Optimizing Quality Control / Quality Assurance Agents of a Global Sourcing / Procurement Strategy

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THE MARKET LEADER IN PHARMACEUTICAL CONSULTING

Developing a Supplier Policy as a Key Element of the Quality System that Assures Success

Why do we need a Global Supplier Program and what are some key practical reasons for designing an effective system?

Developing a Supplier Policy as a Key Element of the Quality System that Assures Success

In today's LEAN highly regulated and competitive world there's a new global expectation of pre-determined quality measures, more predictable mechanisms of delivery and measures to assure long-term sustainability of quality and product safety.

Points to Consider

- You want something that's meeting compliance requirements.
- You want something that provides value to the business.
- You want something that's cost effective to administer and maintain.
- The system MUST influence your supplier positively to assure they win and you win.

Some Design Drivers:

- It's mandated by the International Regulatory Requirements.
- It assures the suppliers operate their business to match your expectations and needs.
- It assures that material is always uniform, within specifications, manufactured to the highest quality standards and safe.
- It helps to mitigate risk.
- Streamlined LEAN systems make good business sense.

Regulations Involved with Supplier Management

- 21 CFR 200.10(b)
  - "FDA regards third party facilities as an extension of the manufacturer's own facility."
- 21 CFR 211.22
  - "The Quality Control Unit shall be responsible for approving or rejecting drug products manufactured, processed, packaged or held under contract by another company."
- 21 CFR 211.84
  - Details the requirements for testing and approval/rejection of components for drug manufacturing.

Other Compliance Expectations

- ICH Q9 Risk Management
  - Requires a detailed evaluation of suppliers and CMO's including auditing and implementing supplier quality agreements.
  - The sponsor's Quality System should drive the management of outsourced activities.
  - Members involved in the supply chain are viewed as partners in determining success.

Other Compliance Expectations

- ICH Q10 Quality Systems
  - Sponsor responsibilities extend to the review of control of outsourced activities as an extension of their own Quality Management System.
  - Sponsor should have adequate procedures for auditing and qualifying supplies prior to and during use in the supply chain activities.

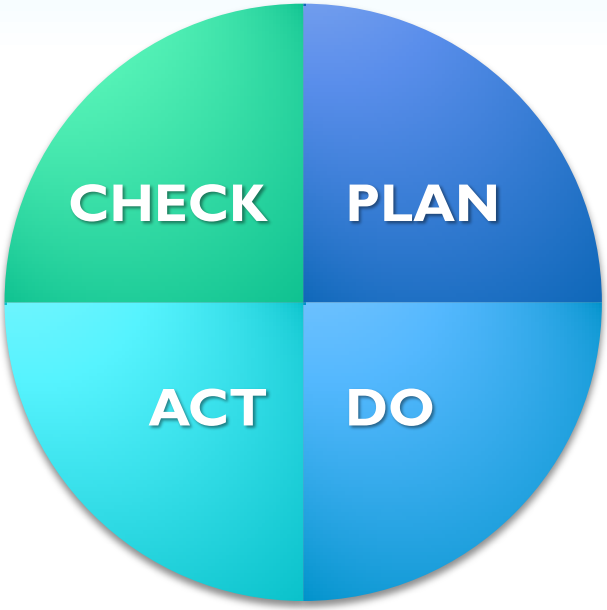
Unacceptable Incidents

- In the absence of strong Supplier Management Systems the potential for failure is high:
  - Heparin – 81 deaths; 800+ adverse events
  - Tainted Glycerin – 300+ deaths
  - TBA (2,4,6 Tribromoanisole) – contamination
    - Due to plastic bottles on wooden pallets treated at a contract CMO.
  - Ritonavir – Recall
    - Pulled from market due to existence of a polymorph that decreased bioavailability of drug for HIV patients.

Developing a Strategy

- Using a lean compliance philosophy we can approach the development of an effective supplier policy around a Deming Cycle; Plan-Do-Check-Act.

Continuously monitor and evaluate performance



Plan and define the process

Qualify the candidate

Carry out the selection process methodology

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Important Tools in the Development of a Best Practice Global Sourcing Strategy

- Process Map of the Process
- Supplier Quality Questionnaire
- Effective Risk Management Strategy
- A Communications Infrastructure
- Audit Program
- Quality Agreements
- Metrics/Analytics Program
  - Use of score cards

Supplier Sourcing Process Map

- Have a defined process map for your supplier process that's logical and considers cross-functional inputs.
- In developing this map understand the "Current State" as this will act as a reference point from which to develop the "Best Practice" "Desired State".
- Transition to the Desired State as the strengths and weaknesses are understood.

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Supplier Questionnaire Tool Composition

- This can vary depending upon the complexity, but should always include quality, cost and performance factors.
- For Quality:
  - Existence of GMP culture
    - Adherence to GMP's and ICH guidelines
  - Implementation of Quality System
    - Existence of policies, SOPs and records
  - Good Compliance Record
    - No citations by regulatory authorities

Supplier Questionnaire Tool Composition

For Process and Technological Capabilities:

- Appropriate facilities for production
- Capacity to deliver
- Strong technological capabilities
- Strong production controls
- Delivery performance record
- Clean environmental record

Supplier Questionnaire Tool Composition

For Personnel and Management Capabilities:

- Strong understanding of key performance indicators for supply chain.
- Strong technical management controls.
- Strong project management expertise.
- No de-barred individuals by FDA or other authority
- Strong in-house acquisition policy to maintain supply capabilities
- Appropriate group chemistry and business culture fit to foster long-term cooperative relationship.
  - Can-do spirit

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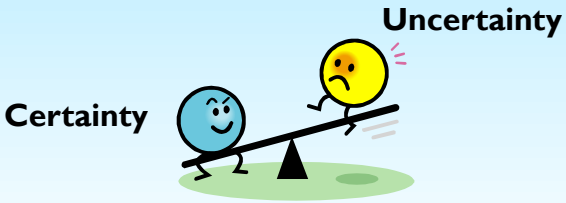
Effective Risk Management Strategy

- Risk, what is it?
  - Certainty and uncertainty
  - The probability of something occurring
  - The potential consequences of the result of something occurring
    - Equipment breakdown
    - Specification failure – wasted batch
    - Test failure – lost productivity



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Effective Risk Management Strategy

- Risk Management is a knowledge management program providing Decision Makers the power to make better Quality decisions.
- It involves identifying potential failure causing issues.
  - Ranking for criticality.
  - Mitigating the effects of these.
  - Where possible, eliminating these.
- Maintenance of sustainable compliance through oversight policy.
  - Determine areas needed.
  - Set out structure for levels required.
  - Execute oversight measures.
  - Review and make adjustments as necessary.

Risk-based Approach Flow Chart Described in ICH Q9 Provides Direction

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Determine Criticality Through Quantitative/Qualitative Models

Example: Compliance Record

Compliance Actions	Historical Database of Compliance Issues				
	No issues	Few issues	Occasional issues	Many issues	Significant issues
FDA violations requiring attention	**Low**	**Medium**	**High**	**High**	**High**
FDA objections voluntary action	**Low**	**Low**	**Medium**	**High**	**High**
Periodic internal audit findings	**Low**	**Low**	**Low**	**Medium**	**High**

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Determine Criticality Through Quantitative/Qualitative Models

- Now rank in terms of priority
  1. GMP fault A
  2. GMP fault X
  n. GMP fault N

Communications Infrastructure

- 4 issues: **What**, **When**, **Whom** and **How**
- **What** needs to be reported should be clearly defined based upon the degree of criticality
- **When** should something be reported?
  - Immediately when it occurs
  - In a monthly report
  - Annually

Communications Infrastructure

- To **Whom** should things be reported
  - QA
  - Senior Management
  - Procurement Specialist
- **How** should it be reported?
  - Telephone
  - E-mail
  - Dashboard
  - Written report

Audit Program

- Have a well defined audit plan and audit checklist to maintain consistency between vendors/suppliers and different auditors
- Define audit schedules/frequencies
- Define audit agendas
- Define reporting mechanism
- Define follow-up strategies

Quality Agreements

Key Points

- Should delineate responsibilities and accountabilities for both the sponsor and the supplier
  - Expectations
  - Timelines
  - Deliverables
- Should discuss change management issues
  - Authority for changes
  - Circumstances permitted

Quality Agreements

Key Points

- Should define communications mechanisms and decision making process
- Should define mechanism for dispute resolution

Metrics / Analytics Program

- Set up an analytical program to continuously provide data for ongoing assessment.
  - Gather data on each batch/lot received and use a dashboard to track performance
  - Trend data and provide to Quality Review Board for assessment.
- Use analytics to separate poor performers from qualifiable candidates.
- Use analytics to provide useful data for supplier profiles
  - Use audit data and data gathered for supplier questionnaire.
- Use data to continuously monitor performance and justify continued use.
- Use to establish "Preferred Vendor" list.

Example of Customer Scorecard

Scores to ± 10

Score Attribute	Ideal Score	Example Score
Documents received	1	0
Material quality OK	3	0
Delivery date Met	2	0
Material in good condition – packaging	1	1
Quantity delivered	3	2
TOTAL	10	3

*This lot would receive a poor rating. Every delivery is scored.

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Tips related to performing appropriate due diligence to develop best practices and assure success

- What to look for from Best in Class performers
- They:
  - Have metrics/analytics and perform tracking of supplier performance
  - Use real-time dashboards to monitor critical attributes and diminish supply chain disruptions
  - Perform industry benchmarking to maintain standards
  - Perform risk analytics to avoid/mitigate supplier related issues
  - Leverage resources globally through standardized policies and practices to reduce duplication of effort or non-added value functions
  - Influence outcomes through use of LEAN 6 Sigma to improve supplier performance

Tips related to performing appropriate due diligence to develop best practices and assure success

- Consolidate the housing of key supplier data through use of a central system
- Use single point of contact for streamlining of business and technical information/data.
- Demand > 80% on-time delivery of material or completion of tasks.
- Have fewer (< 2%) major failures.
  - Use Risk Analysis to screen these suppliers out.

The role of the Quality audit as part of a supplier best practice and what to look for:

Key points:

- They should be a central piece of a multi-factorial strategy to assure quality compliance readiness.
- They should be used in conjugation with questionnaire data gathering tools, Quality Agreements and Risk Analysis
- They can be targeted tools for evaluation of capacity capabilities or some specific compliance issue
- They can be used to assess compliance fit for the transition from clinical supply to full scale commercialized supply.

The role of the Quality audit as part of a supplier best practice and what to look for:

What's important to you as a customer?

- Existence of policies that drive a Quality System Approach to the monitoring and control of supplies and their processes.
- Existence of systems that detect problems early and provide mechanisms to correct them and prevent future occurrences.
- Existence of Risk Analysis and mitigation processes as part of their management strategy

The role of the Quality audit as part of a supplier best practice and what to look for:

What's important to you as a customer?

- The supplier's ability to meet your quality and technical specification requirements
- The supplier's ability to meet your capacity and delivery expectations
- Business fit and whether they are financially stable for long-term partnerships

Audit Reports

Some important points:

- Detail what's working and what's not.
- Explain why failing suppliers don't meet the expectation of your qualification process.
- Detail remediation plans proposed to the supplier for qualification.
- Where there are inspection driven remediation activities, include a statement that the action being taken is acceptable to restore compliance.

Question

Are full-scale mock audits required or can more focused audits be done?

- The issues are:
  - Time: Dozens of audits can be time-prohibitive.
  - Cost: for extensive audit program especially where overseas suppliers are involved, e.g., China.
  - Risk: Possibility of missing something that's a key compliance factor
- Through a Risk Analysis and Mitigation Strategic mandated by ICH Q9, key points/problems can be addressed.

Solution

Using a Risk Analysis approach then, one might advocate targeted audits on a specific supplier process that might critically impact your process.

- Examples might include:
  - A thorough review of technical critical issues associated with the manufacturing of a Purification Resin that's a key component of your process.
    - Rather than looking at their training program and/or facility issues.
  - Focus on the validation of a test method used to release your product.
    - Rather than their own supplier policy.

What can be learned from analyzing historical trends? Lessons learned related to capacity and capabilities.

Ranking of issues based upon field experiences in last 3 years.	
Issue affecting performance	Ranking
Manufacturing errors due to personnel actions	#1
Errors due to documentation mistakes, data, incomplete reviews	#2
Product contaminations or specification failures	#3
Equipment breakdowns causing lost materials	#4
Delays due to silo practices	#5

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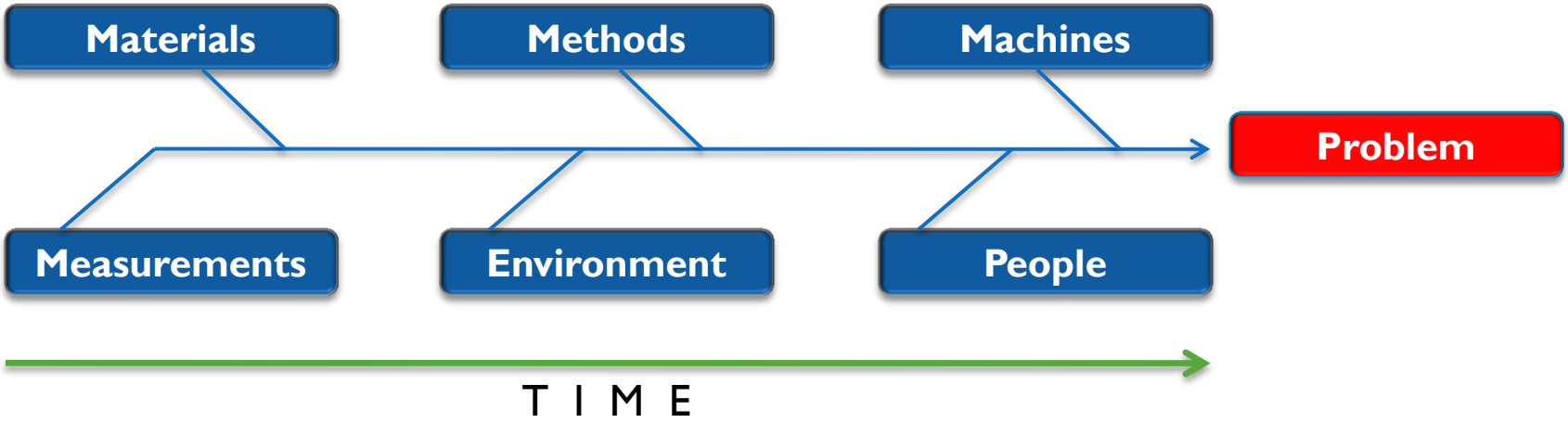
Historical Trends for Capabilities Performance of Suppliers

Capabilities	Subset of Suppliers		
	Top 25%	Middle 50%	Bottom 25%
> 90% on-time delivery of supplies. Includes: • Finished goods • Components • Raw materials • API	X		
75% on-time delivery of supplies		X	
< 50% on-time delivery of supplies			X
Failure rates in production	< 2%	5%	> 5%

What are common QC / QA issues experienced and how can they be ameliorated?

- Recommendation:
  - Always develop a strategy to determine Root Cause
  - Ask 5 Why's; Why did that occur?
  - Perform Fishbone or "Ishikawa" Exercise



What are common QC/QA issues experienced and how can they be ameliorated?

Example 1

- Issue
  - Changes made without notification that might affect product quality. Case of the laboratory method change;
    - Contract laboratory changes method used for test involved in product release.
- Solution
  - Better communication between testing laboratory and client company
    - Enforcement of issues in the Quality Agreement by the host Procurement and QA group.

What are common QC/QA issues experienced and how can they be ameliorated?

Example 2

- Issue
  - Incomplete laboratory investigations due to large number of incidents generated.
  - Caused bottleneck and delays in release of API
- Solution
  - Assessment identified change in method of analysis from HPLC to UPLC resulted in better use of resources and reduced incidence of errors.

What are common QC/QA issues experienced and how can they be ameliorated?

Example 3

- Issue
  - CAPA Programs that are either not followed through on or don't reach root cause remediation.
- Solution
  - Training on root cause analysis together with the implementation of a follow-up policy for close-out of remediation measures.

What can be learned from recent FDA warning letters and activity?

- ~ 20% of the warning letters in the last 2 years related to manufacturing quality related to supplier controls.
- Supplier management contributes to a "Cost of Quality" that's 6x greater than that of other manufacturing industries like semi-conductor and automotive.

What can be learned from recent FDA warning letters and activity?

- Three major factors contribute to this:
  - The cost and availability of resources.
  - Use or non-uniform and inefficient processes.
  - The changing regulatory and commercial environment.
- Why?
  - Supplier management is expanding as the numbers enlarge and the oversight needed increases.
  - As expectations in regulatory content evolve, tighter controls frequently require more resources to implement. As market competition changes, unless growth is sustained, there's pressure to reduce operating costs.
  - Resources are being disproportionately deployed on issues that may require less attention due to lower criticality.

What can be learned from recent FDA warning letters and activity?

Some important points:

- As more and more focus in put on Asian suppliers, regulators perceive this puts more strain on maintaining compliant supply chains.
- The result is this is catching their attention.
- Implementation of Risk Management Strategies is occurring more on a product by product basis.

Supplier Management Programs; Some Trends

- The quality of the Supplier Management Process is inadequate.
- Examples
  - "Your vendor qualification has not provided adequate evidence that the manufacturer can consistently supply raw materials.
  - "Your API suppliers are not monitored and regularly scrutinized to ensure ongoing reliability."
  - "You did not specify how you intend to document and implement supplier audits."
  - "Your firm has not conducted at least one specific identity test and has not established the reliability of the suppliers analysis through appropriate validation of the supplies test results at suitable intervals."

Supplier Management Programs; Some Trends

- Certificates of Analysis
  - "Your firm accepts supplier Certificates of Analysis without having qualified the vendor."
  - "You failed to validate your supplier test results supplied to you on the Certificate of Analysis."
  - "You receive a Certificate of Analysis with the components and discard it without conducting any review."

Some other important points related to supplier management from recent FDA interactions

- FDA has concerns over the concept of supplier "authority."
  - Did the person signing the Quality Agreement have authority to commit to the terms?
- When suppliers support a virtual or blended company structure assure that they are supported by adequate management controls at your company.
- Plan what documentation you require to verify regulatory compliance so as to mitigate your Risk Exposure.
- Assure your document retention policy meets prevailing expectations for the global harmonized regulatory agencies.

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Some other important points related to supplier management from recent FDA interactions

FDA is communicating that where outsourced CMO/CRO vendors are used, in addition to supplier selection, evaluation and qualification processes the following points will receive attention for oversight:

- Ongoing assessment of results
- Issues connected with change management and supplier controls
- Ongoing Risk Assessment and Mitigation Processes

Some other important points related to supplier management from recent FDA interactions

- Onsite receipt of materials from suppliers and associated processes.
- Handling of third party CAPA processes.
- Follow-up remediation action from noted audit deficiencies.

Concluding Thoughts

- Effective Supplier Management in a global environment requires partnership and cooperation at multiple levels as well as cross-functionality.
- Use of the correct tools integrated with strong policies will provide a basis for a successful outcome.
- However, it's important to keep it LEAN and simple!

Questions?

Thank you for this opportunity to share our ideas with you.

For more information, visit:

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