Pathway for Patient Health

QMS Agility – a Fit-for-Purpose Model

Lead your company with agility through time and cost pressures while providing your patients with quality/safe products that meet global regulatory requirements and expectations

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Achieving a Fit-for-Purpose Operation

A Chief Quality Officer Forum Initiative

Mission:

Pathway for Patient Health is a global leader that helps companies achieve a quality breakthrough. We focus on working with purpose-driven organizations to scale quality across the entire organization. We do this because the next quality defect that could happen today, could be the one that is catastrophic…and we believe that every patient life matters.

The QMS Agility initiative was chartered by the Pathway Chief Quality Officer Team, whose mission is: Mobilizing Enterprise-wide Effectiveness. Staying true to this mission, the outcome of the QMS Agility initiative assists companies in optimizing the Quality Management System for maximum agility and business effectiveness. The QMS Agility Team would like to thank the Chief Quality Officer Team for their vision in launching this initiative.

Chief Quality Officer Team Members (as of July 9, 2023):

First	Last	Title	Company
Beverly	Bates	Senior Vice President, Quality Assurance	P&G
Tracy	Founds	Vice President, Global Quality & Safety	Glaukos
Tony	Mire-Sluis	Head of Global Quality	AstraZeneca
Brian	Molloy	Vice President, Quality for Global Operations	Alexion
Karen	Netherton	Vice President, Global Quality	Seqirus
Johna	Norton	Senior Vice President of Global Quality	Eli Lilly
Maire	O'Reilly	Global Head of Quality	Elanco
Anil	Sawant	Senior Vice President, Global Quality Compliance	Merck
Brian	Schultz	Vice President Quality, Safety and Regulatory Affairs	Fisher & Paykel Healthcare
Peter	Shearstone	Vice President, Global Quality Assurance & Regulatory Affairs	Thermo Fisher Scientific
Andy	Wirths	Senior Vice President, Supply Americas	AstraZeneca
Gary	Workman	Vice President, Global Quality	Illumina

Purpose: To provide a mechanism for companies to establish Quality Management System (QMS) agility in a way that is Fit-for-Purpose, based on the risk of their products, strength of their culture and needs of the overall business while remaining compliant with applicable regulations. Each company is encouraged to determine how best to implement the QMS Agility Model for their needs.

Problem Statement: Risk-based processes need to enable cross-functional employees at multiple levels to make similar decisions on available data across varying criticality levels of commodity types and business pressures (such as time and cost). A QMS Agility Model can proactively guide right-sized decisions, reduce exposure to risk, and increase employee trust in the leadership of their organization.

Benefits:

- Enables organizations to move from a standardized approach that is often over-engineered for various products, by using a predefined process that is QMS Agility.
- Assesses QMS adjustments needed to appropriately factor-in Time and Cost Pressures, for product, patient and business success.
- Includes cross-functional alignment on the decisions involved.
- Provides transparency to employees as to when, how and why QMS variations are used, which is linked to predefined, consistent processes.

Participants: The following team members represented the Chief Quality Officer Forum in this initiative:

First Name	Last Name	Title	Company
Ingrid	Cabalza	Corporate QMS Integration & Alliances	Illumina
Mark	Frankenberg	Senior Director, Corporate QA	P&G
Alan	Johnson	Global Quality Director (BPO), Risk Management	AstraZeneca
Shirley	Murphy	Head Knowledge Management, Global Quality Compliance & Systems	Takeda
David	Murray	Senior Director, Quality- Design, Software, Supplier Quality	Illumina
Marla	Phillips	CEO and President	Pathway
Melissa	Smith	Director, Fem Care Quality Assurance	P&G
Eva	Urban	Head Internal Audit & Compliance	CSL Behring

Background:

The QMS Agility initiative was launched by the Pathway Chief Quality Officer Team to improve the way in which the Quality Management System is implemented, by adjusting for:

1. Phase of Development for Products and Systems
2. Regulated versus Non-Regulated Products
3. Time and Cost Pressures

Standardization is Good. Right? Historically, a standardized approach was believed to minimize opportunity for error, increase employee understanding and increase efficiency. However, more recently, it has been recognized that over-engineering solutions for the sake of consistency is quickly spotted by employees, which leads to frustration, the desire to find a faster way through work-arounds, and apathy towards their work. In this regard, standardization leads to the constant trends of failures and waste that have been observed for decades.

Why is That OK? The complexity of plant site operations often involves manufacturing commodities of varying complexity, risk, and regulated status. For example, a company might manufacture for its business partners a product that is intended for Research Use Only (RUO), which is non-regulated product that will never be used in a regulated product and not used for regulated decisions. In the same plant site, regulated product is manufactured of varying complexity and risk. This scenario is often managed through the following modes of operation:

1. Option 1: Develop, manufacture and control the non-regulated and regulated products through the same set of standards and expectations. In this manner, the standards for the non-regulated products would be over-engineered for the intended purpose.
   - *Outcome:* Employee frustration, employee disengagement, employee mistrust in leadership to make good decisions, and business waste.

2. Option 2: Make concessions to your standard QMS procedures to manage non-regulated products. In this manner, employees would not have transparency as to why it is ok to operate differently.
   - *Outcome:* Employee mistrust that the non-regulated product is being sufficiently/appropriately handled (asking "why is that ok?"), and employee frustration when moving to work on regulated product, since it is not clear why so much more needs to be done.

But We Already Have a Different QMS Process for R&D. It might be correctly argued that many companies have already separated the R&D QMS from the Commercial QMS, and that ICH Q8, Q9 and Q10 help guide companies on how to right-size the QMS for various phases of product development. This is an acceptable practice and is one that is encouraged to ensure the right level of development, qualification, documentation, testing, verification, validation and controls are in place in each phase of development. For this reason, the QMS Agility Model includes these approaches to help further guide companies in this direction. However:

- **What About a QMS for Systems Implementation?** Often times, employees are left to determine how best to implement computerized systems under a QMS that is primarily geared for product development. As a result, not only does variation exist in execution from one group of employees to another, and one plant site to another, but the lack of clear guidance results in increased risk of missing critical elements in the QMS. The QMS Agility initiative provides a QMS path for systems implementation to increase the assurance of intended outcome.
- **What About Time Pressure?** Most projects involve pressure from a given timeline. However, in some cases, the timeline is externally mandated (e.g., by regulatory agencies) or is on a critical path. As a result, cross-functional alignment is typically strained, since some groups are demanding to cut out studies, skip steps, and overrule the standardized approach. The Quality group is often holding firm to following the traditional, sequential approach. However, neither group is "right" and neither approach is ok. The QMS Agility Model includes strategies for how to appropriately address Time Pressure and how to overlay these considerations on the Quality Management System.
- **What About Cost Pressure?** In some cases, projects are planned and have the necessary budget to support the work. However, in many cases, the project requires quick cost savings, or long-term return on investment. The QMS Agility Model includes strategies for how to appropriately adjust the

QMS approach to achieve quick cost savings, and also includes separate strategies for how to achieve long-term ROI. Interestingly, the quick cost savings and long-term ROI strategies require completely opposite approaches, so identifying the driver in advance of the project is critical.

A business-smart Quality Management System is critical for improved patient access, employee engagement, and business success. Historically, discussion of business success related to quality has not been acceptable. However, modern experience has proven that without business success, patient success suffers through increased costs, limited inventory, and issues with product performance.

The QMS Agility Model takes-on the complexity of operating a business in a regulated industry with patient lives at stake. Serious solutions are needed for improved outcomes!

Fit-for-Purpose Use Case #1 - Covid: The Covid Pandemic that was identified in 2020 will have lasting impact on how we operate businesses, communities, and health systems. The crisis was rapidly killing hundreds of thousands of people around the world, and the pharmaceutical industry had to act fast. Would this be the right time to methodically follow the 10 year process for developing a new product? No. However, how did industry and regulatory agencies know what was ok, and what was not as it sped its research, development, production, release and approval activities to save humanity? Good question.

Fortunately, the companies involved in vaccine production for Covid were no strangers to regulated product development, and have processes steeped in risk analysis. Although employees rallied around the situation and there was no shortage of heroics, the situation left employees, regulators, health systems, patients, communities, and newscasters feeling uneasy. "How can we be sure", and "How is it possible to have enough data to support the safety". Of course, benefit/risk analyses were in play, and business risk was maximized. Companies ran activities in parallel that would cost large amounts of money if anything failed. But governments and industry worked together to make the situation scientifically and financially possible.

Now that we are post the onset of Covid, we are seeing that lots of good decisions were made, but some steered the development work in the wrong direction, and some completely failed. It would have been nice if employees had strategies in place for how to adjust the Quality Management System for severe time pressures, like those presented by Covid. In a similar fashion, most companies have a strategy and procedure in place to handle stability failures. Pharmaceutical companies have 3 days to determine the validity of the failure, so it is an "all hands on deck" approach. Mimicking the success of this predefined strategy for stability failures, the QMS Agility Model has predefined strategies in place to guide companies through normal-state, time pressures and cost pressures. Additionally, the QMS Agility model guides teams to consider overlaying the Time Pressure Strategies and Cost Pressure Strategies on all QMS pathways, in order to responsibly identify additional efficiencies.

Fit-for-Purpose Use Case #2 – Nonconformance: Oftentimes, the result of a nonconformance is the need to improve a process, update a procedure, change a piece of equipment, etc. The QMS Agility Model can be used in these circumstances to help cross-functional teams establish the project drivers and context.

For example, if an unexpected equipment failure occurs, there may be time pressure to get the operations back up and running. As a result, the team might not have the opportunity to determine if a different type of equipment could be used that would result in great long-term ROI. If time pressure exists, this would prevent the team from having enough time to research alternatives. The FFP Actions would guide the team to implement what is known to work, then use the post-implementation time to develop an upgrade strategy (and budget).

Another likely result of the same scenario is the lack of funds to purchase a new piece of equipment unexpectedly. Therefore, the QMS Agility Model would guide the team to use the Cost Containment Strategy (but to weigh the benefits against the Time Strategy).

Fit-for-Purpose Use Case #3 – Change Control System Update: The QMS Agility Model is a useful tool when updating any of the quality management systems, such as the Change Control System. Following the "FFP Actions – Systems" tab in the QMS Agility Model spreadsheet guides cross-functional teams on mapping out the system needs and the regulatory requirements.

The model provides different methodologies for updating the Change Control system. For example, if Long-Term ROI is desired, the team is guided to spend time understanding the Voice of the Customer ("VOC"). In this case, the customers would include multiple functional groups across the total product lifecycle, as well as IT, Procurement and those using the system. This would be a perfect time to determine if data integration could be employed to increase the level of information supporting change control decisions.

Fit-for-Purpose Use Case #4 – Early Phase Research and Development: The goal of the QMS Agility Model is to avoid standardization just for the sake of standardizing. The model supports the ability of the cross-functional team to make decisions that are fit for the intended purpose ("Fit-for-Purpose").

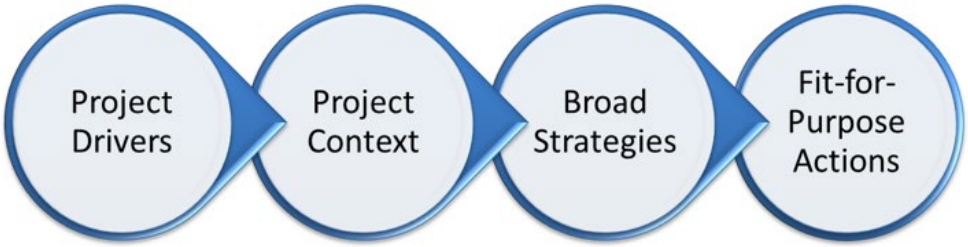
The QMS Agility Model provides clear examples of how to manage documentation, approvals, levels of finalization, rigor of studies, etc. differently across the total product lifecycle. For example, during process development, changes could be document in a laboratory notebook instead of the formalized process implemented post-market.

The QMS Agility Model

How to Implement

Including the QMS Agility Model in Existing Processes. Companies might consider incorporating the QMS Agility Model into the Project Charter development process to clearly establish the project drivers, context, and strategies prior to commissioning the work. The Fit-for-Purpose actions provided in this model guide companies on decisions that must be assessed from a risk management standpoint. Therefore, including the FFP actions (running in parallel versus sequential, completing work iteratively, etc.) in existing risk management processes will ensure the impact of each decision is understood and approved.

The QMS Agility Model consists of 4 distinct steps:



Step 1: Identification of Project Drivers

Goal: Identify if any cost pressures or time pressures are driving the project. These drivers are beyond the normal budgets and timelines used for every project. The strategies are not to be used as a substitute for proper planning, but rather, are for significant drivers that have been pre-approved by the appropriate level of management. The Project Drivers tool is the first step, and is also provided in the QMS Agility Spreadsheet (orange tab).

The Project Drivers discussion tool contains questions that are designed to aid cross-functional teams in identifying Time or Cost pressure drivers that need to be considered to maintain the necessary quality outcomes. These questions are not meant to be all inclusive, so teams should add questions to the list to drive meaningful decisions, or remove questions that are not applicable.

Note: all projects have timelines and budgets, but this discussion tool will help teams determine if there are pressures beyond "Normal State" that need to be addressed with proactive strategies.

1. Discuss the Time and Cost Pressure Discussion Questions
2. Document any key notes/comments
3. Determine if a Time and/or Cost Strategy is needed
4. Complete the Outcome Assessment below the Discussion Questions Table

Discussion Questions	Notes/Comments	Pressure?
Time Pressure Questions:		**Is a Time Pressure Strategy Needed?**
Is the project (product or system) being driven by the need to meet a customer-driven timeline?		
Is there a Potential Market Opportunity or Patient Need that needs to hit an accelerated timeline (e.g. Covid vaccine development)?		
Has there been an External Time Commitment Made or Expectation (Investors, Clients, Customers, Regulators)?		
Is there an accelerated time needed due to social responsibility drivers (e.g. the need to stop sourcing from the rain forest by x date, etc.)		
Is there a critical timeline driven by mfg demands that could lead to inability to supply market?		
Is there an accelerated timeline driven by Regulatory/gov't requirements (e.g. the need to add serialization to packages by x date, etc.)?		
Is the timeline tied to an accelerated critical business domino effect (e.g. moving manufacturing inhouse from a CMO, but internal capacity needs to be created by an accelerated date, or all the dominoes involved will be stopped)		

Cost Pressure Questions (Pressure to Contain-Cost short-term, or for long-term ROI):		**Is a Cost Pressure Strategy Needed?**
Are sales dependent on cost containment? (could be out-priced)		
Is there high intrinsic product or process risk that could lead to significant cost/loss if there is a failure - keeping in mind phase of development? This could lead to investment to protect long-term ROI.		
There is no significant business driver for the project, but is one that "just needs to be done". Therefore, cost containment is key (no real ROI)		
Is there a lack of budgeted money for the project (product or system) that could lead to business threat if costs are not contained?		

Project Drivers Outcome Assessment - Next Steps

1. If the team determines there are no unusual time or cost pressures, then the team will follow the "Normal State" Guide in the "FFP Actions - Product" or "FFP Actions - System" tab (Skip to #4)

2. If the team identifies both Time **and** Cost Pressures, then identify the main driver by answering the following:
   - If you are 2 months away from the project due date, and you need to either go beyond the due date or go beyond the budget, which would win?
   - Go to #3
3. After the team determines the main driver from a Time **or** Cost Pressure perspective (if one exists), then the team will follow the corresponding "Time Pressure" or "Cost Pressure" Strategy in the "FFP Actions - Product" or "FFP Actions - System" tab (Go to #4)
4. Identify further efficiencies/savings:
   - Whether the project is determined to be Normal State or needing a Time Pressure Strategy or Cost Pressure Strategy, the team should assess the Time and/or Cost Strategies for additional efficiencies.
     - First follow the appropriate Guide based on Questions 1-3 above
       - If the Normal State was followed, then the Time and Cost Strategies can be assessed for opportunities
       - If the Time Pressure Strategies were followed, then overlay the Cost Strategies to identify any additional opportunities
       - If the Cost Pressure Strategies were followed, then overlay the Time Strategies to identify any additional opportunities

Step 2: Building the Project Context

Goal: The information gained through the Project Drivers in Step 1 can be used to build the Project Context. This step is especially important in providing clarity for the cross-functional team and in providing transparency for all affected employees. The Project Context tool is the second step, and is also provided in the QMS Agility Spreadsheet (green tab).

The following prompts are provided to guide project teams in building the project context. Without understanding the context, it is difficult to understand how to lead the project in a way that is Fit-for-Purpose. Each team should add their own prompts and/or use the following prompts in templates and processes that already exist.

Project Description: Include whether the project is a product or system, timing needs, budget constraints, end use, end customer (internal and/or external), etc.

Voice of Customer (VOC) Expectations (Scope): Expectations of end-user from a quality, time and cost perspective. For example, if the product is to be used for research purposes only, then clinical trials and validation are not needed.

What are the Time and Cost Pressures? Use the "Project Drivers" outcome to determine if this project can follow "Normal State" processes or if there are time or cost pressures that need to be addressed through time or cost strategies.

- **Important Note:** If a Time Pressure is identified, then follow the SWAT team approach provided in the QMS Agility Spreadsheet. It is not advised to constantly operate in Time Pressure/SWAT Team mode. This is burdensome for people and systems, which historically results in burn-out and failures.
- Quality/ Compliance cannot be compromised but can be met using less efficient processes - iterations of documents, working "at-risk" in parallel (may need to repeat, more waste), may involve a lot of "cleanup" after the project is implemented (e.g., completion of tasks that were not on the critical path).
- Accept that cutting time from a project normally results in inefficiency and higher costs.

Product-Related Projects:

- **Regulated Product?** Non-Regulated products have more quality-requirement latitude, and can follow the "Normal State Non-Regulated Product" column in the QMS Agility Spreadsheet as a guide. Time and Cost pressure strategies might need to be added based on context.
- **Stage of Development?** Preclinical vs. Clinical vs. Commercial. Commercial phase (Full GXP Expectations), Clinical Phase (Partial GXP Expectations), Early Phase Discovery (Non-GXP Expectations), Not Regulated (Minimum Viability)
- **In me, On me, Near me?** Indicates risk to patient (if not any of these, then risk is lower)
- **Inherent Risk?** Sterile vs. Non-sterile; Complexity of Manufacturing Process; Disease state requires high consistency; etc. What do you know about the Inherent Risk that could affect how you lead this project?

System-Related Projects:

- **Informs GMP Decisions?** Determine whether the system is regulated or not. If not regulated, then there is more latitude in meeting quality requirements and business risk should guide the project. Time and Cost pressure strategies should be considered for greater efficiency and savings.

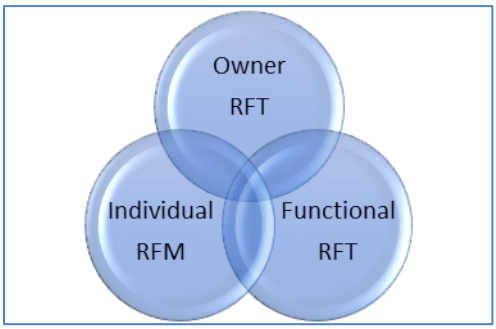
Right-First-Time Metrics (RFT):

Identifying what is truly “right first time” can be difficult for teams that typically use standard metrics. However, if a product is going to be used by a customer for research purposes only, then 70% of target might be “right” for that circumstance. The following information is provided to help guide teams in perhaps shifting paradigms to establish metrics that are relevant and realistic for the project context.

- **Quality - RFT Metric Considerations:**
  - If the product is for research use only, or in early phase R&D, then a RFT Quality metric could be 70-130% of target. Achieving this would be Right First Time.
  - If in later phase development, then typical quality metrics would apply (such as 90 - 110% for active assay, etc.). These expectations must be met, even if following Time and/or Cost Pressure Strategies.
- **Time - RFT Metric Considerations:**
  - If the project has high time pressures (such as COVID vaccine manufacturing), then 100% on time might be necessary = SWAT team approach and Time Strategies.
  - If running in Normal State, then an acceptable timeline metric might be to exceed the timeline by no more than +10%. This would be considered RFT.
- **Cost - RFT Metric Considerations:**
  - If cost pressures are driving the project, then the budget might need to be 100% on-target. The budget could be set for short-term gains, or to invest in long-term ROI. The project might take longer to identify efficiencies/ innovation.

- If running in Normal State, then an acceptable spend metric might be to hit the budget by at least <110% of budget. This could be considered RFT.
- If led by Time Pressure Strategies, then going over-budget by 20% might be Right First Time to hit an aggressive timeline.

Decision Makers: It is important to gain alignment from the functional leaders affected by the project in question. Instead of a single decision maker, alignment is key. For example, a product development project might require early stage alignment from the Head of R&D, Head of Regulatory Affairs and even Head of Marketing initially, then alignment to include the Head of Quality and Head of Operations as the project progresses towards clinical trials. Each company should assess which leaders to involve, and at what stage.



Right-From-Me (RFM) Objectives: As the project is being established, each team member needs to establish measurable objectives that are "Right from Me". They need to overlap with the objectives of the Owner (and vice versa) and with their Functional Area.

Step 3: Assessing Broad Strategies

Goal: As a result of assessing the drivers in Step 1 and Project Context in Step 2, the cross-functional team will have information related to any extenuating drivers for the project, or if the project can operate in "Normal State". In Step 3, the cross-functional team can assess the broad strategies for Normal State, Time Pressure, Short Term Cost Containment, and Long-Term ROI in a side-by-side comparison. Assessing the differences between Normal State and the other strategies will give the cross-functional team an understanding of key differences in how to approach project. This comparison is the third step, and is provided in Appendix I and in the QMS Agility Spreadsheet (blue tabs).

The purpose of the Broad Strategy Comparison is twofold:

1. Enable the cross-functional team to have a deeper understanding of how projects of varying drivers are to be run differently (e.g., long-term ROI versus short term cost containment). This is especially important in understanding the difference between Normal State and any other project driver that might be involved.
2. Enable the cross-functional team to determine if there is a possibility to overlay time and/or cost strategies to increase the impact of the outcome. Any strategy that is overlayed on the main project driver should not dominate the project direction, but rather, enhance the outcome as agreed upon by the proper level of management.

Step 4: Fit-for-Purpose Actions Guide

Goal: The ultimate outcome of the QMS Agility tool is to provide information to guide cross-functional teams on "how" to implement a Quality Management System that is agile, right-sized, and always meets regulatory

requirements. The Fit-for-Purpose Actions are located in the QMS Agility Spreadsheet as 2 separate tabs, labeled: (1) FFP Actions - Product, and (2) FFP Actions - System (purple tabs).

Within each tab are columns for each of the outcomes from Step 3: Normal State Strategy, Time Pressure Strategy, Short Term Cost Strategy, and Long-Term ROI Strategy. For product development projects, there is also a column for "Non-Regulated Products".

The cross-functional team can use the information in the column most relevant to the project drivers and context outcome. The rows in the spreadsheet correspond to typical actions that are needed in developing and launching/implementing products and computer systems. The "FFP Actions – Product" and "FFP Actions – System" tabs both start with a row entitled "SWAT Team Development". This row provides direction if the Time Pressure Strategy is chosen by the cross-functional team, and also provides an indication for the other strategies that the SWAT Team approach should not be necessary. This note is to warn teams, leaders and companies to refrain from operating in SWAT Team mode on a regular basis due to high risk of burn-out and failure.

The information in each column in the FFP tabs is to be used as a guide and to supplement information that the company might already have established in formalized processes. Importantly, the cross-functional team is able to compare every row of information across each of the strategy columns, so it is clear how the strategy chosen by the team is to be led differently than the other strategies. Additionally, the team may identify opportunities to overlay strategies more easily as each action can be readily compared across strategies.

The QMS Agility tool provides a column for companies to take notes on what elements of the strategy will be included in the plan. This column is entitled "Your Company's Plan for this Project". The company is also able to capture the actions that were actually taken during the project, with an opportunity to explain any differences from the original plan and impact to regulatory requirements. This column is entitled "Actual Actions Taken with explanation to regulatory impact".

Once the cross-functional team has identified the best strategy for the project by assessing the Broad Strategies outlined in Step 3 (Appendix I), consulting the Fit-for-Purpose Actions Guide (Excel Spreadsheet Tool) will then give the team actionable steps to help implement the strategy effectively.

It is recommended that the team determine how best to implement the actions, based on the context of the project, the complexity of the work, and the maturity of the team. For example:

1. **Mature Systems:** The company may already have extensive actions in place to handle the various project drivers. The Fit-for-Purpose guide can then be consulted for any additional improvements and ideas.
2. **Inexperienced Team:** In some cases, a team might either consist of fairly new employees, or the project-type is quite different than what the company has worked on previously. In either case, the team would be considered inexperienced. As a result, running an effective and compliant Time Pressure Strategy might not be possible. This strategy requires deep knowledge in regulations and product impact to ensure studies running in parallel are supported and also support the necessary outcomes. Inexperienced teams might not have robust systems in place to ensure iterative approaches are closed out. In this case, the Fit-for-Purpose Guide on Time Pressure Strategy might be too advanced for the team to run in

totality. An inexperienced team should consider running at Normal State, and implementing some improvements from the Time Pressure Strategy, as appropriate.

3. **Complex Project:** Oftentimes, a global launch involving multiple plant sites poses complexity that needs to be managed with agility. Plant sites typically have separate work instructions following corporate guidelines, so the QMS Agility Model can be used to guide site implementation within each individual system. Consulting the QMS Agility Model enables each site to reference the suggested actions to add to their processes, replace their processes, or to inform their decisions on how best to proceed.

Conclusions:

The QMS Agility Model enables teams to implement Quality Systems with agility based on the context of the product or computer system project. In some cases, the information in the QMS Agility Model will support procedures and practices already in place at a company. However, in other cases, the QMS Agility Model may provide a more effective way to build an agile Quality System framework with pre-determined strategies to support the project drivers and context, while remaining compliant with regulatory expectations and requirements.

The QMS Agility Model enables teams to pre-plan for time and cost pressures in a responsible way, while providing transparency to employees at all levels. Through this model, senior leaders can empower employees across plant sites to lead product and computer system projects that consistently align with relevant strategies and achieve the desired outcome.

Important Notes:

1. **Totality of Regulations:** The QMS Agility Model primarily addresses GMP regulations. Each company must assess all other regulations that are pertinent to its business, intended use of its products and intended target markets. These regulations include, but are not limited to social regulations, labor laws, emissions standards, sustainability, etc.

2. **Regulations Always Met:** Although the QMS Agility Model incorporates Cost and Time Pressure Strategies, GMP quality regulations and expectations must always be met. These regulations and expectations vary across the product lifecycle, across commodity types and across markets, but they must always be met.

Appendix I: QMS Agility Comparison Chart – Broad Strategies

Normal State Strategy, Time Pressure Strategy, Short-Term Cost Strategy, and Long-Term ROI Cost Strategy

The following table provides a side-by-side comparison of broad considerations for running a project under the following strategies: (1) "Normal State", (2) Time Pressure, (3) Short-Term Cost Pressure, and (4) Long-Term ROI Cost Pressure. These broad considerations are critical to understand before moving forward. Once the team finalizes how best to manage the project for the given context, then the Fit-for-Purpose Actions associated with the chosen strategy can be found in the accompanying excel tool.

	Normal State Strategy	**Time Pressure Strategy**	**Short Term Cost Strategy**	**Long-Term ROI Cost Strategy**
Project Examples:	• New product launch • Addressing update to regulations • Addressing a quality system failure/ compliance gap • New Quality System • New Laboratory Information/Management Systems • New Environmental Monitoring System • New Manufacturing/Material Control System.	• New product to meet an unmet medical need must be 1st to market for competitive advantage • Regulatory / Government / Or Sustainability Requirement Deadline • Improve Defects/Regulatory Gaps in Existing Systems. • Replace existing software with new system (enhanced functions) by critical date to avoid renewal of licenses/fees. • Replace system that is integral to other workstreams by given date.	• Supplier change needed due to increased pricing • Supplier has raised prices, so cost containment elsewhere is needed • Critical product with low margins • Comply with a new Regulatory commitment (bring system into "new" compliance) • Fix or add functionality but must not exceed budget • Need to get back to "Up and Running"	• Improved process efficiencies desired. • Improved package design for better end user experience. • Higher process automation to reduce resource constraints. • Improve reliability, yields or reduce process variability (i.e., cut inventory and risk buffer stocks) • Look for synergies - simplified standard processes for multiple process steps. Simple innovative solutions.
Purpose:	**MUST deliver a compliant product** according to the project charter.	**MUST deliver a compliant product** very fast to meet time commitment.	**MUST deliver a compliant product** with minimal Cost (Limited Budget)	**MUST deliver a compliant product** that reduces long-term costs (Invest in Outcome)

Focus:	MUST comply with applicable regulations and deliver product/process/system with the quality needed to meet the intended use/purpose. Define quality as priority and assign funding so quality risk level is appropriate.	MUST comply with applicable regulations and deliver product/process/system as fast as possible to meet a deadline or commitment. Define Time as priority and assign funding so no time is lost getting funding to start.	MUST comply with applicable regulations and lead the product/process/system with cost containment as a priority. Define Cost as priority and identify shared resources so project is managed within budget requirements.	MUST comply with applicable regulations and lead the product/process/system with long-term cost savings as a priority. Define as priority provide team with appropriate funding to enable investment in long-term outcomes.
Project Charter:	• Stage gate reviews set for important product-related decisions, and includes appropriate escalation process. • Project Charter elements are closely monitored, based on alignment from all impacted functional areas. • Value in seeking external input (benchmarking, Consultants etc.). • Contracts tied to schedule performance	• Stage gate reviews occur frequently (daily) to ensure project is on time and remains in scope, and includes an approved, direct escalation process. • Project Charter MUST focus on Time Impact in ALL decisions. • No time to seek external input for additional options. Likely need to focus on what is known, due to time constraints. • Contracts tied to schedule performance – Penalty clauses	• Stage gate reviews occur at regular frequency with focus on cost/spend and assessment of scope creep. Includes an approved, direct escalation process. • Project Charter MUST focus on Cost/Spend in ALL decisions. • Value in seeking external input (benchmarking, Consultants etc.). Allow time for competitive bids. • Contracts tied to cost/price commitments	• Stage reviews occur at regular frequency with an emphasis on innovation and voice of customer to know future needs. Includes appropriate escalation process. • Prject Charter MUST focus on Impact to ROI in all decisions. • Value in seeking external input (benchmarking, Consultants etc.). • Contracts tied to long-term cost containment – reward for innovation

Resources and Decision Process for Project:	• Establish a Project Lead who is a vested subject matter expert from end-to-end. • Establish a committed team that can own the project drivers and outcomes • Determine if resources will be internal, complemented with consultants and/or contractors, or will be outsourced. • Ensure proper investment is obtained from senior leaders, as well as clear objectives and measures	• 100% Dedicated SWAT teams with authority to make decisions and spend money. • Use experts and accumulated knowledge to cut design time - stay with proven design elements where possible • Look for external support to reduce/meet timelines (outsourcing, contractors, etc.) • Ensure resources are sufficient to meet critical dates (Number of people, commitment, capabilities).	• Lean Teams - small number of experts (Time is not a factor). • Use shared resources (not charged to project) where possible. • Robust decision processes to ensure decisions are accurate and represent best cost alternatives. • Build on what is known, instead of creating something new. • Identify if external partners can result in reduced costs.	• Team to include diverse, experienced team members who can assess future state and needs. • Heavy time spent in planning and optimizing options. • Experienced decision-makers to ensure patience is employed to assess multiple alternatives.
Strategy for Product Development:	• Design a well-studied product/process to minimize risk related to variability in manufacturing and across end users • Learn as much as possible about the product/process/system, failure modes, end users to reduce possibilities of failure and harm. • Build upon what you know from other products/processes/systems that are similar • Increase the formalization of the QMS as the product/system moves through stages of development, with the goal of increasing product quality assurance.	• Design the product/process such that it is "good enough" for manufacturing suitability and avoidance of risk to the end user. • This approach is most appropriate when there are other products, processes, systems and experiences to build upon • Post-launch, increase the studies needed to handle larger variability and further understand end user variability. • This has a higher likelihood of production/system downtime if wide ranges of variability cannot be studied in advance. • Base planning around minimizing tasks/actions that take significant time (New development,	• Design the product/process such that it is "good enough" for manufacturing suitability and avoidance of risk to the end user. • Maximize as much efficiency as possible from company and industry-wide knowledge. • This approach is most appropriate when there are other products, processes, systems and experiences to build upon • Do as much sequentially as possible to reduce risk of failure/rework/ cost. • Focusing on cost savings will likely increase project timeline. • Assess opportunities to minimize environmental impact, freight costs, etc. due to extra weight, etc.	• Upfront research to increase input from end user (voice of customer), human factor aspects with product and packaging technology, as well as internal customers for improved workflows, etc. • Research new industry capabilities for line efficiencies, testing efficiencies and waste reduction, etc. • Work is often run in parallel to research all relevant aspects of the product/process/system simultaneously, to gain the most long-term benefit. • Risk based decisions focused on evaluation of improvement options.

		characterization, Testing, establish new suppliers, facilities, etc.). Start tasks as early as possible, and in parallel • Capabilities – assess fit with the already-established validation Master Plan. Outsource where fit is poor.	Could serve as "double duty" to get savings in short-term and long-term costs.	• Assess balance of project effort versus benefit (avoid analysis paralysis).
Quality Considerations - Part of Implementation plan:	• Ensure regulatory requirements for product type, phase of product development, intended use and intended markets are understood, and form the minimum requirements for the product • Design studies to generate data that support specifications, process controls and product understanding - including the impact of material variability • Establish the desired quality for the product/system (not to be confused with compliance) that creates the user experience your company is trying to achieve (more of a Brand decision)	• Define exactly the minimum quality/compliance requirements that MUST be met. Define where there is flexibility on time (finalize studies later that are started during development) and how the requirements will eventually be met. • Define a clear path for change management and communication - project will be impacted by change as work will start with incomplete data/information. • Use Risk based criteria for quality decisions - Must vs Nice to Have - Must protect the patients/customers from Harm.	• "Risk Based" - Look for opportunities for Innovation within framework of quality to save cost • Is a task really critical/needed? Sequential execution - no cost risk - avoid potential rework and multiple iterations of work. • Must be Right First Time - take time to do it right - adequate time for reviews and approvals (catch mistakes before they happen) • Work carefully (work and reviews) so as to identify failures fast - work/review times will likely be slower than normal.	• "Risk Based" - Look for opportunities for Innovation within framework of quality. Not looking to speed project, but looking to avoid cost of quality maintenance - reduce ongoing quality demands (documents, reviews etc.) through digital solutions, technology, and other innovations. • Value to define exactly what level of quality/compliance is required and use most effective technologies to comply. Minimize manual effort and resource time - as these are variable costs that increase over time.

Testing/ Validation of Product/ Process:	• Pharmaceuticals: follow Quality by Design (ICH Q8) principles to understand the design space in a way that will minimize failures and unknown impact of variability. There are no regulations for product development in pharma. Follow good scientific method and regulator expectations related to current-GMPs • Medical Devices: follow ISO 13485 requirements for product development through the entire product lifecycle. • Build upon what is known about this product, process or system and of other similar products, processes or systems – internally and externally.	• Plan studies to support the workflows to deliver data on time • Use risk-based study decisions - enough information to make informed decisions to allow subsequent work to start. • Make required data delivery dates explicit so teams are always aware of commitments - follow up frequently • Plan work around materials/capacities to minimize delays • Critically assess need for data - is study critical? Maximize use of existing data internally/ externally • Stay (where possible) within validated conditions (Equipment Limits/Ranges, Shipping conditions). Expand post launch. • Expert review of Plan - to ensure studies will not be repeated if information is already known	• Plan studies to identify efficiencies (but determine realistic possibility upfront so cost is not accrued) • Use risk-based study decisions to minimize waste • Make required budget explicit so teams are always aware of commitments - follow up frequently • Critically assess need for data - is study critical? - Maximize use of existing data internally/ externally • Stay (where possible) within validated conditions (Equipment Limits/Ranges, Shipping conditions), to avoid rework • Expert review of Plan - to ensure studies will not be repeated if information is already known	• Plan studies to identify long-term efficiencies (may require innovation and automation) • Explore new automation possibilities to reduce time, waste and manhours involved in on-going testing post launch • Explore possibilities for continuous manufacturing, process analytic technology (and parametric release if accepted by regulatory agencies). • Explore artificial intelligence on production line to avoid failures • Explore the limits of the validated ranges to expand design space for reduction in rejected product and failure investigations
Evidence:	• Adjust the formality of documentation and approval to appropriate levels for phase of development • Use a stage gate model to drive appropriate go/no-go decisions in a timely manner by the right level of leadership	• Have a high tolerance for business risk in the interest of time. No need to have 100% of the evidence complete before proceeding (business risk of rework, waste, cost) • Do not deviate from the planned strategy (Avoid Scope creep/study creep)	• Have a low tolerance for business risk of failures and increased costs. Need to have as much evidence as possible before proceeding. Deadlines may be longer to be more "sure" before proceeding to next step • Do not deviate from the planned strategy (Avoid Scope creep/study creep)	• Scope creep is acceptable in the interest of innovation and efficiencies. Look for evidence to "fail fast" so true innovation can be identified more quickly while reducing waste/cost. • Determine how to test/validate innovative technologies that might be new to the market • Understand the balance

		• Immediate escalation of threats to timeline	• Immediate escalation of threats to budget	between researching/exploring and time/cost
Maintenance of System:	• Post-market surveillance is expected, and must follow agency regulations and reporting. • Formal investigation of complaints and failures is critical, with scientifically sound root cause identification and trend analyses. • Effective Corrective Actions and Preventive Actions are critical to reduce the risk of repeat failures. • Vigilance is critical to patient safety, consumer satisfaction, study of product effectiveness and intended use, and Brand preservation	• If Time is appropriately deemed as the number 1 priority, then an iterative approach to finalizing and/or expanding upon quality might have been in place during development. - Quality/Compliance MUST be defendable. - Ensure all partially completed work/studies supporting quality decisions is progressed to completion (final approved documents etc.) - Continuous improvement upon scientific studies post-launch is likely necessary (in addition to typical continuous improvement efforts) • Continue to optimize the process/ quality using science and risk-based thinking/decisions	• If Cost is deemed to appropriately be the number 1 priority, then it is likely that additional studies to expand ranges, etc. will be needed post-launch - this can be started once budget is available, but tracking failure/loss as a result of minimal design space and supply chain rigor is important to inform budget decisions. Containing short-term investment needs to be compared to the short-term losses - Take time to look for new efficiencies and economies of scale, and determine a strategy around quick returns/savings or long-term ROI.	• Spend effort to identify most effective and simplest ways to maintain the validated state. Build elements into the design to reduce these long-term recurring costs. • Reduce long-term risk - Automated data trending, AI continuously looking for patterns, trends, analyzing audit trails looking for "flags" - to reduce manual processes and oversight