QMS Agility through a Fit-for-Purpose Model

Pathway Chief Quality Officer Forum Initiative

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Fit for Purpose Initiative

Problem Statement:

- Current risk-based processes are not sufficient to:
  - Enable cross-functional employees, at multiple levels, to make similar decisions on available data across the product lifecycle
  - Allow cost and time to drive our QMS. Only quality.

- The Result?
  - Over-engineered solutions
  - Inconsistent decisions
  - Cross-functional tension
  - Exposure to risk
  - Employee mistrust in the leadership of our organization

Before we dive into the Model

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1. We already know that R&D quality does not need to be the same as Commercial Quality
   - We have delineated the reduced requirements in SOPs
     - Examples: full specifications, analytical method validation and process validation are not needed to go into Phase I clinical trials
   - Some organizations have a separate Quality Department that resides in an R&D division

2. We intuitively knew that rapid response to COVID was more critical than fully understanding all aspects of vaccine safety
   - Risk of death versus risk of side effects
   - Resulted in re-engineering our Quality Management System

3. We already understand that moving to a highly automated production or document system requires budget and strong forecasted sales and volume
   - We choose solutions that optimize ROI, but are less than ideal/desired by employees

QMS Agility

The Fit-for-Purpose Model guides these situations for:

- Increased consistency of decisions across plant sites, products/projects and the product lifecycle
- Increased transparency of decisions so employees at all levels can understand = buy-in and co-ownership of success

Not reducing quality, just aligning quality to be fit-for-purpose

It's time to move away from illusion of black and white

We live in a world of gray

Today's Process

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Portfolio Management (Quality, Cost, Time)

Project/ Product 1	Project/ Product 2	Project/ Product 3	Project/ Product 4
Timeline Budget	Timeline Budget	Timeline Budget	Timeline Budget

Quality Management System

Standardized Approach (even if cost and time are the appropriate drivers)

Risk Assessments: Quality, Compliance, Safety/Patient (generally not business risk at this level)

New Product Development | Supplier Management | Change Control | All Other Systems

QMS Agility

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Portfolio Management (Quality, Cost, Time)

Research Use Only	Government Track/Trace Requirem't	Unplanned Equipment Upgrade	COVID Rapid Response
Driver = Time	Driver = Time	Driver = Cost	Driver = Time

Quality Management System

Fit-for-Purpose

Risk Assessments: Quality, Compliance, Safety/Patient and Business

New Product Development | Supplier Management | Change Control | All Other Systems

Why Change What We are Doing?

"We don't have cross-functional arguments about the standard Quality approach in our company"

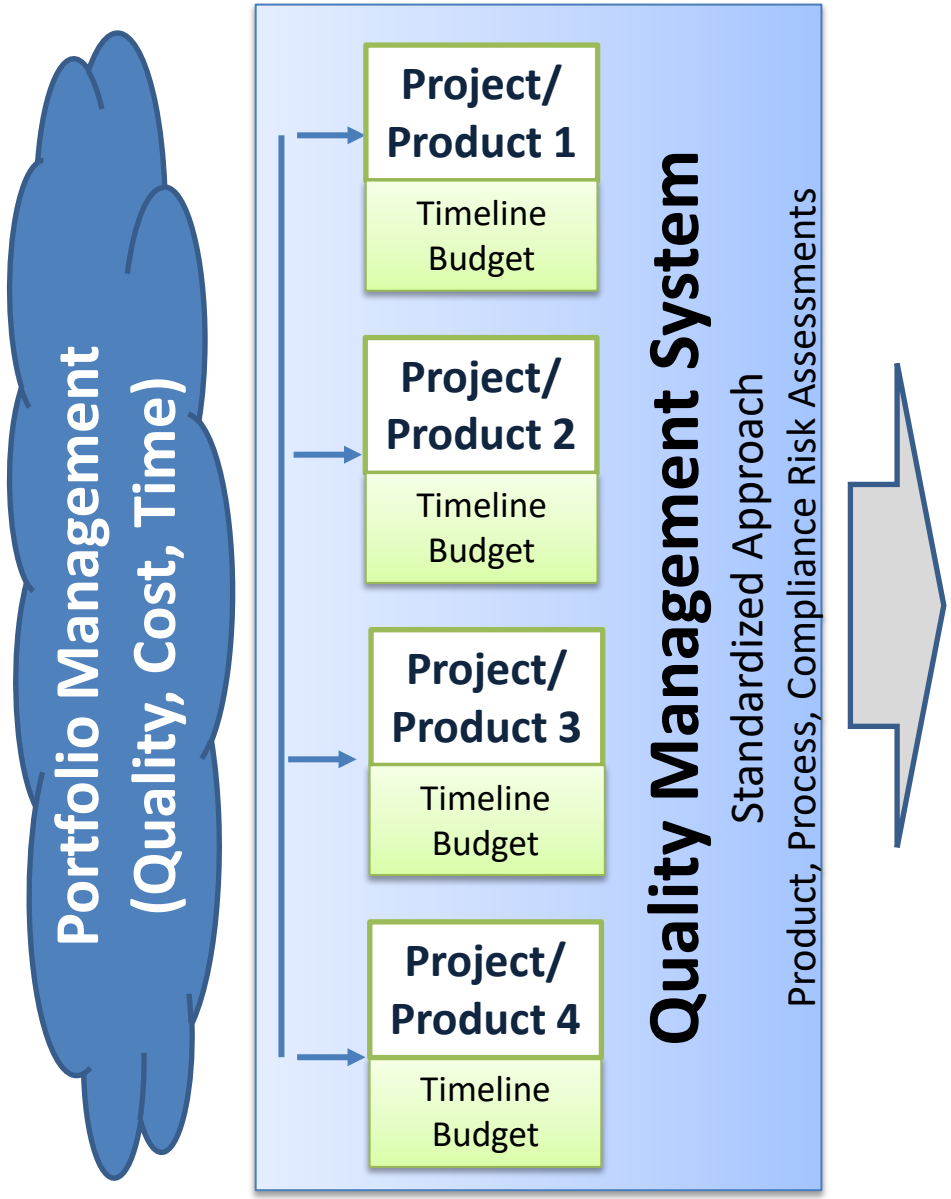
This might be true when the plan is pretty straight-forward

- However, do your cross-functional groups agree, or tolerate?
- And what happens in atypical situations (which are actually "typical")?

Tolerate

Tension

Outcome



1. Quality is viewed as a roadblock (passively and assertively)
2. Tension between groups (spoken and unspoken)
3. Stress across systems with conflicting goals

Introducing…

The Fit for Purpose Model

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The New QMS Model

1. **Build Context:**
   - Start by putting the project into a holistic context – why are we doing this?
2. **Calculate the Driver:**
   - Score Quality, Cost and Time factors to identify what is appropriately driving the project
3. **Fit-for-Purpose Considerations:**
   - Based on the driver, follow the fit-for-purpose guide in the new Quality Management System to create a successful implementation plan

Reminder: We are Always Meeting Regulatory Requirements

Step 1: Build Context

- Problem Statement
- Project Goal
- Product Type:
  - In me, On me, Near me?
  - Inherent Risk
- Voice of Customer
- Right First Time Metrics
  - Quality
  - Cost
  - Time
- Decision Maker
  - Alignment amongst Head of Quality, Head of R&D, Head of Operations

Step 2: Calculate the Driver

Quality Factors:

Criteria	How to Score
Level of GMP Regulatory Expectations?	Full GMP Expectations = 5 PreClinical/Partial GMPs = 3 Non-GMP Product/Process, or NA = 1
Do we need to conduct validation studies?	Yes = 5 Partial val. = 3 Not needed = 1
Do we need to conduct product quality studies to ensure patient safety?	Yes = 5 Partial needed = 3 No = 1
High intrinsic product/ process/system risk that could impact quality/safety	Yes = 5 No = 1
Addressing a GMP Failure or compliance gap?	Yes = 5 No = 1

Step 2: Calculate the Driver

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Time Factors:

Criteria	How to Score
Potential Market Loss/ Market Opportunity or Patient Need	Yes = 5 No = 1
External Time Commitment Made or Expectation (Investors, Clients, Customers, Regulators)	Yes = 5 No = 1
Faster Time needed due to social responsibility drivers	Yes = 5 No = 1
Timeline driven by mfg demands that could lead to inability to supply market	Yes = 5 No = 1
Timeline driven by Regulatory/gov't requirement	Yes = 5 No = 1
Timeline tied to critical business domino effect	Yes = 5 No = 1

Step 2: Calculate the Driver

Cost Factors:

Criteria	How to Score
Investment needed to take advantage of a significant business opportunity	Yes = 5 No = 1
Lack of budgeted money could lead to business threat	Yes = 5 No = 1
No added benefit or risk. Just needs to be done (= cost containment)	True = 5 False = 1
High intrinsic product or process risk that could lead to significant cost/loss if there is a failure - keeping in mind phase of development	Yes = 5 No = 1
Sales dependent on cost containment? (could be out-priced)	Yes = 5 No = 1

Step 3: Fit-for-Purpose Considerations

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Example of when **Time** is the appropriate Driver

- Need to stop using a supplier due to social responsibility issues

Strategy: Planning / Design	
Quality Considerations • Define exactly the minimum Quality / Compliance requirements that MUST be met. Define where there is flexibility on time and how these will eventually be met. • Use Risk based criteria for Quality Decisions - Must vs Nice to Have - Must protect the patients / customers from Harm **General** • Time is critical. Base planning around "minimizing" actions that take significant time • Look for opportunities for overlap / parallel activities • Studies - Plan these carefully to minimize time - generate the data in parallel • Validation Master Plan - see if you fit within existing processes / ranges - align development to fit. Outsource where the fit is poor. • Accept there will be "cost" risk: People / Resources / Support	
Supplier Qualification	
Strategy	• Use existing suppliers (no time to ID a new supplier) • Allow for single source • Onboard now – qualify later (fast)
Verify	• Might take a new supplier, but would not require full supplier qualification process • Supplier could go through qualification later as project progresses (for example, might go beyond research-use only)
Control	• Supplier Management post qualification

Step 3: Fit-for-Purpose Considerations

Example of when **Cost** is the appropriate Driver

- Unplanned upgrade for a piece of equipment for Product X

Strategy: Planning / Design	
Quality Considerations • Define exactly the minimum Quality / Compliance requirements that MUST be met. Identify opportunities to invest in systems that can cut time or cost. • Use Risk based criteria for Quality Decisions - Must vs Nice to Have - Must protect the patients / customers from harm **General** • Maximize as much efficiency as possible from company and industry-wide knowledge. • Do as much sequentially as possible to ensure costs can be minimized • Identify duplication or outdated activities that need to be eliminated. • Ensure resources are used appropriately to minimize full-time-equivalent (FTE) costs • Identify automation that could increase quality assurance, and decrease resource requirements	
Process Development Control Strategy	
Strategy	• Conduct studies to identify economies of scale • Work to improve yield to drive down costs • Process changes need to be balanced with the impact of approvals
Verify	• Determine if automation could reduce production time • Increase verification to detect issues sooner and reduce waste
Control	• Follow QMS requirements to support all process changes

Step 3: Fit-for-Purpose Considerations

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Example for a System Implementation

Time Driver

- Use current service providers due to time constraints.
- Identify a quick solution that works, versus an ideal solution.
- Use the system as-is, then iterative approach to add features that meet your needs.
- Look to leverage OEM qualification data where possible.

Cost Driver

- Consolidate service providers to gain discounts for expanded contracts.
- Assess the amount of manual intervention, versus the cost of upgrading to a better system.
- Map data flow and decisions to identify redundancy or opportunities for efficiency.

COVID Case Study

How the FFP Model methodically would have guided the response to COVID

Step 1: Setting the COVID Context

- Problem Statement:

  Covid-19 was a Global Crisis – It was ravaging populations and economies and the world desperately needed billions of doses of a safe/effective vaccine to help combat the disease

- Project Goal

  Develop, manufacture and distribute billions of doses of a safe / effective Covid-19 Vaccine in the absolute shortest possible time to help the world manage the covid 19 crisis

- Product Type:

  Injectable Vaccine – ("In me")

  Inherent Risk – High. This was a new vaccine, for a new disease with limited science knowledge (Then)

- Voice of Customer

  World was desperate for prevention / treatment options to a disease that was killing hundreds of thousands of people and destroying economies.

- Right First Time Metrics

Quality	Vaccine had to be Safe & Effective. Other Quality elements needed to be flexible
Cost	Not a limiting factor. The Pandemic was a global crisis
Time	Absolutely Critical. Each day was costing thousands of lives ← SWAT Team Approach

- Decision Maker

  This was a commitment from the CEO

Step 2: Scoring the COVID Drivers

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Driver	Criteria	How to Score	Your Score	Notes/Comments
Quality Driver	Level of GMP Regulatory Expectations?	Full GMP Expectations = 5 PreClinical/Partial GMPs = 3 Non-GMP Product/Process, or NA = 1	5	Yes - this was a vaccine product that had to be manufactured in appropriate facilities
	Do we need to conduct validation studies?	Yes = 5 Partial val. = 3 Not needed = 1	3	Yes - But there was some flexibility in this. A lot of concurrent validation activities.
	Do we need to conduct product quality studies to ensure patient safety?	Yes = 5 Partial needed = 3 No = 1	5	Yes - Vaccine had to be demonstrated to be safe and effective.
	High intrinsic product/ process/system risk that could impact quality/safety	Yes = 5 / No = 1	5	Yes - Very high risk product. Limited disease knowledge / limited science understanding
	Addressing a GMP Failure or compliance gap?	Yes = 5 / No = 1	1	No this was not a compliance gap
Time Driver	Potential Market Loss/ Market Opportunity or Patient Need	Yes = 5 / No = 1	5	This was a desperate patient need
	External Time Commitment Made or Expectation (Investors, Clients, Customers, Regulators)	Yes = 5 / No = 1	5	Yes - CEO had committed to deliver
	Faster Time needed due to social responsibility drivers	Yes = 5 / No = 1	5	Yes - Covid 19 was a world crisis
	Timeline driven by mfg demands that could lead to inability to supply market	Yes = 5 / No = 1	5	Demand was for "Billions" of doses so extreme risk of not meeting this demand. Timelines were 100% critical
	Timeline driven by Regulatory/gov't requirement	Yes = 5 / No = 1	5	Yes - Urgent demands from both governments & regulators
	Timeline tied to critical business domino effect	Yes = 5 / No = 1	5	Scored as Yes - as the disease itself was threatening businesses, global economies and supply chains.
Scores	**Quality Focus Score**	**Total:**	76	Very important as well but Time was even more critical
	Faster Time Score	**Total:**	100	Highest Score
	Cost Containment Score	**Total:**	20	Not a factor

World had a desperate crisis – Time was absolutely critical, but Vaccine had to also be Safe and Effective

Step 3: Fit for Purpose Considerations

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Activity	Fit for Purpose Considerations
Product Specs / Process controls	• Process & Control Strategy - **No time to "perfect" – Approved based on early data**. Evolved later to improve yields / cut variability. • Flexible approach **Run at risk with appropriate oversight / controls**: - **Parallel/concurrent (not sequential) activities** (e.g. Ship ahead of clearance, Use materials at risk while being released) - **Higher tolerance for errors / variance** • Robust Technical & Quality teams to provide Oversight – and strict Quality Gates
Facility Fit/ Design	• **"Use what you have"** Risks assessed and known. Implement controls / oversight to mitigate/manage these risk. No compromise on dose safety / efficacy. • **"Allow Manual / less robust Controls**" - while improving in parallel • No compromise on regulatory requirements – e.g. Sterile products
Process Validation	• **Risk Based Approach** - Approved Strategy with special oversight / controls on disposition • **More flexibility on non-critical deviations** • Keep regulators informed of plans / progress
Supplier Qualification	• **No time for supplier development – take them as they are.** Audited /Assessed but used at risk "As found" – with oversight / Control • Work in parallel on development / Improvements
Stability / expiry	• **Accelerated stability studies** • **Use existing knowledge and science** • Keep regulators informed of plans / progress

Aligns well with proposed FFP Model !

Next Steps

Next Steps for the Model

1. **Finalize the Model – pilot studies**
   - Separate Product and Systems into 2 different models
2. **Link into the Pathway Quality Maturity Model**
   - Culture has to be mature enough to be agile
3. **Publish for open-source use**

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Ideas/Suggestions?

Want to Stay Informed?