Efficient Process as Driver of Business Success

Companies in the pharmaceutical industry are regulated in virtually every aspect of their business. Quality departments look closely at the CFR regulations when producing traditional products (21CFR210/211), biologics (21CFR600), medical devices (21CFR820), and must also recognise the many guidance documents that help them implement suitable procedures to run their processes. If these processes work, delivering the requisite output, we have a definition of a "Quality System". This Quality Management System (QMS) of procedures then drives quality which in turn drives a company's performance. If it is done right, the QMS is not a burdensome formality nor a 'bureaucratic monster' rather, it becomes a supportive system that enables growth and improved business performance.

How do we know that a company's QMS is driving the desired success and how do we prove that it is not a drag on the system? There needs to be a monitoring system in place to ensure oversight and provide the indicators that enable management decision making.

The 2008 guidance document of ICH Q10 (International Committee of Harmonisation) defined the pharmaceutical quality system. The 'guidance' document provided an exact a set of instructions to enable the industry to set up systems, procedures, and elements of managerial oversight. When it came time to discuss managerial oversight, it went even further, offering not only guidance, but making this oversight a formal requirement.

It may be surprising to the layperson that such oversight structures needed to be created and enforced. One rightly imagines it would be a natural consideration for any company to have established tactical monitoring systems in place to optimise performance and maximise results, to say nothing of maintaining high quality standards. But the heterogeneity of the pharmaceutical industry made international guidance and enforcement a necessity and inspections by various authorities are now the norm. These regulations will be updated overtime and will be followed by ever-increasing regulation – as evidenced by a quick review of *CDER Guidance Agenda New & Revised Draft Guidance Documents Planned for Publication in Calendar Year 2022*.

The ICH Q10 guidance, in this instance, is detailed – 20 pages in length - and clearly advises senior management of their commitment and how to perform their duties (Section 2.1) (emphasis added):

1) *Participate* in the design, implementation, monitoring, and maintenance of an effective pharmaceutical quality system
2) *Demonstrate* strong and visible support for the pharmaceutical quality system and ensure its implementation throughout their organisation
3) *Ensure* a timely and effective communication and escalation process exists to raise quality issues to the appropriate levels of management
4) *Define* individual and collective roles, responsibilities, authorities, and inter-relationships of all organisational units related to the pharmaceutical quality system. Ensure these interactions are communicated and understood at all levels of the organisation. An independent quality unit/structure with authority to fulfil certain pharmaceutical quality system responsibilities is required by regional regulations
5) *Conduct* management reviews of process performance and product quality and of the pharmaceutical quality system

6) *Advocate* continual improvement
7) *Commit* appropriate resources

Clearly management has an *active* responsibility to "participate, demonstrate, ensure, define, conduct, advocate, and commit" (to) the process.

And further to perform regular reviews, since then referred to as "Quality Management Review" (QMR), (Section 2.6) …

a) Senior management should be responsible for pharmaceutical quality system governance through management review to ensure its continuing suitability and effectiveness.
b) Management should assess the conclusions of periodic reviews of process performance and product quality and of the pharmaceutical quality system.

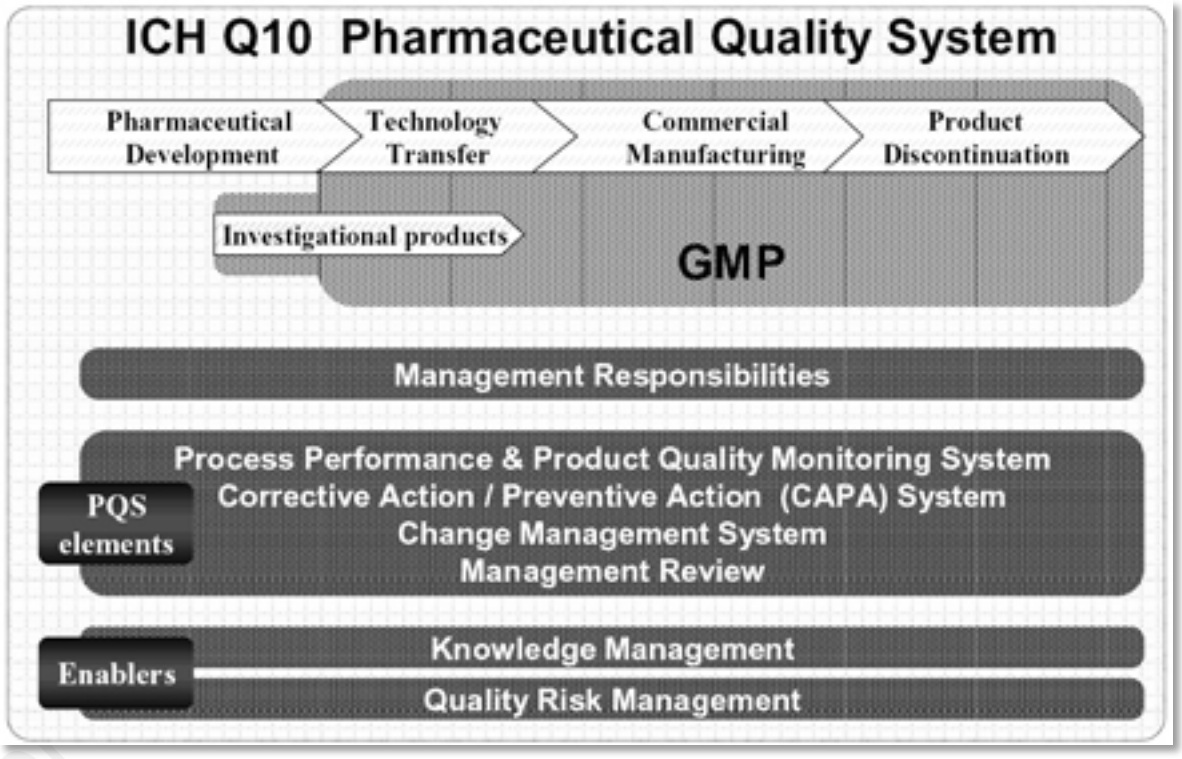


Figure 1 ICH Q10 – Management Responsibilities

The guidance goes on to clearly frame how management should consider continuous improvement processes and work on continued monitoring of the delivered product quality (Figure 2). The guidance documents describe several additional elements and important aspects of establishing a working quality management system, but this

article focuses on the management review and resulting decisions for the organisation, product quality, and continuous process improvement.

> 3.2.1. Process performance and product quality monitoring system
>
> Pharmaceutical companies should plan and execute a system for the monitoring of process performance and product quality to ensure a state of control is maintained. An effective monitoring system provides assurance of the continued capability of processes and controls to produce a product of desired quality **and to identify areas for continual improvement**. The process performance and product quality monitoring system should:
>
> a) Use quality risk management to establish the control strategy. … The **control strategy should facilitate timely feedback / feedforward and appropriate corrective action and preventive action**;
> b) **Provide the tools for measurement and analysis of parameters** and attributes identified in the control strategy (e.g., data management and statistical tools);
> c) **Analyse parameters and attributes identified** in the control strategy to verify continued operation within a state of control;
> d) Identify sources of variation affecting process performance and product quality **for potential continual improvement activities** to reduce or control variation;
> e) Include feedback on product quality from both internal and external sources, …
> f) **Provide knowledge to enhance process understanding, enrich the design space,… and enable innovative approaches to process validation**.

Figure 2 ICH Guideline Q10 - emphasis added

If nothing else, the guidance answered an important question. As agreed by all the international authorities and industry representatives: 1. regulatory compliance and 2. business interests were to be the responsibility of one (and only one) office of a pharmaceutical company.

If the guidance and associated processes work, delivering the requisite output, we have a definition of a "Quality System" (Figure 3.). This Quality Management System (QMS) of procedures which drives quality throughout the organisation, which in turn drives a company's performance. If it is done right, the QMS is not a burdensome formality nor a 'bureaucratic monster' rather, it becomes a supportive system that enables growth and improved business performance.

Figure 3 Benefits of a Quality System

By establishing, for example, regular QMR meetings, companies invite cross-functional managers to review an abundance of data and quality metrics. This data is collected in the various locations, departments, processes, workflows, and document management systems of the organisation.

These metrics are collected for typical quality events like deviations, corrective & preventive actions (CAPA), changes, complaints and recalls, audits, laboratory/out-of-spec result investigations, and many other trackable activities. For each of these parameters, various criteria can be envisioned which further describe performance in this quality process. Such criteria can be on-time delivery, effectiveness, re-occurrence, or calculated in correlation to other metrics such as in relationship to production volume, analysis, or time.

Clearly in a large company, with a branch network spanning time zones, it is common that the number of criteria / parameters in a QMR-meeting may quickly reach an unmanageable number. If one considers a typical hour-long meeting, there may be only time for one data point per minute, creating an enormous challenge for management. This time constraint makes it unrealistic for those responsible to digest the data and to consider possible actions, to say nothing of addressing trends or effects which the data may have brought to light.

The organisation is, furthermore, obligated to collect and compile this data for presentation. This has, historically been done manually, via paper and pencil, using excel to compile and collate, creating various graphs for the relevant parameters of quality processes. The guidance and regulations envisage that these graphs will

provide a visualisation that follows the purpose of straight forward interpretation and delivery of a message, which may be realised in well-defined graphical displays. However, the presentation ends up as a collection of individual graphs in a variety of formats thus increasing the already challenging task of interpretation where each graph's axes and layouts must be explained. Ultimately there is no time for meaningful data interpretation, or joint discussion of the parameters in the meeting, to say nothing of defined action to address or capitalise on the observed effects.

The solution to break this cycle and move into an upward spiral of improved performance has two main elements, both pointing in the same direction:

1. Quality over Quantity

In the attempt to produce better results and deliver change through effective action the QMR-team must focus on fewer metrics to enhance the effect of joint analysis, cross-functional evaluation, and aligned decision making. This can be achieved by alternation of presented quality processes and their performance parameters to ensure a more manageable number per meeting.

The downside of this procedure lies in the reduced visibility and decreased ability to react to internal trends in the data. This increases the lag already inherent in the delivery of the metric parameters due to the frequency of the QMR meetings (in most instances monthly or quarterly cycle).

2. Data Availability and Capability for Preparation

The performance data of the reviewed quality processes in a QMR-meeting are core elements of managerial practice. The ability to understand the various data and processes, by any relevant leadership function on any level of the organisation, will support management's ability to manage, grow, and direct the company's activities. The metrics on each level, from shopfloor unit to department and site, or even corporate network aggregation, can deliver the basis for this growth.

This effective collection and distribution of data empowers every manager to better understand the functionality and performance of their area of responsibility. A process that allows review of the metrics, securely, anywhere at any time, provides additional benefits. In the case that data is available in advance of meetings it will allow management to be properly prepared. This will lead to in-depth discussion of the relevant metrics, for which proactive action will lead to the most promising performance improvements.

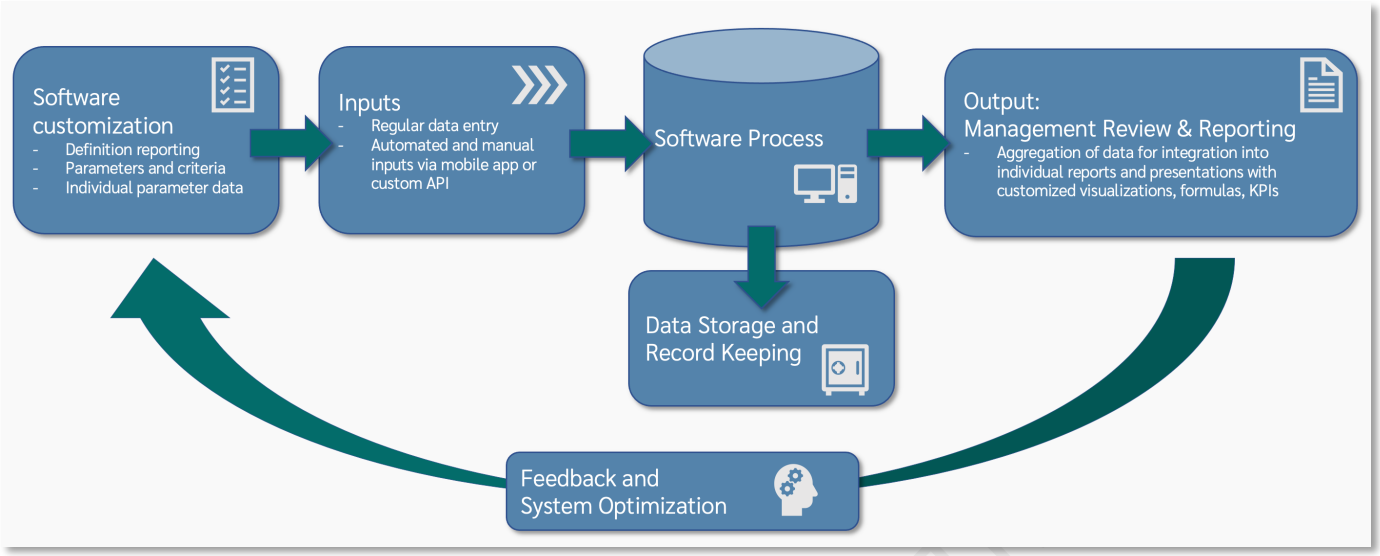


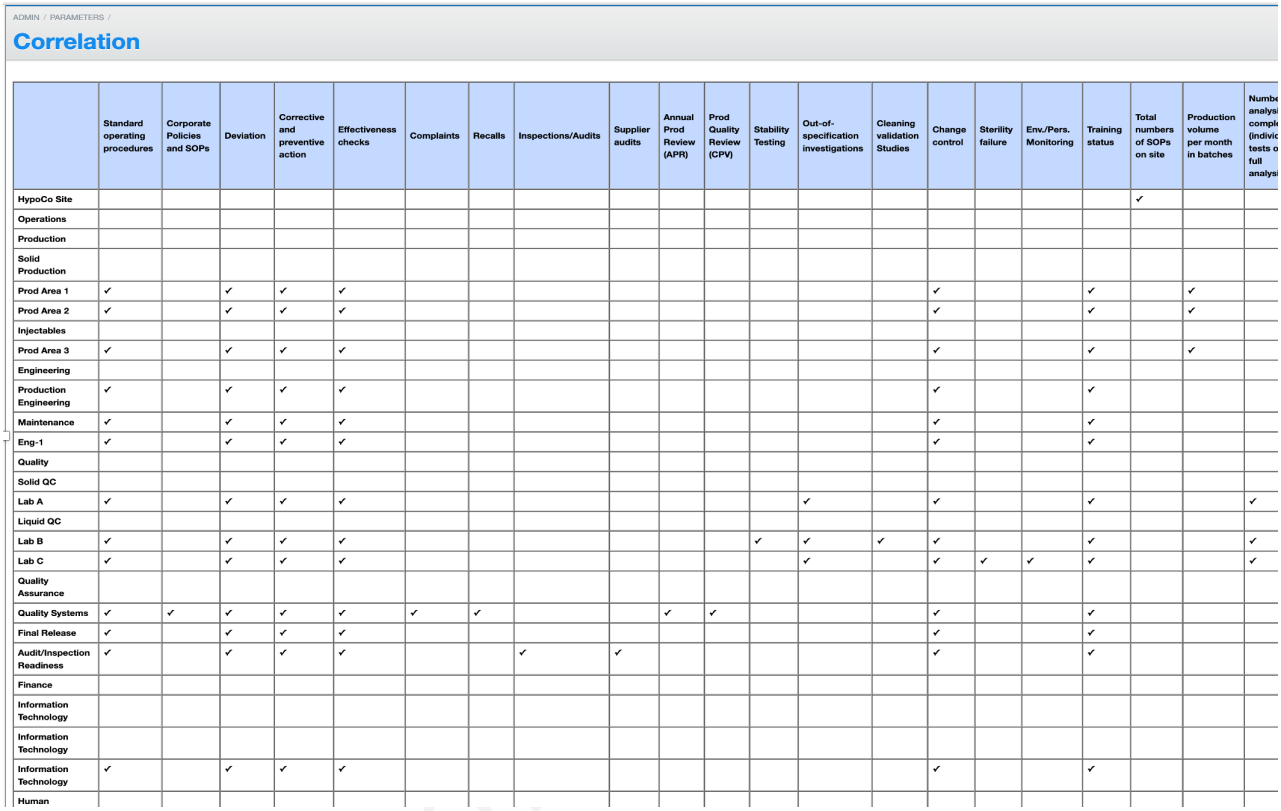
Figure 4

These outcomes can only be realised using specialised software. Simplified gathering of data, aggregation on all levels of the company - starting on the shopfloor, will allow leaders on all levels to use the data to analyse performance in their own area of responsibility as well as in comparison to other areas or departmental overview.

There is also the capability to aggregate into networks of sites to support global functions. High data availability with secure access from anywhere at any time to support core job of each manager (manage and improve performance).

- The properQMR process allows management to fulfil their regulatory obligations, while simultaneously creating a platform for feedback, regulatory and audit transparency, and process improvement.
- Data entry, calculations of derived parameters (ex. KPIs), detailed analysis, and presentation in graphical and contextual format are delivered in one useable format.
- The solution allows users to analyse trends in their data which can be visualised, aggregated, and differentiated by unit, department, geographical location, etc. At the same time, end-to-end encrypted data is available to management in real time and can be analysed on any desktop or mobile device.

- Finally, any interaction with the software is stored in a revision-proof audit facility, providing maximum transparency and security for management, auditors, and regulators.



ADMIN / PARAMETERS /

Correlation

	Standard operating procedures	Corporate Policies and SOPs	Deviation	Corrective and preventive action	Effectiveness checks	Complaints	Recalls	Inspections/Audits	Supplier audits	Annual Prod Review (APR)	Prod Quality Review (CPV)	Stability Testing	Out-of-specification investigations	Cleaning validation Studies	Change control	Sterility failure	Env./Pers. Monitoring	Training status	Total numbers of SOPs on site	Production volume per month in batches	Numbe analysi compl (indivic tests o full analysi
HypoCo Site																			✓		
Operations																					
Production																					
Solid Production																					
Prod Area 1	✓		✓	✓	✓										✓			✓		✓	
Prod Area 2	✓		✓	✓	✓										✓			✓		✓	
Injectables																					
Prod Area 3	✓		✓	✓	✓										✓			✓		✓	
Engineering																					
Production Engineering	✓		✓	✓	✓										✓			✓			
Maintenance	✓		✓	✓	✓										✓			✓			
Eng-1	✓		✓	✓	✓										✓			✓			
Quality																					
Solid QC																					
Lab A	✓		✓	✓	✓								✓		✓			✓			✓
Liquid QC																					
Lab B	✓		✓	✓	✓							✓	✓	✓	✓			✓			✓
Lab C	✓		✓	✓	✓								✓		✓	✓	✓	✓			✓
Quality Assurance																					
Quality Systems	✓	✓	✓	✓	✓	✓	✓			✓	✓				✓			✓			
Final Release	✓		✓	✓	✓										✓			✓			
Audit/Inspection Readiness	✓		✓	✓	✓			✓	✓						✓			✓			
Finance																					
Information Technology																					
Information Technology																					
Information Technology	✓		✓	✓	✓										✓			✓			
Human																					

Figure 5 Parameter Matrix

How do we know that a company's QMS is driving the desired success? There needs to be a monitoring system in place to ensure oversight and provide the indicators that enable management decision making.

By integrating a specialised software platform into the data collection and review process, managers are equipped with a solution that allows them to monitor and measure their organisation's data. The ability to do so in real time in a secure environment, provides them with an advantage over their paper-and-pencil-based competitors. Once a company has established a tactical monitoring system, they are able to easily optimise their performance and maximise their results, all while maintaining high quality standards demanded of them by the regulators and their customers.