Definitions

Decision Maker(s): Person(s) with the competence and authority to make appropriate and timely quality risk management decisions.

Detectability: The ability to discover or determine the existence, presence, or fact of a hazard.

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

Hazard: The potential source of harm (ISO/IEC Guide 51).

Product Lifecycle: All phases in the life of the product from the initial development through marketing until the product's discontinuation.

Quality: The degree to which a set of inherent properties of a product, system or process fulfils requirements (see ICH Q6A definition specifically for "quality" of drug substance and drug (medicinal) products.)

Quality Risk Management: A systematic process for the assessment, control, communication and review of risks to the quality of the drug (medicinal) product across the product lifecycle.

Quality System: The sum of all aspects of a system that implements quality policy and ensures that quality objectives are met.

Requirements: The explicit or implicit needs or expectations of the patients or their surrogates (e.g., health care professionals, regulators and legislators). In this document, "requirements" refers not only to statutory, legislative, or regulatory requirements, but also to such needs and expectations.

Risk: The combination of the probability of occurrence of harm and the severity of that harm (ISO/IEC Guide 51).

Risk Acceptance: The decision to accept risk (ISO Guide 73).

Risk Analysis:
The estimation of the risk associated with the identified hazards.

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 of information about risk and risk management between the decision maker and other stakeholders.

Risk Control: Actions implementing risk management decisions (ISO Guide 73).

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 Reduction: Actions taken to lessen the probability of occurrence of harm and the severity of that harm.

Risk Review: Review or monitoring of output/results of the risk management process considering (if appropriate) new knowledge and experience about the risk.

Severity: A measure of the possible consequences of a hazard.

Stakeholder: 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. For the purposes of this guideline, the primary stakeholders are the patient, healthcare professional, regulatory authority, and industry.

Trend: A statistical term referring to the direction or rate of change of a variable(s)

Risk Rating Scales

1.1 Risk Estimation – Severity/ Consequences Tables

The following severity ratings can be used to estimate degree of severity of an identified hazard. Product performance means a combination of Safety, Efficacy, Identity, Purity and Quality. The criteria also includes levels of compliance with GMP Rules.

***Table 1 – SEVERITY* Rating Criteria**				
Ratings		**Effect**	**Patient Product Impact Criteria**	**GMP Compliance Impact**
S-1	**1**	None	No impact at all on product performance or patient safety.	No impact on GMP compliance.
	2	Minor Inconvenience	Patient not concerned. No patient injury. No noticeable effect on product performance.	Very low impact on cGMP compliance
S-2	**3**	Moderate Inconvenience	Patient not concerned. No patient injury. Slight / cosmetic effect on product performance. May result in minor complaint.	Low impact on GMP compliance.
	4	Minor Dissatisfaction	Customer experiences some minor nuisance and becomes slightly annoyed. Complaint probable but no patient injury.. Minor/cosmetic effect on product performance.	Some impact on GMP compliance but no excursion from Marketing Authorisation.
S-3	**5**	Moderate Dissatisfaction	Moderate user dissatisfaction, No patient injury. Performance degraded, but product remains safe and operable. Likely complaint.	Minor direct non - compliance with GMPs. No excursions from marketing authorization.
	6	Major Dissatisfaction	Major user dissatisfaction, product non-performance evident but safe, no resulting injury to patient.	Major non - compliance with GMPs. Possible excursions from marketing authorization.
S-4	**7**	Marginal Health Hazard	A failure that can cause transient adverse reaction to a patient and compliant. May not require treatment and has no long-term health consequences.	Major non - compliance with GMPs. Possible excursions from marketing authorization. Recall unlikely.
	8	Moderate Health Hazard	A failure that can cause a moderate harm or adverse reaction to a patient or user but will not result in chronic harm. The harm will require treatment. Product performance is either partially or completely degraded. Product complaint expected.	Major non - compliance with GMPs. Probable excursions from marketing authorization. Possible recall.
S-5	**9**	Critical Health Hazard	A failure that can contribute (indirectly) to a death or severe or chronic harm, Product performance is degraded.	Critical non - compliance with GMPs. Direct excursion from marketing authorization. Probable recall.
	10	Catastrophic Health Hazard	A failure that can by itself cause (directly) death or a significant harm to a patient or user.	Critical non - compliance with GMPs. Loss/ restriction of GMP License probable. Multiple excursions from marketing authorization. Probable recall.

1.2 Example Probability of Occurrence Rating /Scoring Table

The following table was used to assign the probability of occurrence of the identified harm. This assessment is based on (a) the experience of the risk assessment/audit team (b) analysis of marketplace feedback such as adverse events and complaints (c) internal failures and non-conformances and (d) historical or trend experience.

***Table 2 – OCCURRENCE* Rating Criteria**					
Rating		**Likelihood of Occurrence**	**Probability of Failure** ***(Qualitative Criteria)***	**Possible Failure Rate** ***(Quantitative Criteria)***	
O-1	**1**	Almost Impossible	Failures are highly unlikely.	Once every 6 –100 years	≤ 2 per billion
	2	Remote	Rare numbers of failures are likely to occur.	Once every 3 –6 years	≤ 3 per 10 million
O-2	**3**	Very Slight	Very few failures are likely to occur.	Once every 1 – 3 years	≤ 6 per million
	4	Slight	Few failures are likely to occur.	Once per year	≤ 6 per 100,000
O-3	**5**	Low	An occasional number of failures are likely to occur.	Once every 6 months	≤ 1 per 10,000
	6	Medium	A medium number of failures are likely to occur.	Once every 3 months	≤ 0.03%
O-4	**7**	Moderately High	A moderately high number of failures are likely to occur.	Once per month	≤ 1%
	8	High	A high number of failures are likely to occur.	Once per week	≤ 5%
O-5	**9**	Very High	A very high number of failures are likely to occur.	Once every 3–4 days	≤ 30%
	10	Almost Certain	Failures almost certainly will occur.	More than once per day	> 30%

1.3 Example Detection Rating / Scoring Table

The following table was used to determine the level of detectability of a harm or failure mode if it did occur. This assessment is based on (a) the experience of the risk assessment/audit team (b) analysis of inspection and test programs within the company and at suppliers and sub-contractors (c) analysis of in-process controls during production (d) historical or trend experience, including complaints.

***Table 3 – DETECTION* Rating Criteria**

Rank	Detection	Criteria
1	Certain	The listed Controls will almost certainly detect the Cause of Failure and/or the subsequent Failure Mode. Defect is obvious and can be kept from affecting customer. Tests are validated.
2	Very High	The listed Controls have an excellent chance of detecting the Cause of Failure and/or the subsequent Failure Mode. All units are automatically inspected. Tests are validated.
3	High	The listed Controls have a good chance of detecting the Cause of Failure and/or the subsequent Failure Mode. SPC as above with 100% inspection surrounding out of control conditions. Tests are validated
4	Reasonable	The listed Controls have a reasonable chance of detecting the Cause of Failure and/or the subsequent Failure Mode. SPC used with an immediate reaction to out of control conditions. Tests are validated
5	Moderate	The listed Controls may detect the Cause of Failure and/or the subsequent Failure Mode. Process is systematically monitored (SPC) and manually inspected. Tests are validated
6	Uncertain	It is uncertain that the listed controls will detect the Cause of Failure and/or subsequent Failure Mode. Manual/automated inspection with mistake-proofing. Units are systematically sampled and inspected using AQL sampling. Tests are validated.
7	Unlikely	It is unlikely that the listed Controls will detect the Cause of Failure and/or the subsequent Failure Mode. Units are systematically sampled and inspected using AQL sampling. Units are manually inspected. Tests partially validated
8	Very Unlikely	The listed Controls will very likely not detect the Cause of Failure and/or the subsequent Failure Mode. Units are irregularly sampled and inspected using AQL sampling. Control tests are not validated.
9	Extremely Unlikely	It is extremely unlikely that the listed Controls will detect the Cause of Failure and/or the subsequent Failure Mode. Occasional units are checked for defects. Control tests are not validated.
10	None	Action will / can not detect the Cause of Failure and/or the subsequent Failure Mode, or there is no action possible. Defect caused by failure is not detectable