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Here are some simple action plans from the example:

EXAMPLE: Action plans		
Set up Project Management Office (PMO)	3 months	Short-Term
Make organizational changes to handle this new approach	6 months	Short-Term
Select a vendor for batch release support system	1 year	Short-Term
Bring the preventative maintenance (PM) system into compliance	1 year	Short-Term
Implement a dashboard for batch release system	2 years	Long-Term
Select a vendor for a Manufacturing Execution System (MES) & an Enterprise Resource Planning (ERP) system	2 ½ years	Long-Term
Implement ERP	3 years	Long-Term
Implement MES	4 years	Long-Term
Upgrade lab management system	5 years	Long-Term
Upgrade document management system	7 years	Long-Term
Upgrade ERP	8 years	Long-Term

Lastly, manage this new way of doing business. Include check-points along the way and make adjustments as necessary. Remember that change management and open communication are critical. Tools to use include metrics, key performance indicators, and project management methodologies.

Adopting a proactive approach will be a path of continuous improvement that will move your Life Sciences organization forward. Quick fixes will no longer be needed.

Set the stage

Realize that your company won't achieve Operational Excellence overnight. After all, most likely it has taken decades for your company to get where it is today. But by taking a holistic view

of your organization and linking Quality Systems with Operational Excellence, you can move in that direction. It's a journey that requires a strong commitment throughout your organization, which means bottom up dedication and top down support. It means changing perceptions, changing directions, and changing the course of your business. It will, however set the stage for improved customer satisfaction; more efficient and streamlined operations; a stronger, more strategic advantage in the marketplace; and higher quality drug products. Is your company ready to begin this journey? Can it afford not to?

About the authors

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INSIGHTS

Quick Fixes Won't Work Anymore. A Proactive Approach Will

How to build in quality to achieve Operational Excellence

In your Life Sciences organization, does Operational Excellence seem to clash with Quality Systems? Or, is your organization one of the talented few that has successfully joined these concepts together? If you have, congratulations! But, if not, like many pharmaceutical, biotechnology, and medical device firms, you know that when Operational Excellence meets Quality Systems sparks tend to fly.

It's really not surprising. On the surface, it would appear that the two concepts don't have much, if anything, in common. They have different objectives, different drivers, and different pressures. Even different funding sources and different sponsors. Not to mention different perceptions associated with each.

PERCEPTIONS	OPERATIONAL EXCELLENCE	QUALITY SYSTEMS
Pace	Fast	Slow
Mindset	Efficiency	Compliance
Media	Machines, Widgets	Paperwork, Files
Personnel	Productions, Operations	Quality Assurance, Quality Control

But while Operational Excellence and Quality Systems may indeed have opposing attributes, they actually share the same goal – producing a safe and effective product to serve the patient's needs. Patient first. Period.

Moreover, they are both equally committed to doing this in the best manner possible. So, does it really matter how a Life Sciences company gets to the end product, as long as the goal is always a quality product and Operational Excellence and Quality Systems each contribute to that goal? Or could Quality Systems fit nicely under the umbrella of Operational Excellence and take advantage of the resulting synergy? Can Operational Excellence and Quality Systems join together and take advantage of a best of breed approach? The answer to each of these questions is a resounding yes.

What if you could align all initiatives, projects, concepts, systems, and initiatives that fall under Operational Excellence and Quality Systems into a single strategy? You can. Balancing efficiency and quality in a single approach translates into improved customer satisfaction, reduced costs, and a stronger, more strategic advantage. Change your perceptions and results will follow.



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In the beginning...

To understand how perceptions about Operational Excellence and Quality Systems developed, first consider the competing pressures you face.

External pressures such as legislation, patients, and regulators and internal pressures including employee retention, priorities, production schedules, and budgets all vie for your attention. Each group within your organization is doing exactly what they think they should do to address these pressures. Furthermore, each group is acting in their best interests to take care of their part of the business in the best way possible. For example, finance may be driving Sarbanes-Oxley compliance issues; Quality may be addressing regulatory concerns; and, the production group may be focused on statistical process control initiatives. As a result, responses to internal and external pressures tend to be siloed and reactive. Frankly, it may seem easier and quicker to take care of business making as few waves as possible. Each Life Sciences company, however, continues to grow and evolve, leaving an unfortunate trail of fragmented systems in place. An article by *Business Management* opined that while these one-off initiatives may prevent regulatory fines in the short term, they often compound risk and compliance costs in the long run. In essence, the pressures companies face have caused them, in many cases, to be motivated more by fear and less by strategy.

To determine whether your organization has taken a piecemeal approach to solving their challenges, quickly answer these questions:

- How many change control systems are there in your company?
- How many document management systems?
- How many compliance groups?
- How many CAPA systems?
- How many distinct continuous improvement efforts?
- How many databases using similar information?

You probably have answered 'more than one' in most, or perhaps all, of these areas. The point is not that one is the optimal answer, but that fewer is better. Fewer change control systems, consolidated document management systems, fewer software licenses, and aligned initiatives will provide a lower total cost of ownership and greater consistency across the company.

Nobody can argue that these systems i.e. CAPA, change control, etc. weren't implemented with good intentions. Of course they were. Nobody plans for disparate, fragmented systems. These solutions were put in place in an effort to continually diffuse the most immediate and pressing threats.

This reactive nature has unfortunately left many companies at a significant disadvantage. Without a long term strategy and only quick fixes on the fly to address regulatory inspections, many companies are burdened with solutions from yesteryear that have compromised efficiency, compliance, or possibly both.

Think about the various activities and systems that are in place to support your organization. Where do you think your firm would place on the grid below?

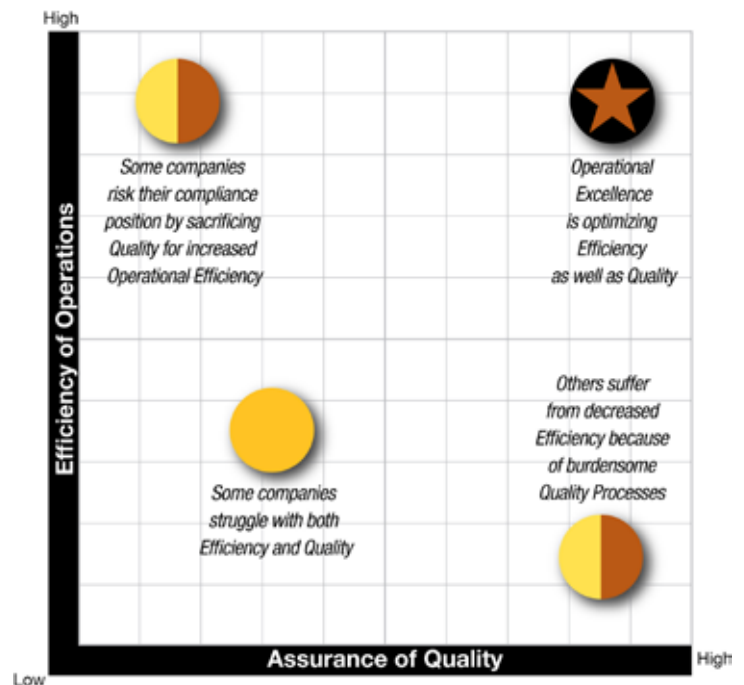


Figure 1

Too often, companies have evolved underestimating the necessity of balancing Efficiency of Operations with Assurance of Quality. There is, however, a better way.

Connecting the dots: Drawing value from a proactive approach

If you want to move beyond piecemeal solutions, you need to look at your challenges differently and address them in aggregate. We advocate adopting a proactive approach. This approach is not simply a short-lived fad or initiative, but a new and better way of doing business.

A proactive approach means taking responsibility for your own destiny. It's going where you want to go, not going where you just end up. A proactive approach is building compliance into your operations or in other words, Quality by Design (QbD). It's putting scientific processes in place to fully understand your end-to-end processes and products. This includes developing specifications and operating ranges for operation inputs, raw materials, and finished products, and designing robust production through adequate design and control of equipment and facilities. Furthermore, a proactive approach is building quality into operations, which means you won't have to rely on an inspection to call out defects; instead an inspection will fulfill its intended quality check. It means establishing and maintaining procedures and systems to support Right First Time operations.

A proactive approach creates and promotes a culture of continuous improvement, i.e. finding better, more efficient ways to do business. Contingent on open communication throughout the organization, it's about building relationships between departments and encouraging people to work together. It also means having the right information at your fingertips in a dashboard or similar format that will help enable batch release, maintain plant operations, or facilitate critical decision-making. All of these things are possible and achievable with an innovative mindset that is necessary for a proactive approach.

Why should I look at systems holistically & move to a proactive approach?

First and foremost, the FDA is advocating Quality by Design. The FDA's Guidance for Industry "Quality Systems Approach to Pharmaceutical cGMP Regulations" issued September 2006, describes a quality systems model (management responsibilities, resources, manufacturing operations, and evaluation activities) that can yield long-term benefits that will far outweigh any implementation costs.¹ The ICH Guidance for Industry, "Q8 Pharmaceutical Development" states: "It is important to recognize that quality cannot be tested into products, i.e. quality should be built in by design."² Furthermore, "the FDA's Process

Analytic Technology (PAT) initiative is a clear message to the industry that the time has come to invest in modern process technologies."³ These can range from a simple in-line sensor to state of the art technology; nonetheless it is built-in quality. The FDA recognizes the benefits of built-in quality and has published these guidances and others to guide the industry.

Looking more broadly at the global regulatory environment, the EMEA (European Medicine Evaluation Agency), the Japanese Ministry of Health, Labour, and Welfare (MHLW) and the FDA are also developing harmonized guidance through the International Conference on Harmonization (ICH). A draft of ICH Q10 Pharmaceutical Quality System, issued May 2007, describes a harmonized pharmaceutical quality system across a product's lifecycle, emphasizing an integrated approach to quality risk management and science.⁴ This guidance may have many potential benefits including 1) harmonizing the concept of quality systems for pharmaceutical industry between the three regions, 2) promoting improved manufacturing processes, thus reducing undesired variability and leading to more consistent product quality, and 3) demonstrating industry and regulatory commitment to robust quality systems and technical innovation which will ensure the consistent availability of drug products globally. The bottom line is that many are already recognizing and embracing the benefits of implementing quality by design, continual improvement, and quality risk management.

Local and global mandates aside, complex decentralized systems have a high total cost of ownership. As reported in *Business Management* magazine, "The fragmented approach to governance, risk management, and compliance is riddled with manual tasks, duplicative processes, errors, and high costs."⁵ According to AMR Research, the cost of compliance around the world was estimated at US\$27 billion in 2006 – and this figure doesn't quantify the financial impact of distractions, delays, and loss of competitive advantage."⁶ Beyond operating costs, when companies choose not to comply with the law, FDA deals with these problems very decisively. The fines associated with consent decrees are considerable: Abbott was fined US\$100 million in 1999; Wyeth was fined US\$30 million in 2000; and Schering Plough was fined US\$500 million in 2002, all for equitable remedy of disgorgement. Opting for quick fixes, and a reactive approach, therefore, can not only make you lag behind your competition, but it can also be quite an expensive route to take.

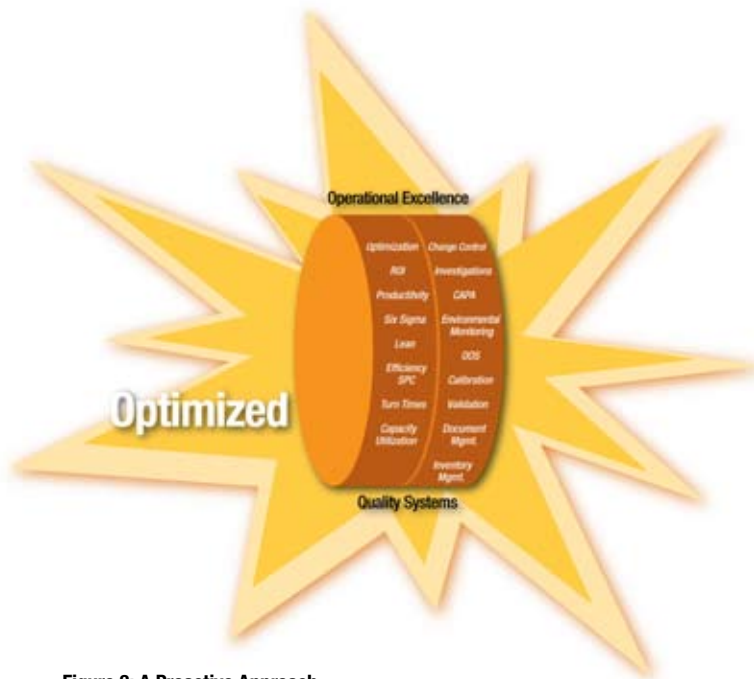


Figure 3: A Proactive Approach

What benefits can I expect by taking a proactive approach?

Less FDA oversight. As stated in the September 2006 guidance document referenced within, the FDA has concluded that modern quality systems, when coupled with manufacturing process, product knowledge, and the use of effective risk management practices, can facilitate changes to equipment, facilities, and processes without the need for prior approval regulatory submissions. Manufacturers with a robust quality system and appropriate knowledge can implement many types of improvements on their own. Which in turn will yield much more flexibility and much better relationships with the regulators. In addition, an effective quality system lowers the risk of manufacturing problems resulting in shorter and fewer FDA inspections.

High quality product entering the marketplace. A proactive approach will reduce your number of recalls, returned or salvaged products, and defective products entering the marketplace. A single scrapped batch can represent between US\$3 million and US\$4 million to the enterprise.⁷ Looking at this in a more positive light, fully developing and understanding the quality attributes throughout your product lifecycle ensures the delivery of a high quality product to your patients.

Dollars to the bottom line. This is difficult to quantify, but one analyst made this prediction: “We forecast that, by managing risk and applying scientific- and systems-based approaches throughout development and manufacturing, the top 30 pharma companies alone can protect up to US\$60 billion of future revenues, and reduce cost of goods sold (COGS) by up to 16 percent.”⁸ Furthermore, “Companies that embrace the new manufacturing paradigm can decrease internal failures from 16 percent to less than 1 percent, reduce COGS from 20 percent to 17 percent, and achieve process performance levels of 4.5 sigma.” Once more for just those top 30 companies, annual savings of approximately US\$10 billion and incremental revenue of US\$600 million for a drug with peak annual sales of US\$1 billion is achievable.⁹ With these kinds of numbers, it’s hard not to take notice.

Getting started

Initiating a proactive approach is a 3-step exercise that includes assessment, analysis, and action.

Step 1- Assessment

The assessment phase documents the current state for all aspects of your business. The deliverable from this step is an “as is” snapshot of your organization.

First determine the scope of your assessment. Ideally all parts of your organization should be assessed. Limiting the scope to only quality systems is a great place to start, but you should also look at all of your GXP areas and all of your support areas, including finance, information technology, human resources, marketing, and sales.

Next, set up a ranking system with definitions to document the assessment. This will become important as you proceed to Step 2. The ranking system can be a green-yellow-red type of ranking, a numerical ranking (i.e. 1 to 5 or 1 to 10), or one designated by maturity states. (Refer to Figure 2 which uses a maturity state ranking based on efficiency of operations and assurance of quality.) You will also need to define the criteria to associate with your ranking. For instance, one end of the scale should be used for those things that should be continued and activities that are optimized, value added, and compliant. The other end of the scale should be used for things that should be discontinued, or those that are non-value added, non-compliant, or start-up activities.

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To prepare for ranking, several methods should be used to gain a complete understanding of the current state prior to ranking. Benchmarking against accepted standards and operating norms, regulations, and regulatory guidance, such as ICH Q10, works well for processes, policies, and procedures. Another method is to interview process owners throughout the organization who can provide additional insight into operations. Reviewing data such as process maps, organizational charts, metrics, and statistical process control charts can also be used for ranking.

Next, rank the individual pieces of the business based on the scope selected. Operational items may include processes, systems, policies, procedures, and initiatives. Structural items may include organizational reporting structures, facility locations, and facility layout. Other items may include company culture or resource utilization. Measures such as metrics, key performance indicators, and financial reports can be used to facilitate ranking.

This phase will provide a thorough assessment of your organization and its state of affairs. Spend as much time as needed. If you find that more information is needed, this step can be quickly revisited.

Here is a simple example providing an “as is” snapshot of computer systems:

EXAMPLE: Ranking of computer systems		
Red Non-Compliant, Inefficient	Yellow	Green Compliant, Efficient
Resource Planning, OTS, outdated	CAPA, OTS	Deviation & Investigation Management, OTS
Preventive Maintenance (PM), OTS	Laboratory Data Management, OTS /customized	Document Management, OTS /customized
Audit Tracking, spreadsheet	Change Control Management, home grown	
	Calibration, OTS	

OTS = Off the shelf software

Step 2- Analysis

The analysis phase quantifies implementation options to be used for Step 3. The deliverable from this step will be the costs of implementing needed changes for alignment with a proactive approach. The Final Business Plan for Q10 can serve as a helpful reference.

Review the ranking from Step 1. Analyze the data both collectively and granularly. Based on the ranking, begin formulating opportunities for improvement. Tools to use include discussion groups, SWOT (Strengths, Weaknesses, Opportunities, and Threats) analyses, start-stop analyses, risk assessments, or gap assessments.

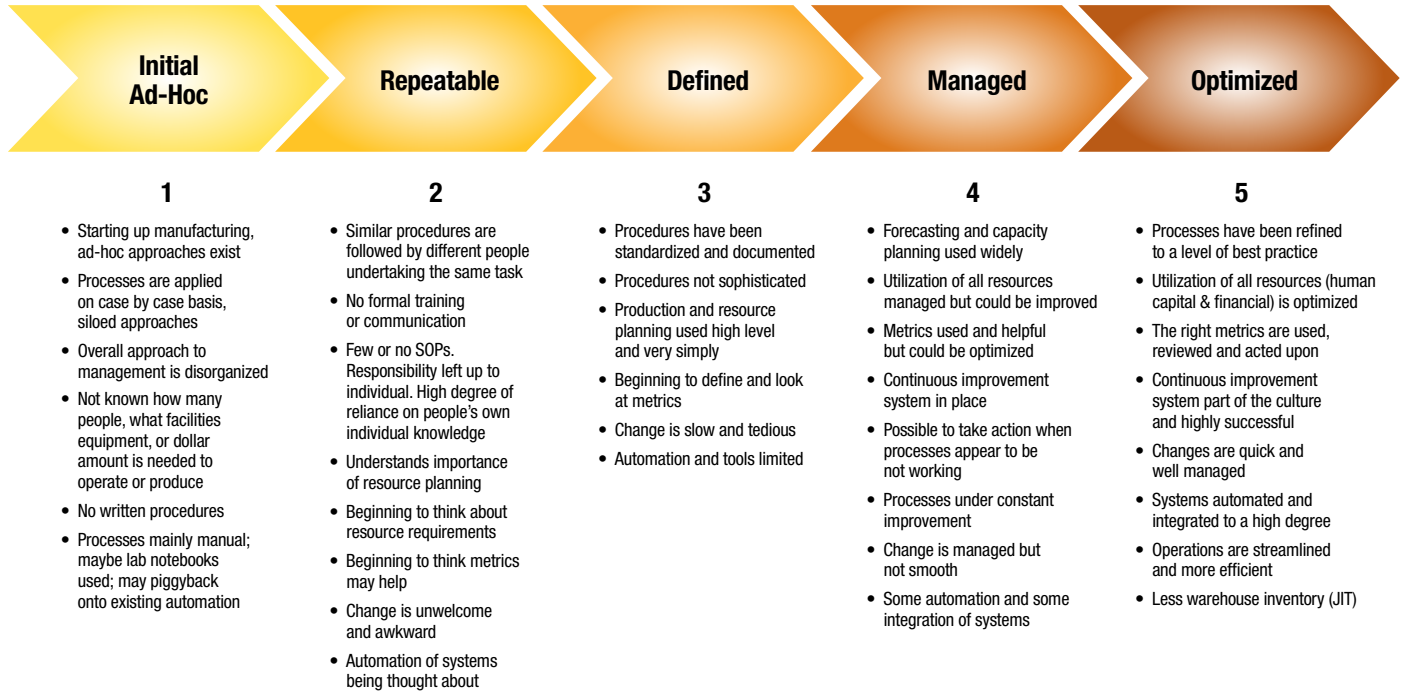
Based on the scope selected in Step 1, develop the desired end state. This is the chance to refocus your company and align all objectives. For example, if the scope was quality systems, list the desired attributes of your quality systems. In other words, knowing what you now know about the “as is,” describe the end state you want to achieve. Use these questions to move you through this process.

- How can you better understand your end-to-end process to improve Right First Time (RFT)?
- How can you integrate your process and technology to support Quality by Design (QbD)?
- How can you access real time data for science-based decision making to improve the predictability of your drug development and manufacturing processes?
- How can you improve your IT architecture to meet the needs of your business?
- How can you build compliance into your operations?
- How can you balance your processes and systems with respect to efficiency and compliance?
- How can you better align your organization and culture to support a proactive approach?
- What changes can you make that would yield a true investment in efficient, high quality operations?

Continuing with our example from Step 1, here is a simple description of an end state.

EXAMPLE: Desired end state for computer systems
• No red ranked systems; preferably few to zero yellow systems
• Batch release supporting systems (i.e. Change Control, CAPA, Deviation Management, and Investigation Management) on a single system with a dashboard
• Manufacturing Execution System (MES) in place with PM and Calibration included
• Upgrade systems as needed to ensure software is supported and aligned with current regulatory requirements

Efficiency of Operations



Assurance of Quality

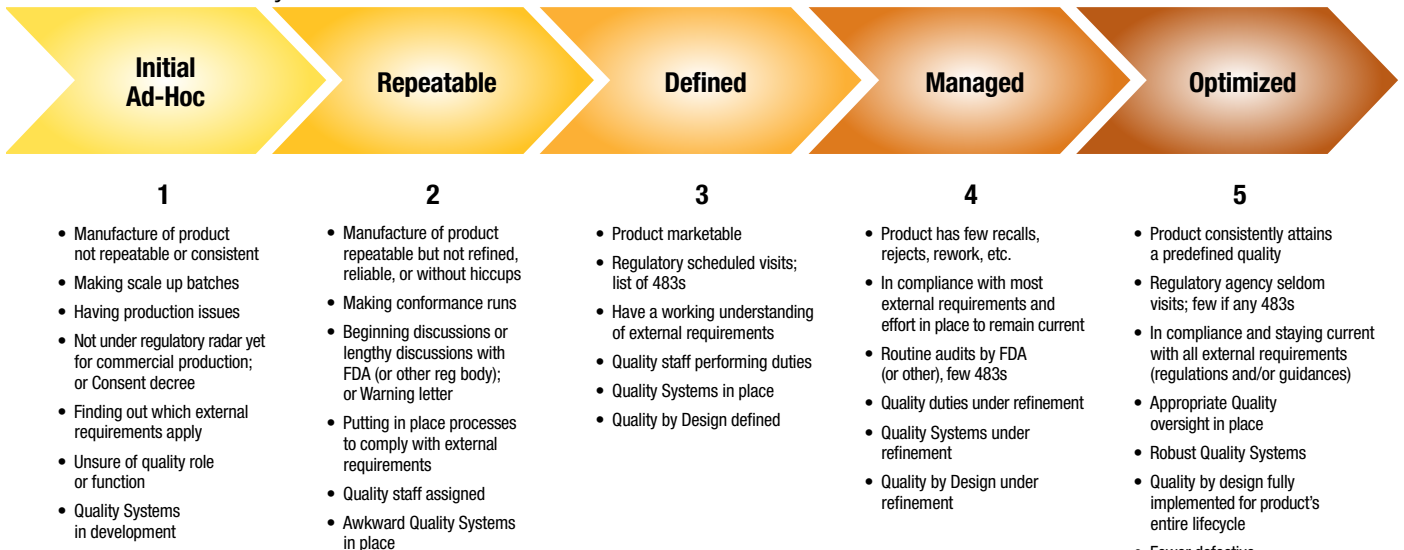


Figure 2: Typical Maturity States
 Moving toward optimization puts all of your systems, processes, and programs into balance to achieve business benefits.

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Once the end state is defined, begin listing the incremental changes that may be needed to achieve your end state. Calculate the costs of the changes using different resource requirements and different timelines. Quantify all of your options for moving your current state to a future state, if desired, and eventually to an end state. Tools to use include a risk benefit analysis.

Some suggestions include calculating:

- The cost of current state operations; i.e. complexity of operations, number of operating sites, etc.
- The return on investment (ROI) from efficiency improvements and lower internal failures, i.e. the ROI realized by improved process performance
- The cost of getting drug products to the market sooner
- Cost avoidance of not preparing and reviewing regulatory submissions
- The cost of design, redesign, or enhancement of current systems
- The cost of compliance consequences

Spend adequate time on this step. This analysis will be the basis for developing strategies and action plans. Once completed, you can move to Step 3.

Step 3 – Action

This is the step where you design your path forward and begin implementation, moving from your current state to your end state.

First, review your analysis. Prioritize items that require change and select the best options for moving forward. Develop a timeline if needed. The data from Step 2 will provide the detail needed for informed decision-making. Factors to consider in these activities may include:

- Low hanging fruit
- Changes with the largest return on investment
- Known inefficiencies, gaps, non-compliant areas
- Complexity of operations, i.e. number of facilities, number and position/s of product/s in product lifecycle etc.
- Resource requirements, i.e. money, people, materials, equipment, facilities
- Time requirements
- Incremental states, i.e. milestones

Then, develop short-term as well as long-term plans to move your company toward its future state and eventually its end state. Your short-term plans should include “low hanging fruit” – those things you need to quit doing immediately (i.e. non-value added), as well as those that require only minimal enhancement or replacement. They should also include setting up a sustainable business model, whether this is a Project Management Office (PMO) as a part of the organization or other dedicated resources. Long-term plans should include step-by-step plans to achieve your long-term goals. These should include changes that may take 2 to 10 or more years, such as replacing stand-alone software systems and implementing a full-blown MES and/or ERP system or building a new facility. These tactical and strategic plans need to be agreed upon at all levels, in all functional areas; in short, throughout your entire organization.

A few suggestions to consider when developing plans for a proactive approach:

- Cross-utilize your teams. For instance:-
 - Leverage the strength of the cGMP document control group to assist in the development of a document management system for a non-GMP group like pharmacovigilance.
 - Encourage the SOX project team to reach out to other functions such as Quality Assurance for their expertise.
- Assign a job task for an individual or a group to:
 - Stay current with Freedom of Information Act (FOIA) documents, new guidance documents, updates to the USP, new legislation, etc.
 - Stay engaged with the regulatory bodies, e.g. provide comment during comment periods on regulations.
- Eliminate turf issues by using a Project Management Office (PMO) approach. Use a PMO to provide a consistent approach, integrated teams, concise communications, and knowledge transfer.
- Employ ongoing continuous improvements efforts by incorporating them into the fabric of the organization. Whether the effort is Six Sigma, Lean, or something else, it is necessary to build this function into your organization. Change is here to stay.
- Locate your functional areas in close proximity to facilitate effective communication. For example, “place the lab and production in close proximity.”¹⁰ When people are near each other, they will talk.