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Technical Operations		
Standard Procedure	**Risk Management Process**	Page 1 of 14
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1. Objective

To define a global process and related rules for risk management and in particular provide guidance for a coordinated Risk Management process in Tech Ops.

The output of this process is:

- To provide the list of Risks impacting Tech Ops business activities and respective Action Plan for the mitigation
- To report to the **M**anagement **C**ommittee (MC), the consolidated treatment decisions and applicable mitigation actions related to the Strategic Plan

2. Scope

Applies to:

- All Tech Ops Functions as listed in section 3 Definition
- All products identified in the strategic plan
- Operational risks with influence on the Tech Ops business

Does not apply to :

- Occupational Health & Safety. These risks are considered through the EHS global Approach
- External environment. These risks are considered at company level as described in Merck KGaA Corporate Risk Management Guideline (2008-02-06) refer to category "Business Environment" specified under section 5.1.1.

3. Definitions and Abbreviations

Consolidation

The grouping by product of all Segment Operational risks and their assessment as per the global severity and occurrence criteria.

Harm

Damage to health, including the damage that can occur from loss of product quality or availability

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Operational Risk

Risk related to internal processes, employees, systems, or external events

Risk

The combination of the probability of occurrence of Harm and the severity of that Harm

Risk Assessment

A systematic process of organizing information to support a risk decision to be made within a Risk Management process. It consists of the *identification* of hazards and the *analysis* and *evaluation* of risks associated with exposure to those hazards

Risk Communication

The sharing information about risk and risk management between the decision maker and stakeholders

Risk Review

The review or monitoring of outputs/results of the risk management process (if appropriate) new knowledge and experience about the risk

Risk avoidance

Decision not to become involved in, or action to withdraw from, a risk

Risk reduction

Actions taken to reduce the probability, negative consequence, or both, associated with a risk

Risk retention

Acceptance of the burden of loss or consequence from a particular risk

Risk transfer

Sharing with another party the burden of loss for a risk

Monitoring

Monitoring is the follow up of the implementation of the Action Plan

Strategic Plan

The selection of the list of the finished products or products families

Segment

Group of activities in Tech Ops which must be considered for performing the Risk Assessments under the cover of the Segment coordinator. The defined Segments are:

- Input Materials
- Manufacturing Sites
- Processes
- Outputs

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Tech Ops Functions

The following Functions in Tech Ops:

- Biotech Product Development
- Biotech Manufacturing & Process Development
- Pharma Manufacturing Global Market
- Pharma Manufacturing Regional Markets
- Quality Management
- Supply Chain
- Engineering & Technology
- Purchasing

4. Rules

4.1 Process

The Risk must be managed through the following steps (see flow chart in Annex 1):

1. Strategic Plan - Product Panel
2. Risk Assessment
   - Risk Identification
   - Risk Analysis
   - Risk Evaluation
3. Risk Control
4. Consolidation
   - Consolidation of risk and mitigation actions
   - Recommendation of Treatment Decision
5. Validation of Risk Treatment Recommendations
6. Action Plan
7. Monitoring & Risk Review

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4.2 Strategic Plan- Product panel

The basis of the Risk Management process is the selection of the list of the finished products or finished product families which are integrated in a strategic plan. For these products or product families, a risk assessment according to this standard must be performed.

The drivers for product impact rating which must be considered are at least (not exhaustive):

- Revenue
- Strategy Company
- Portfolio strategy

This plan must be provided by Tech Ops to the Segment coordinators as a written and signed statement.

4.3 Risk Assessment

Risk Assessment must be done by the site under the cover of a Segment coordinator according to the different Segments defined which are:

- Input Materials
- Manufacturing Sites
- Processes
- Outputs

The processes and actions summarized under these Segments are defined in Annex 3. The segment coordinator is also shown in Annex 2, chosen by the function having the highest influence on these segment activities.

4.3.1.1 Risk Identification

Risk identification is the process to find, list and characterize element of risk.

The Output of the risk identification is a List of scenarios with their consequences

4.3.1.2 Risk Analysis

Risk analysis is the process to assign values to the probability and consequences of a risk.

This means definition on failure modes, their consequences and causes.

Output of risk analysis is the List of risks with value assigned

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4.3.1.3 Risk Evaluation

Risk evaluation is the process to prioritized risks according to risk evaluation criteria in relation with the incident scenario that lead to those risks. This evaluation must be performed according to a common risk scale (see Annex 4).

Output of the risk evaluation is List of prioritized risks

4.4 Risk Control

Risk Control (= risk treatment) is the process to select/decide the most appropriate option to deal with a risk based on the risk assessment. Effort and costs for implementing the different options and the expected benefits from these options are important elements to consider in this decision process.

Risk treatment actions can be

- Risk avoidance
- Risk transfer
- Risk reduction
- Risk acceptance

For all prioritized risk, the risk evaluation, the proposed treatment decisions and applicable mitigation actions must be defined. The Table for risk level treatment defined in Annex 5 must be used to define the risk level and prioritized risk form the risk evaluation.

Output of risk control (treatment) is:

- List of risks of levels 1 and 2

- Proposed risk treatment decisions and mitigation actions for level 1.

4.5 Consolidation

Consolidation consists in combining all collected information for each product/product family defined in the strategic plan.

Consolidation must be done on risks but also on mitigation actions to allow the maximum of synergies between these latter.

In addition, proposed treatment decision must be reviewed by the Segment coordinator to confirm, modify or invalidate those considering the global picture of all contributors involved in the particular segment. *(example: a major risk identified by a site could be reviewed and considered acceptable at TechOps level if a full backup strategy with a second site is in place. In such a case the proposed mitigation action will be invalidated)*

The reviewed treatment decision are called treatment recommendation

Output of the consolidation is the List of consolidated risk with respective treatment recommendations and applicable mitigation actions

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4.6 Validation of Treatment Recommendations

The recommended treatment actions can be accepted, changed or refused. If actions are accepted, the necessary resources must be given to allow implementation of actions.

Resulting out of this Management decisions an Action Plan must be generated and communicate. The reason for each rejected risk must be reportd in the Action plan. Responsibilities and timelines for implementation must be specified.

Output of the validation of Treatment Recommendation is an Action Plan

4.7 Monitoring and Risk Review

Strategic plan must be updated yearly. Any change of strategic plan must trigger new Risk Assessment(s).

The Risks must be reviewed on a regular basis.

In case of change which might impact a Risk Assessment, the Site must assess the need to update the Risk Assessment and to communicate the Risk Assessment to the Segment coordinator. A new consolidation must be done.

5. Responsibilities

5.1 Sites are responsible

- To perform Risk Assessment and provide Risk Assessment results
- Develop and propose treatment decisions and applicable mitigation actions
- Implement validated Action Plan
- Provide follow-up status as agreed

5.2 Segment coordinators are responsible

- Define Risk Management approach
- Define specific tools used to perform the Risk Assessment
- Support the sites to perform the Risk Assessment and provide training if required
- Provide the Strategic plan to sites
- Collect the list of risk by product from the Site
- Consolidate Risks
- Review treatment decisions
- Consolidate treatment decisions and applicable mitigation actions
- Monitoring of action plan execution

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- Risk Review

5.3 Tech Ops is responsible

- Develop and provide Strategic Plan

5.4 Tech Ops Management Committee is responsible

- Validate the risk treatment recommendations and generate Action Plan
- Risk Communication

5.5 Tech Ops Functions are responsible

- Participate and support Segment Coordinator to set the appropriate Risk Management approach for the specific segment as specified in the responsibility matrix in Annex 1

5.6 Tech Ops Controlling is responsible

- Develop clear costs assessments and calculation with regard to figures presented

6. References

Merck KGaA Corporate Risk Management Guideline (2008-02-06)

7. Annexes

- Annex 1: Process flowchart of Risk management
- Annex 2: Responsibilities matrix
- Annex 3: Definition categories
- Annex 4: Severity and Occurrence criteria for Consolidation
- Annex 5: Risk Level for treatment

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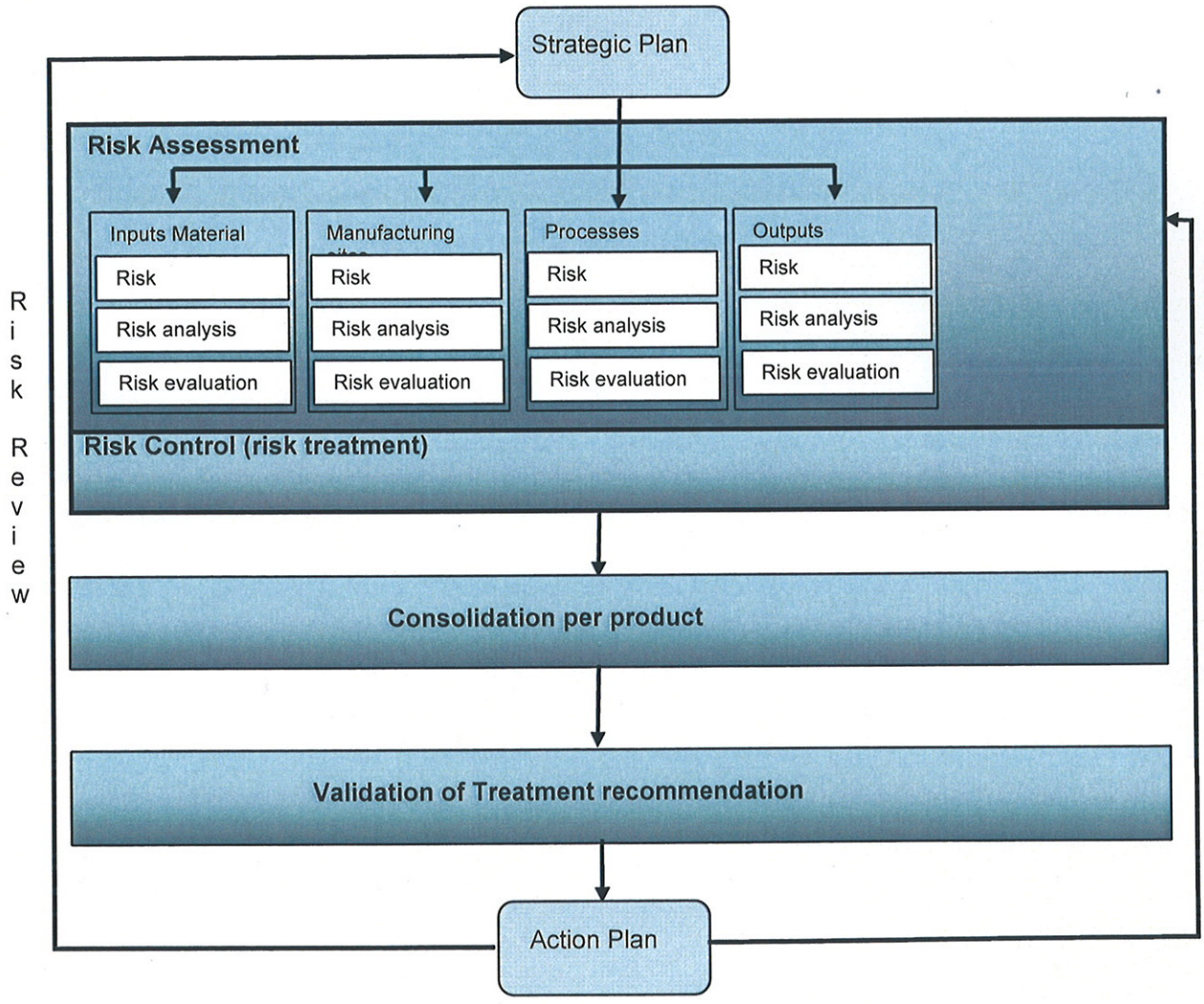
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8. Revision history

Version n°	Effective Date	Reason for and Description of the Change	Replacement of previous QM TechOps Documents
01	As per first page header	First version	N/a

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Annex 1
Risk Management Process flowchart



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Annex 2
Responsibilities Matrix

Segment	Tech Ops Function								
	Biotech Prod. Dev.	Biotech Manuf&Process Dev.		Pharma Manuf. Global Market	Pharma Manuf. Regional Market	Quality Mngt	Supply Chain	E&T	Purch.
		CoE Biotech	CoE F&F						
Input Materials & Services						I	I		L
Manuf.sites		I		I	I			L	
Biotech Processes	I	L					I		
Solid Form Processes	I			L	I		I		
Fill & Finish Processes	I	I	L	I	I		I		
Outputs						I	L		
Ext. Manufacturing	I	I	I	I	I	I	I	I	I

Legend
I: Involved
L: segment coordinator

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Annex 3
Definition of the Categories

Input Materials & Services

- API
- Excipients
- Diluents
- Primary and Secondary packaging components
- Services providers
- Subcontractors
- Critical materials in contact with product (e.g. chemicals, filters, ...)

Manufacturing Sites

- Facilities
- Production Equipments
- Utilities
- Premises (e.g. Flow and Classification)
- IT Hardware

Processes

- Biotech API processes
- Solid non-sterile forms and Semi-liquid non sterile forms
- Liquid sterile forms
- Liquid non sterile forms
- Packaging processes
- QC processes
- QA processes
- Planning/Inventory processes
- Shipping and Distribution processes

Outputs

- Shipping & Distribution of Finished Products
- Shipping & Distribution of Semi-finished Products
- Shipping of Biotech API

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Annex 4
Severity and Occurrence (Probability) criteria for Consolidation

Severity Criteria

Category	Severity	Ranking
Very High	Business interruption >1 month Market supplied <50%	5
High	Business interruption >1 months Market supplied <75%	4
Moderate	Business interruption >1 week Market supplied <90%	3
Low	Business interruption >1 week Market supplied by product of same family	2
Very Low	Business interruption <24h Market supplied 100%	1

Business interruption:

Time between the demand of the market and the delivery

Market supplied:

Capacity to fulfill the market demand

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Occurrence Criteria

Category	Probability of Occurrence	Ranking
Very High	More than 1x in 1 years	5
High	1x in 1 year	4
Moderate	1x in 5 years	3
Low	1x in 10 years	2
Very Low	1x in 20 years	1

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Annex 5
Risk Level of Treatment

P \ S	1	2	3	4	5
1	1	2	3	4	5
2	2	4	6	8	10
3	3	6	9	12	15
4	4	8	12	16	20
5	5	10	15	20	25

RPN	Risk Level	Priority	Measure
> / =15	1	HIGH	Risk Treatment is mandatory and action plan must be developed and will be presented to MC Mitigation Actions must be validated.
>10 ; <15	2	MEDIUM	Risk Treatment is mandatory and action plan must be considered at site level
<10	3	LOW	No action required

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