ACTIVE PHARMACEUTICAL INGREDIENTS COMMITTEE

1.1 Risk assessment for Audit trail review definition for Weighing and Dispensing step

1) Scenario:

The WMS (warehouse management system) is a component of the company ERP system (enterprise resource planning); it is interfaced with the LIMS system and with the ERP system. It supports the execution of operations related to the handling of materials used in production, from the receiving of raw materials to the shipping of finished products

2) Business process mapping

The business process mapping utilizes the 6 FDA systems and their subsystems

➔ FDA Process: Production control system

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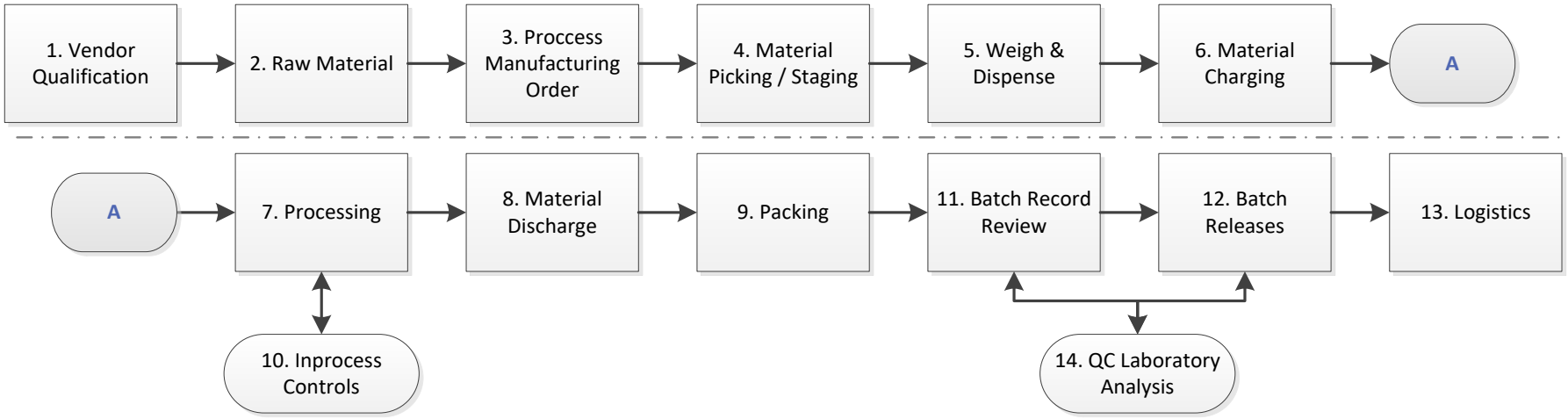
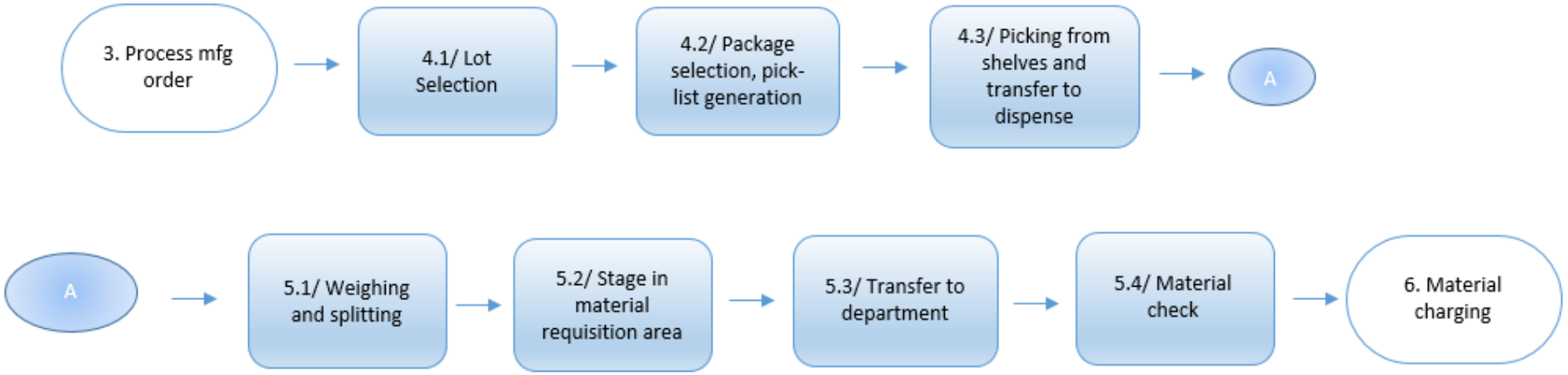


➔ Sub-Processes 4 – Material Picking/staging and 5 - Weigh & Dispense



3) Data (paper/electronic) and system identification

a. System identification: (see section 3 step A)

	4.1	4.2	4.3	5.1	5.2	5.3	5.4
Step	Lot selection	Package selection, pick-list generation	Pick-up from shelves and transfer to dispensing rooms	Weighing and splitting	Stage to requisition area	Transfer to production department	Material check
GxP Data	electronic	electronic	electronic	paper/ electronic	electronic	electronic	paper/ electronic
System	WMS	WMS	WMS	WMS Scales Label printing system	WMS	WMS	WMS

b. Data Identification: (see section 3 step B)

Step	4.1 Lot selection	4,2 Package selection, pick-list generation	4.3 Pick-up from shelves and transfer to dispensing rooms	5.1 Weighing and splitting	5.2 Stage to requisition area	5.3 Transfer to production department	5.4 Material check
System 1: WMS							
GxP Data elements	Lot number * Quantity *	Package ID *	Material position	Net Weigh Tare * Package ID Package labels	Material position * Time in temporary storage	Material position Time in temporary storage	Gross weight Package ID Scale ID
System 2: scales							
GxP Data elements				Net Weigh Tare * Package ID Scale ID			Gross weight Package ID Scale ID
System 3: printing system							
GxP Data elements				Package labels			

c. Highlight electronic GxP data that can be modified/deleted or re-processed after creation (see section 3 step C): as indicated by an asterix in above table.

4) Data and System categorisation

a. Data severity assessment (see section 4.1)

This example will focus on the WMS system only. The scales systems and printing systems should be handled in a separate assessment.

The WMS is used for intermediates and APIs manufacturing.
According to the severity definitions, the API categorization results in **very high severity data**.

b. System profiling (see section 4.2, decision tree figure 3)

System 1: WMS -> cat 6

System 2: Scales -> cat 4
System 3: Labelling -> cat 4

c. System assessment: (according to checklist 4.3 table 2)
Only the gaps are in below overview.

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ID	Topic	Sub topic	Question	Category	Acceptance criteria	Does the system meet the criteria?	Description of gap	Comments
26	Audit trail	Audit trail review	Are audit trails reviewed according to the applicable procedures?	2 / 3 / 4 / 5 / 6	The company's requirements on audit trail review shall be taken into account and should be supported by a risk-based approach to define the process and frequency for execution.	NO	Audit trail review is not adequately performed on data identified as GMP-critical since consultation of the audit trail database requires IT skills	none
18	Data lifecycle management	Archival/retrieval	Does the system have an archival strategy documented and is the GxP data retrieval process periodically verified?	1 / 3 / 5 / 6	The system shall have an archival strategy documented. GxP Data and associated meta data shall be archived if system modifications impact the functionality to read or to process existing files. GxP Data shall be archived at the retirement of the system. Data archival storage time shall be defined per the company's Retention Schedule. GxP Data retrieval of archived records shall be tested on a periodic basis, as required by applicable regulation, using a statistically relevant sample.	NO	Archiving is not planned for the system; a plan should be prepared to avoid system crash	none
30	Security/User Access Control	Access Approval	For contractors; Is an agreement in place with the service provider capturing the data integrity responsibilities of the service provider?	1/ 2 / 3 / 4 / 5 / 6	An agreement shall be in place with the service provider (Quality Agreement, Service Level Agreement, etc.), capturing the responsibilities of the service provider.	NO	An agreement is in place but it does not provide details over the GMP versus non-GMP functionalities and actions allowed for GMP ones.	none

5) Risk Assessment (FMEA to calculate the gaps and their current individual Risk Priority Numbers (RPN)) (see section 5)

ID#	Checklist ID	Step	Function/Requirement or Data flow Step	Potential Failure Mode	Effect	Severity	Occurrence	Detectability	RPN
1	18	Data lifecycle management	Archival/retrieval	Archiving is not planned for the system; a plan should be prepared to avoid system crash	possible loss of data	4	2	4	32
2	26	Audit trail	Audit trail review	Audit trail review is not adequately performed on data identified as GMP-critical since consultation of the audit trail database requires IT skills	manipulation of data possible	5	3	4	60
3	30	Security/User Access Control	Access Approval	Agreement with the service provider (Quality Service Level Agreement) is in place but it does not provide details over the GMP versus non-GMP functionalities and actions allowed for GMP ones	possible manipulation of data and configuration items	3	3	3	27

6) Risk management (see section 6)

The above table shows that 4 of the 5 gaps have a high RPN (Red). Actions have been defined to address these issues immediately. Additional actions have also been defined to mitigate the other gaps

In the next table the RPNs are recalculated after implementation of the defined actions.

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ID#	Checklist ID	Step	Function/Requirement or Data flow Step	Potential Failure Mode	Effect	Severity	Occurrence	Detectability	RPN	Intermediate Action	Severity	Occurrence	Detectability	RPN	Long term Recommended Action	Severity	Occurrence	Detectability	RPN
1	18	Data lifecycle management	Archival/retrieval	Archiving is not planned for the system; a plan should be prepared to avoid system crash	possible loss of data	4	2	4	32	define a data archiving plan and validated archiving of data	4	0	4	0	N/A (coverd by intermadiate action)	4	0	4	0
2	26	Audit trail	Audit trail review	Audit trail review is not adequately performed on data identified as GMP-critical since consultation of the audit trail database requires IT skills	manipulation of data possible	5	3	4	60	define queries to be run by IT and validate them	5	2	1	10	develop audit trail reports accessible to specified users	5	1	1	5
3	30	Security/User Access Control	Access Approval	Agreement with the service provider (Quality Service Level Agreement) is in place but it does not provide details over the GMP versus non-GMP functionalities and actions allowed for GMP ones	possible manipulation of data and configuration items	3	3	3	27	provide the supplier with a list of GMP-critical functionalities and actions allowed	3	2	3	18	audit the supplier to ensure that the personnel involved in the WMS is aware of responsibilities defined in the	3	1	2	6

To close out the risk in a documented and formal way, an additional column can describe the objective evidence that has been implemented to remediate the gaps.

Function/Requirement or Data flow Step	Potential Failure Mode	Effect	Severity	Occurrence	Detectability	RPN	Intermediate Action	Severity	Occurrence	Detectability	RPN	Long term Recommended Action	Severity	Occurrence	Detectability	RPN	References
Archival/retrieval	Archiving is not planned for the system; a plan should be prepared to avoid system crash	possible loss of data	4	2	4	32	define a data archiving plan and validated archiving of data	4	0	4	0	N/A (coverd by intermediate action)	4	0	4	0	1) data archiving plan XXX 2) validation report XX
Audit trail review	Audit trail review is not adequately performed on data identified as GMP-critical since consultation of the audit trail database requires IT skills	manipulation of data possible	5	3	4	60	define queries to be run by IT and validate them	5	2	1	10	develop audit trail reports accessible to specified users	5	1	1	5	1) WMS audit trail queries and report specifications doc. nr. XXX 2) validation report doc. nr.XX
Access Approval	Agreement with the service provider (Quality Service Level Agreement) is in place but it does not provide details over the GMP versus non-GMP functionalities and actions allowed for GMP ones	possible manipulation of data and configuration items	3	3	3	27	provide the supplier with a list of GMP-critical functionalities and actions allowed	3	2	3	18	audit the supplier to ensure that the personnel involved in the WMS is aware of responsibilities defined in the	3	1	2	6	1) attachment to Quality Service agreement doc. nr. XXX 2) audit (or paper audit) report doc. nr.XX