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Integration of Q9 Quality Risk Management When Conducting GCP Regulatory Inspections and Audits

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Objectives

- Conducting Quality Risk Management within your own organization
- Applying Risk assessment to audits and inspection
- CRO Risk Model and applicability
- Recommendations from FDA and MHRA on conducting risk assessments



Applying Risk Evaluation to Site Auditing

- Goal of Risk evaluation is to develop more effective audit strategies to identify sites to audit by assessing risk:
 - Assign priority to risk identified
 - Reviewing results of audits and inspections
 - Pre-identified sponsor or CRO issues
 - Conducting data trends across sites to pinpoint data outside of expected range
 - Review of monitoring visit reports for high-impact trends
 - Absent PI/Lack of oversight
 - Large number of protocol deviations/violations
 - Serious issues with IP prep, administration and accountability



Q9 Concepts

Initial Quality Risk Mgt. Assessment

Identify Risk – Assess Impact on Patient Safety,
Product Quality, and Data Integrity

Perform Risk Assessments and
Hazard Analysis/ Evaluation

Risk Reduction/Strategy and Operations Controls

Risk Acceptance/Test and Implement Controls

Review Events/Monitoring System

**Most
Interactive**

**Least
interactive**



Implement Q9 Process



Steps for Conducting Risk Assessment

- Step 1: Begin by collecting information from stakeholders, in-house specialist, external consultants
- Step 2: Ask questions to identify risk
 - What is the cause of the risk?
 - What can be done to prevent the threat from occurring?
 - If the threat does occur, what is the plan of action?
 - How will the plan for dealing with the threat be implemented?
- Step 3: Measure the risk
- Step 4: Make adjustments to the project plan to eliminate threats (risk) & identify opportunity to add value
- Step 5: Define & follow action plan & post-review



So how is Risk applied to Clinical Trials?

- Measure progress of project(s) – ID Quality metrics
 - How? By tracking how close actual performance is to the planned deliverable
- In order to properly ID risk, need metrics to measure the effectiveness of the risk assessments currently in place by asking:
 - Do I have risk events that occur without warning
 - Did we track risk and assess the appropriate risk?
 - What was the impact of the Risk?
 - Have I seen new trends arising as a result of risk , i.e., (new trends arising as a result – deviations, violations, re-audits, inspections, regulatory action)
 - What effect did the risk have on Stakeholders (re-monitoring efforts, conducting internal investigations/audits, re-training)?



QA RISK INDEX

RISK CONTROL INDEX	LOW RISK	MEDIUM RISK	HIGH RISK
FREQUENCY OF USE 3 = Used often 2 = Medium use 1 = Seldom use	A one-off process or vendor used on a small Study	Used on >1 or 2 studies	Preferred Provider or part of a SOP within CRO
REGULATORY RISK 3 = High risk 2 = Medium risk 1 = Low risk	Minor findings	Major findings	Critical Findings patient safety, data integrity
BUSINESS RISK 3 = High risk 2 = Medium risk 1 = Low risk	Small one-off studies with smaller sponsors	Studies with mid to large pharma	High Income Study with Large Sponsor



QA RISK EXAMPLE

RISK CONTROL INDEX	VENDOR A	VENDOR B	VENDOR C
FREQUENCY OF USE	Used rarely for archiving FDA regulated records = 1	Used on >1 or 2 studies for monitoring = 2	Preferred Provider - Assigned highest score of = 3
REGULATORY RISK	Original training record lost, but scanned copy available; Minor finding = 1	Major findings – some monitoring visit reports were missing = 7	Critical Findings on unreported SAEs, data integrity issues = 9
BUSINESS RISK	Small one-off studies with smaller sponsors, but not all processes documented = 2	Critical Risk – Risk for company not using qualified/trained monitors = 9	High Income Study with Large Sponsors and FDA reportable = 9



MHRA Model Recommendations

1. Recommends comprehensive risk assessments
2. Inspect only if there is a reason
3. Provide authoritative, accessible advice easily and cheaply
4. Write regulations in terms which are easily understood, implemented, and enforced consulting with all interested parties when they are being drafted
5. Avoid requesting unnecessary information or multiple request of information from businesses
6. Quickly ID the businesses that persistently break regulations for further regulatory sanctions
7. Regulators should allow or even encourage economic progress and only to intervene when there is a clear case for protection
8. Regulators should remain independent but be accountable for the efficiency and effectiveness of their activities
9. No new regulator should be created where an existing one can do the work, focusing on the right size and scope
10. Consider how regulations can be enforced using existing systems and data when new policies are being developed



FDA Recommendations on Implementation:

- Implement a risk-based approach to trial inspections (e.g., site selection process) and consider when appropriate:
 - Iterative monitoring processes that enhance reliability without duplication
 - For sites and trials based on appropriate risk factors, alternatives to traditional on-site monitoring
 - Standardize data collection. Borrow from work already accomplished in information technologies such as software development, data management, data transfer formats
 - Training
 - Pre-testing of forms and procedures
 - Standardize data format (e.g., CDISC) to facilitate data auditing
 - Standardize data storage to facilitate real-time trial audits, transparency of data and data sharing



Summary: Quality Risk System

- Allows organizations to develop systematic risk systems to reduce probability of known risk and to identify emerging risk at the lowest levels
- Implementation of risk assessment allows organizations to understand and be prepared for:
 - Questions on what might go wrong
 - Probability of reoccurrence
 - Consequences of severity
- Proactive means to identify and control potential quality issues
- Allows management to make informed decisions on prioritizing risks
- Easily applied to auditing

