Guidance Number: 83

Table I. Probability and Severity Ranking Scales

Risk Level	Probability	Severity
Low (1)	**Regulatory requirement**- No regulatory requirement exists to investigate non critical events. Not included in regulatory filing. **GMP** – There is no industry accepted practice to conduct investigations on non critical events. **Direct impact system** – It is a non-GMP impact system. **Direct product quality impact** – It has no direct product quality impact. **Risk to patient** – It has no direct risk to patient.	**Regulatory/GMP** – No issues during a regulatory inspection. **Direct impact system** – No impact. **Direct product quality impact** – No impact to product quality. **Risk to patient** – No risk to patient.

Risk Level	Probability	Severity
Moderate (3)	**Regulatory** – Some requirement exists to investigate non critical events. Not included in regulatory filing. **GMP** – It maybe considered an industry standard to conduct investigations on this type of events. **Direct impact system** – It is an indirect impact system. **Direct product quality impact – there may be** an indirect product quality impact. **Risk to patient** – It may present a moderate risk to the patient. e.g., Blister pack not formed correctly.	**Regulatory/GMP** – May result in a comment/minor observation during a regulatory inspection. **Direct impact system** - May have a GMP impact as it is an indirect impact system (if impact is mitigated with secondary system then severity moves to low). **Direct product quality impact** – May indirectly impact product quality (if impact is mitigated with secondary system then severity moves to low). **Risk to patient** - May result in an indirect risk to patient (if impact is mitigated with secondary system then severity moves to low).
High (5)	**Regulatory** – A formal requirement exists for investigating this type of events. Included in regulatory filing. **GMP** – It is an industry standard to conduct investigations on this type of events. **Direct impact system** – It is a direct impact system. **Direct product quality impact** –It has a direct impact to product quality. **Risk to patient** – It has a direct risk to patient.	**Regulatory/GMP** – May result in a FDA-483/major or critical observation during a regulatory inspection. **Direct impact system** – Results in impact as it is a direct impact system (if impact is mitigated with secondary system then severity moves to moderate). **Direct product quality impact** – Impacts product quality. **Risk to patient** – May result in a direct risk to patient.

Event	Probability/mitigation	Severity/mitigation	Risk score	Classification
Solvent recovery operations	1- Indirect system (mitigated to low with isolated recovered solvent testing), no regulatory requirements, no product impact	1 – Testing of isolated recovered solvent, no impact to patient	1 - Low	Event
Clean by testing failures (CBT)	3- Direct impact equipment, CBT failures trended and reviewed periodically.	1- Rinsate testing is performed on all equipment prior to use, no impact to patient	3 - Low	Event
Power failures with no impact to product	3- Potential to affect all systems, confirm no impact to product, no regulatory requirement.	1- When no impact to product there's no impact to patient. Product tested to final release specification.	3 - Low	Event
Documentation omissions with back up electronic	3- Potential to affect all systems, confirm back up electronic data	1 – No impact to patient	3 - Low	Event

Event	Probability/mitigation	Severity/mitigation	Risk score	Classification
data	available, documentation errors trended and reviewed			
Deviations from SOP with no impact to product	3- Potential to affect all systems	1- No impact to product quality. No risk to patient.	3 - Low	Event
In-process Control missed	3- Direct impact system. GMP standard to document and evaluate in-process control results.	1- In-process data available for other intervals which comply with acceptance criteria. Product tested to final release specifications.	3- Low	Event
Excursions from process manufacturing descriptions	5- Process parameters are filed	1 – No impact to patient	5 - Moderate	Deviation from regulatory filing
Equipment Out of Calibration	3- Indirect impact system. May have an indirect impact on product quality. GMP standard to investigate.	3- May result in a comment or minor observations during a regulatory inspection. Mitigated when calibrated equipment is OK and product quality is sustained.	9- Moderate	Deviation
Labeling Issues	5- Specifications are filed.	3- May result in indirect risk to patient. Can be detected/mitigated at several points within the company and distribution channel.	15- High	Deviation
OOS	5- Specifications are filed	3- OOS may impact patient and OOS product not released to market	15 - High	Deviation
Stability failures	5- Stability specifications filed	5 – Product is in dating and in the market	25 - High	Deviation
Foreign Matter/ Contamination	5- Direct impact, GMP standard to investigate, potential for introducing foreign matter from various sources: raw materials, environment, people and equipment.	5- Impacts product quality. May result in a direct risk to patient. If product is released, may result in customer complaints and major observation during a regulatory inspection, and/or recall.	25 - High	Deviation

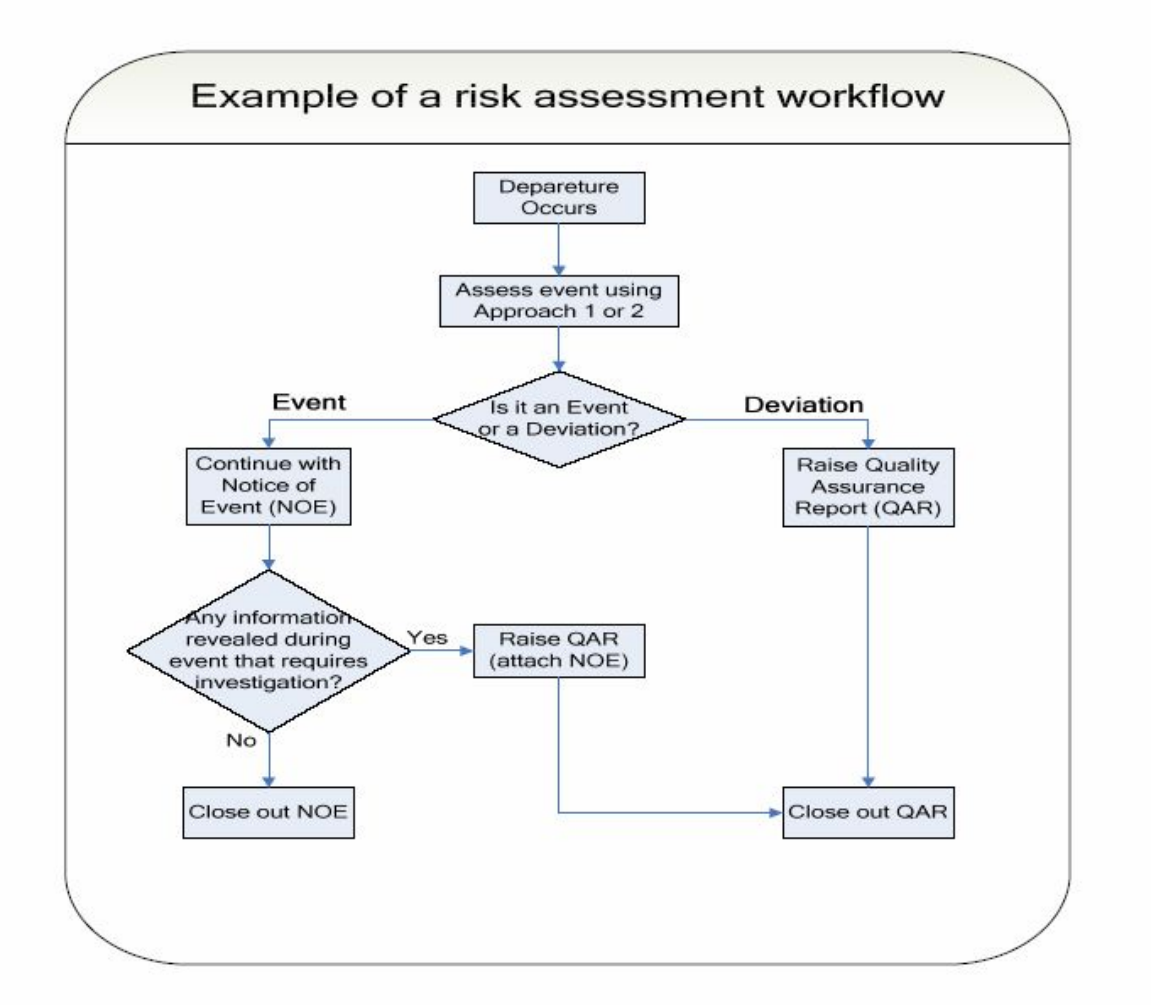
Example of a site risk assessment questionnaire based on the Individual Assessment Approach:

Quality Assessment				
If you answer YES to any of the following questions raise a QAR. If the answer to any is unknown (due to lack of information available at the time), explain in comments section, continue with Event and when information is available, reassess and, if answer is Yes, raise a QAR.		Yes	No	Unknown
1	Is it outside the registered parameters?	☐	☐	☐
2	Does the event impact a critical process parameter or yield of a critical process step?	☐	☐	☐
3	Is it a validation batch?	☐	☐	☐
4	Was there an error in batch manufacture that could have a direct impact on product quality; e.g. wrong material charged, a significant manufacturing step not completed or completed incorrectly?	☐	☐	☐
5	Have any of the test specifications (including in-process tests) not met?	☐	☐	☐
6	Has any foreign matter been introduced to the batch?	☐	☐	☐
7	Has the equipment been used prior to passing cleaning or the cleaning interval or cleaning procedure not followed?	☐	☐	☐

* QAR: Quality Assurance Report or Deviation Report

Quality Assessment				
If you answer YES to any of the following questions raise a QAR. If the answer to any is unknown (due to lack of information available at the time), explain in comments section, continue with Event and when information is available, reassess and, if answer is Yes, raise a QAR.		Yes	No	Unknown
8	Is there any equipment in the final API steps (post final polish filtration) not intact (including consumables or cleaning equipment)?	☐	☐	☐
9	Were there any raw material testing, packaging or contamination issues that would impact the batch quality?	☐	☐	☐
10	Does the issue affect the reliability or fitness for use of the finished product?	☐	☐	☐
11	Will this issue cause the product or its labeling to be mistaken for or applied to another product?	☐	☐	☐
12	Will additional testing or evaluations need to be performed to assess the product quality prior to release?	☐	☐	☐
13	Is this a recurring issue?[1]	☐	☐	☐
14	Does this event implicate drug product batches released to the market?	☐	☐	☐

* QAR: Quality Assurance Report or Deviation Report



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