control and storage conditions.	1	Have environmental Policy	Supplier Questionnaire

Section 6: Determination of the risk profile and worst-case scenario for excipient manufacturer

Overall Risk Score of Excipient Manufacturer High Level GMP Elements (A1)	**Worst case scenario (highest score, when applicable) (Worst Case of A1 = B1)**	**Excipient Manufacturer Risk Profile**	**Reference**
16	NA	Low Potential risk	NA

- **Low potential risk**: $0 \leq$ score ≤ 16
- **Medium potential risk**: $17 \leq$ score ≤ 32
- **High potential risk**: $33 \leq$ score ≤ 48

Section 7: Determination of the Overall risk profile for excipient and excipient manufacturer

Overall Risk Score of Excipient or worst-case scenario (C or D)= X	Overall Risk Score of Excipient Manufacturer or worst-case scenario (A1 or B1)= Y	Overall Risk score for Excipient and Excipient Manufacturer Risk Profile X+Y	Overall Risk Profile for Excipient and Excipient Manufacturer Risk Profile	Reference
18	16	34	Low Potential risk	NA

The overall risk profile score will result in the following overall risk profile of the excipient and excipient manufacturer.

- **Low potential risk:** $0 \leq \text{score} \leq 35$
- **Medium potential risk:** $36 \leq \text{score} \leq 70$
- **High potential risk:** $71 \leq \text{score} \leq 105$

Section 8: Life cycle management

Criteria	Details/Number
Number of lots received	10
Total Number of defected lots	0
Type/ severity of defect	Nil
The review of PQR of last 2 years for monitoring and trend analysis of excipient quality. Observation of trends in drug product quality attributes.	Satisfactory
The information with respect to loss of relevant quality system and/or GMP certification by excipient manufacturer	No information
Observed organizational, procedural or technical/process changes at the excipient manufacturer	No information

5.0 SUMMARY & CONCLUSION:

Risk Assessment for ascertaining appropriate good manufacturing practice of Excipient Potato Starch (GMO free Starch) supplied has been performed by risk scoring on the basis of quality and safety of excipient, use and function of the excipient and various excipient manufacturer high level GMP elements.

It is concluded by performing risk assessment for ascertaining appropriate Good manufacturing practice of Excipient Potato Starch (GMO free Starch) supplied having low potential risk hence re evaluation or reassessment of manufacturer will be performed in minimum of every 48 months and not to exceed 54 months through Quality questionnaire or Specification acceptance agreement or certification (e.g. government or industry) or site defined documentation.

6.0 REPORT APPROVAL:

Report Prepared by:

Department	Name	Designation	Signature	Date
QA				

Report Reviewed by:

Department	Name	Designation	Signature	Date
Warehouse				
Quality Control				
Production				
R & D				
QA				

Report Approved by:

Department	Name	Designation	Signature	Date
QA				