Procedure: Device Risk Management

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# Purpose

The purpose of this procedure is to describe the requirements for integrating Quality Risk Management (QRM) within the Quality Management System (QMS) at [Company]

Refer to **Appendix 1 - Overview of the QRM process**.

# Scope

The scope of this procedure includes the Quality Management System for [Company]

QRM is required within all aspects of the QMS where a hazard may be identified. QRM is associated with Good Manufacturing Practice (GMP) and product quality and safety.

The following table describes areas where QRM is routinely applied (but not limited to):

|  |  |
| --- | --- |
| Area | Example systems where QRM is routinely applied |
| Quality systems | * complaints * non-conformances/deviations * corrective and preventative actions (CAPA) * change control * internal audits * validation and qualification * supplier evaluation and management * product quality review |
| Product lifecycle | * product development (as appropriate) * laboratory control and stability testing * manufacturing, technology transfer or contract manufacturing * distribution * inspection * submission/review processes |

The following is excluded from the scope of this procedure:

* Business, administrative or other risks not covered by the QMS and/or that are not GMP.

# Responsibilities

Amend to reflect company structure.

|  |  |
| --- | --- |
| Position | Responsibility |
| Quality Manager (or delegate) | Ensure risk management is carried out so the quality management system is adequate and effective.  Lead risk management when required.  Train others to lead and carry out risk assessments.  Periodically review risk assessments for adequacy and completeness.  Coordinating QRM across various functions and departments of the company  Approves risk assessments to ensure they are appropriately documented and decisions are justified using a scientifically-based approach |
| Validation staff, Originators of CAPA, deviations, CC, etc. | Carry out risk assessments and ensure completion of actions. |
| All staff | Participate on risk management teams or in risk assessments as appropriate. |

# 

# General requirements

|  |  |
| --- | --- |
| Important: | * The level of effort, formality and documentation of QRM is commensurate with the level of risk. QRM is used to focus effort on areas of greatest risk to GMP and product quality & patient safety. * QRM must not be used to justify non-compliance with GMP or any other requirement mandated by a regulatory authority. * This QRM SOP systematically defines the risk, based on scientific knowledge and experience, for the hazard being considered. Factual evidence and/or expert assessment must always be used to reach conclusions. * Different situations may require different levels of effort proportional to the level of risk. In some cases, the order of steps in this SOP may need to be flexible, depending on the situation and the availability of data. |

Risk management is integrated into the QMS to assist in decision making to:

* ensure product quality
* provide continued assurance of patient safety
* ensure integrity of data
* ensure regulatory compliance
* reduce risk

## Initiating QRM

QRM is initiated when a hazard is either:

* detected - has occurred
* perceived - near miss or yet to occur (identification may be dependent on staff risk tolerance)

The following stages may be completed by either a single subject matter expert (SME) or a risk team, depending on the situation. Specific requirements for selecting a risk team are detailed in **Section 4.2 - Forming a risk management team** of this SOP.

|  |
| --- |
| * **Describe the problem** – define the “problem statement” including relevant assumptions identifying the potential for risk * **Gather data** – assemble background information and/or data on the potential hazards relevant to the risk assessment * **Gather resources** – identify a leader / facilitator and the necessary resources * **Define deliverables** – specify timelines, deliverables and appropriate level of decision making for the process * **Choose QRM tool** – establish and document the risk assessment strategy or tool to be used before commencing risk analysis (refer to **ISO 14971**). |

Risk assessment document numbers should be assigned and registered in accordance with local document management procedures.

## Forming a risk management team

Risk teams are typically formed when the risk scenario or hazard is complex, impacts multiple departments, or has a high impact to the site.

The risk team members should be selected based on staff knowledge and experience of:

* the area/process being assessed
* QRM principles

The risk team must document as part of the risk assessment record:

* team members and their roles within the risk team – it is recommended that the team includes a representative from QA
* any resources required
* the escalation process for different levels of management decisions, based on the results of the risk assessment
* proposed timeline

QRM activities are usually undertaken by interdisciplinary teams including SMEs from appropriate areas. As people perceive risk differently, different people may attribute:

* different or additional potential risks to a situation or problem
* different probability of each hazard occurring
* different severities to each hazard

Consequently, it is very important that all aspects of QRM are documented, including justification for why decisions have been made.

## Performing risk assessment

A risk assessment generally comprises three stages:

* Risk identification (in detail)
* Risk analysis
* Risk evaluation

These stages consider three questions for the defined problem statement in order to identify hazards:

1. What might go wrong?
2. What is the likelihood (probability) it will go wrong?
3. What are the consequences (severity) if it does go wrong?

The risk assessment is documented in **Form FM812-1 – Risk Assessment Spreadsheet** which facilitates the activities required in Sections 4.3.1 to 4.3.3 below.

### Risk identification

For each of the hazards (problem, event etc.) identified, make a list of everything that may go wrong associated with the hazard with respect to GMP and product quality/safety. There may be multiple risks identified for a single hazard.

Consider:

* known information or data
* site knowledge and experience, particularly for risks associated with facility, processes and products
* regulatory and/or customer expectations
* stakeholder concerns

Document the list of identified risks according to the type of risk approach used.

### Risk analysis

For each of the risks identified in **Section 4.3.1– Risk identification**, estimate the severity and probability.

*Detectability* may be included in the risk analysis if applicable to the situation and if data is available by asking the following question:

“What is the probability it can be detected if it does go wrong?”

Refer to **Appendix 2 – FMEA 3x3 Risk Analysis and Evaluation** for example criteria that may be used during FMEA risk assessments.

|  |  |
| --- | --- |
| Important: | The better the data, the more confidence in the risk assessment result. If data used during risk analysis is poor, then the risk team or Quality Manager may require additional measures to ensure the risk is adequately controlled. |

|  |  |  |
| --- | --- | --- |
| Criteria | Description | Example of Evidence |
| Severity | Severity of the risk if it were to occur (also called severity of harm or consequence) | Past records – investigations, corrective actions, recalls, complaints, studies etc.  Stability or trending data  Expert knowledge or experience, including published literature or advice from external experts  Experiments, prototypes or models |
| Probability | Probability that the risk will occur (also called likelihood of occurrence or frequency) |
| Detectability | Detectability that the risk will be detected if it does occur – identifies current controls that are in place that can detect the risk.  **Note:** Detection after finished product is released, such as product complaints or adverse events, should not be included in detectability assessments because they do not protect patient safety. | Real time displays, charts or logs – temperature, pressure, pH etc.  Alarms  Sampling, in process and testing results  Product inspection  Number of rejects, stoppages, interventions, machine jams etc. |

Document the risk analysis results according to the type of risk approach used. If other risk tools not specified by this SOP are used, the quantitative or qualitative criteria used must be documented within the risk assessment record.

### Risk evaluation

Risk evaluation compares the level of risk found during risk analysis (**Section 4.3.2 – Risk analysis**) with the company’s level of risk tolerance by using risk evaluation criteria to generate a risk score (e.g. high, medium or low or risk priority number, etc.).

Refer to **Appendix 2 – FMEA 3x3 Risk Analysis and Evaluation** for evaluation criteria that may be used during FMEA risk assessments.

The risk score is used to:

* decide the level of risk
* assign priority to the highest risk(s)
* identify what risks are not acceptable and must be controlled

Document the risk evaluation results and indicate risks that require risk control measures to be implemented.

When risk control measures are:

* required to be implemented to mitigate the risk, go to **Section 4.4 – Controlling risk**
* not required because all risks are acceptable (control measures may already be in place), go to **Section 4.5 – Closing a risk assessment**

## Controlling risk

|  |  |
| --- | --- |
| Important: | Unacceptable risks must be controlled unless a written justification, indicating why the risk should be accepted, is approved by the Quality Manager. |

Determine appropriate risk control measures for those risks identified as unacceptable in **Section 4.3.3 – Risk evaluation**.

### Designing risk controls

Consider the following questions to design risk control measures:

* What can be done to reduce, control or eliminate the severity or probability of the risk?
* What can be done to improve the detectability of the risk?
* What is the appropriate balance between benefits, risks and resource? Should the activity generating the risk be avoided all together?
* Will the risk control measures be effective?
* Are new risks introduced by implementing the risk controls?
* Will the risk be acceptable once the risk control measure is implemented or does the risk require further control?

Document the risk controls in the risk assessment record.

Examples of risk control types are listed in the following table (other control types not listed below may also be used if appropriate).

|  |  |
| --- | --- |
| Risk Control Type | Description |
| Procedural | Documented in an SOP requiring staff to complete an activity in a particular manner. |
| Training | Training of relevant staff to communicate risk associated with a specific event (e.g. deviation).  Frequency of routine training is increased or training type is changed to include an assessment. |
| Change in functionality | The functionality of a system is changed so that the risk is controlled (e.g. by reducing probability or severity). |
| Testing/monitoring | New or additional actions to test or monitor a product or process. |
| System access or authorisation | Limit system access for critical process steps to specific/senior staff roles. |

### Determining residual risk

The residual risk, when the risk control measure is applied, is evaluated using the same criteria used to evaluate the original risk. If the residual risk is not acceptable, then further risk control measures are need. Additional risks may also be introduced with the control measure – this should be assessed as part of the risk control strategy.

### Implementing risk controls

Submit the risk assessment record to the Quality Manager to approve the implementation of risk control measures.

When the Quality Manager is satisfied that the risk control measures are appropriate and will not cause other impacts to GMP activities, processes or areas, then the risk controls may be approved to be implemented.

Risk control implementation may be actioned as:

* a corrective and preventative action (CAPA)
* a change control (procedural control or documentation update)
* a site project (requiring a change control for the project)

## Closing a risk assessment

Complete all risk assessment records and documentation according to the risk tool used. All risk management must including the following requirements:

* Risk description
* Areas/stakeholders impacted by the hazard (e.g. departments)
* Tools and criteria employed (if different from those listed in this SOP and associated forms)
* Records from risk assessment and risk control
* Justification for decisions made during risk assessment and risk control
* Outcomes and effectiveness of risk control (when risk control is required)

Any additional records associated with the risk assessment should be collated with the risk assessment (e.g. copies of CAPA or change control record, data used to justify decisions, monitoring/control data etc.).

### QA approval

Submit the risk assessment package to the Quality Manager for review and approval. The Quality Manager confirms that:

* All documentation is compliant and correct
* Decisions are documented
* Conclusions are appropriate and justified.
* Mitigating actions are in place for unacceptable risks

The Quality Manager assigns a review frequency according to **Section 4.5.2– Assigning risk review frequency**.

### Assigning risk review frequency

Routine review of QRM is required to:

* take into consideration any new knowledge or experience
* continue to use the same approach for events that might impact on the original quality risk management decision – including planned events (e.g. results of product review, inspections, audits, change control) or unplanned events (e.g. root cause from failure investigations, recall)
* reconsider risk acceptance decisions

The Quality Manager uses the following table as a guide to assign a review frequency to the risk assessment before approving the risk assessment record. The Quality Manager may assign tighter review frequencies is required.

|  |  |
| --- | --- |
| Frequency | Guidance description |
| Annually | High risk to GMP or product quality, impacts to events, processes, systems or equipment and/or when significant changes are planned (including to systems or processes used as control measures). |
| 3 years | Medium risk to GMP or product quality, impacts to events, processes, systems or equipment and/or when significant changes are planned. |
| 5 years | Low risk to GMP or product quality. |
| Not required | Risk assessments with low/medium risk to GMP or product quality, that did not require risk control, and that are completed as part of other quality systems that are routinely reviewed during annual product quality review (e.g. change controls, deviations, CAPA, internal audits, complaints etc.). |

## Trending QRM metrics

The Quality Manager reports to senior management the following metrics and trends over a 12 month period on a routine basis [industry standard would be quarterly]:

* number of risk assessments opened each month
* number of risk assessments closed each month
* number of high/critical risks for the site

The QRM metrics and trends should be included in the annual Product Quality Review (PQR).

Appendices

# Appendix 1: Overview of the QRM process



# Appendix 2: FMEA 3x3 Risk Analysis and Evaluation Criteria

The following 3x3 qualitative and quantitative criteria are based on the approach in GAMP 5 and ISPE.

[This section defines only one way that risk can be evaluated; refer to ISO 14971, or investigate other risk management processes, to help you determine what the most appropriate option for your company is. Once decided, then describe your approach in this section.

Update the risk analysis spreadsheet to reflect your approach.]

**Risk Severity**

Assign severity for each risk. Use either a qualitative approach (Critical/Major/Minor) or quantitative approach (ranking 1-3).

|  |  |  |
| --- | --- | --- |
| Severity level | Ranking | Severity description |
| Critical | 3 | Situation may result in:   * death, permanent impairment or life-threatening injury, or * product quality ruined or quality requirements systematically breached, or * product withdrawn from sale, or * regulatory penalty will result |
| Major | 2 | Situation may result in:   * injury or impairment requiring professional medical intervention, or * significant product quality reduction or quality requirements breached, or * regulatory consequence |
| Minor | 1 | Situation will result in:   * self-limiting, temporary and / or trivial effect on consumer, or * small product quality reduction not impacting effectiveness or efficacy, or * isolated quality deviation |

**Risk Probability**

Assign probability for each risk. Use either a qualitative approach (high/medium/low) or quantitative approach (ranking 1-3).

|  |  |  |
| --- | --- | --- |
| Probability level | Ranking | Probability description |
| High | 3 | 41- 100% chance of occurring |
| Medium | 2 | 10 – 40% chance of occurring |
| Low | 1 | Less than 10% chance of occurring |

**Risk Evaluation Matrix to Assign Risk Class**

Determine the risk class for each risk based on the severity and probability.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  | | Severity | | | |
|  |  | | Critical (3) | Major (2) | | Minor (1) |
| Probability | High (3) | | Unacceptable (9) | Unacceptable (6) | | Undesirable (3) |
| Medium (2) | | Unacceptable (6) | Undesirable (4) | | Acceptable (2) |
| Low (1) | | Undesirable (3) | Acceptable (2) | | Acceptable (1) |
| Unacceptable = Risk Class 1 | | Undesirable = Risk Class 2 | | | Acceptable = Risk Class 3 | |

**Note:** Assign risk controls based on the risk class when detectability will not be included in the evaluation.

**Risk Detectability**

Assign detectability for each risk. Use either a qualitative approach (high/medium/low) or quantitative approach (ranking 3-1). Note that the ranking for detectability is in the reverse order to severity and probability – ability to detect presents low risk.

|  |  |  |
| --- | --- | --- |
| Detection level | Ranking | Detection description |
| High | 1 | Detection of the hazard is perceived to be highly likely (e.g. 1 event in every 1 operation) |
| Medium | 2 | Detection of the hazard is perceived to be reasonably likely (e.g. 1 event in every 2 operations) |
| Low | 3 | Detection of the hazard is perceived to be unlikely (e.g. less than 1 event in every 3 or more operations) |

**Assign Risk Priority**

When detectability will be included in the evaluation, then assign a risk priority according to the risk class and the level of detectability.

|  |  |  |  |
| --- | --- | --- | --- |
|  | Detectability | | |
| Risk Class | High | Medium | Low |
| 1 | Medium Risk Priority | High Risk Priority | High Risk Priority |
| 2 | Low Risk Priority | Medium Risk Priority | High Risk Priority |
| 3 | Low Risk Priority | Low Risk Priority | Medium Risk Priority |

**Determine Risk Control**

Use the following risk priority table to determine if risk control is required.

|  |  |  |
| --- | --- | --- |
| Qualitative Risk Priority | Quantitative Risk Priority (RPN) | Risk Control |
| Low | 1-4 | No control required |
| Medium | 5-9 | Risk control may be required although in some circumstances this may not be considered necessary. |
| High | 10-27 | Control required. |

**Note:** RPN = severity x probability x detectability

# Definitions

Amend as required or delete.

|  |  |
| --- | --- |
| Term | Definition |
| Detectability | The ability to discover or determine the existence, presence, or fact of a hazard |
| Failure mode | Different ways that a process or sub-process can fail to provide the anticipated result |
| Harm | Damage to health, including the damage that can occur from loss of product quality or availability |
| Hazard | The potential source of harm |
| Quality risk management | A systematic process for the assessment, control, communication and review of risks to the quality of the drug product across the product lifecycle |
| Risk | The combination of the probability of occurrence of harm and the severity of that harm |
| Risk acceptance | The decision to accept risk |
| Risk analysis | The estimation of the risk associated with the identified hazards |
| Risk assessment | A systematic process of organising 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 of information about risk and risk management between the decision maker and other stakeholders |
| Risk control | Actions implementing risk management decisions |
| Risk evaluation | The comparison of the estimated risk to given risk criteria using a quantitative or qualitative scale to determine the significance of the risk |
| Risk identification | The systematic use of information to identify potential sources of harm (hazards) referring to the risk question or problem description |
| Risk management | the systematic application of quality management policies, procedures and practices to the tasks of assessing, controlling, communicating and reviewing risk |
| Risk priority number (RPN) | A numeric assessment of risk assigned to a process, or steps in a process, as part of failure mode effects analysis (FMEA). Each failure mode gets a numeric score that quantifies likelihood of occurrence, likelihood of detection and severity of impact. The product of these three scores in the risk priority number for that failure mode.  RPN = severity rating x probability rating x detection rating |
| Risk reduction | Actions taken to minimise the risk to reduce its probability or impact. |
| Risk review | Review or monitoring of output/results of the risk management process considering any new knowledge or experience about the risk |
| Risk tolerance | The level of risk perceived as acceptable to any one stakeholder (may also be called risk appetite) |
| Severity | A measure of the possible consequences of a hazard |
| Stakeholders | Any individual, group or organization that can affect, be affected by, or perceive itself to be affected by a risk. Decision makers might also be stakeholders. Possible stakeholders include the patient, healthcare professionals, regulatory authorities and industry. |

Document Information

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| ISO 14971 | Medical Device Risk Management |
| ISPE - GAMP 5 | A Risk-Based Approach to Compliant GxP Computerised Systems |
| FM812-1 | Risk Assessment Spreadsheet |

List all controlled procedural documents referenced in this document (for example, policies, procedures, forms, lists, work/operator instructions

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