ICH Q10

'AN OPPORTUNITY FOR US ALL'

The ICH Q10 Guideline 'Pharmaceutical Quality System' was signed off as a Step 4 document at the ICH meeting in Portland, Oregon, in June 2008.

The Q10 Guideline was then introduced into the regulatory systems of FDA, EMEA and Japan over the next few months and was highly influential in shaping how modern quality management approaches evolved and developed within the Pharmaceutical Industry.

NSF's Neil Wilkinson was the EU Industry topic leader within the ICH Q10 Expert Work Group and was an active participant in the Q10 journey – from the early conceptual discussions with FDA around the need to modernise the Pharmaceutical Industry and associated regulatory procedures, to the ICH 'Q' discussions leading to the agreed ICH Quality Vision and the subsequent Guidelines Q8, Q9 and Q10 (and Q11) needed to deliver it, through to the writing of the Q10 document.

It is critical that Q10 should not just be looked at as a Quality Guideline, relevant only to the 'Quality Folks' in a company. It should be seen as an essential key business system that drives good business performance and improvement.

But what about that old Pharmaceutical Industry argument – 'we are a heavily regulated Industry and have our own GMPs'?

Well, this article will attempt to convince you that this is not valid – to improve the performance of the Pharmaceutical Industry and to facilitate more science and risk-based regulatory approaches something new was needed – enter ICH Q10.

BACKGROUND – THE NEED TO CHANGE

The Pharmaceutical Industry is currently facing significant challenges both in the external economic environment in which we operate and internally with the need to modernise and make pharmaceutical manufacturing more efficient.

To continue to operate with a focus on 'blind compliance' leading to inefficient ways of working is no longer an option.

External pressure from governments seeking reductions in the costs of healthcare spending, including the cost of drugs, and a sustained slow down in the introduction of new drugs from the R&D based Industry are significant challenges we face as an Industry.

Additionally, internally, the Pharmaceutical Industry is well behind other Industries in terms of manufacturing understanding and efficiency, Quality Management and continual improvement approaches. It was recognised, in part, that regulatory agency processes have played their part in the situation by making changes and improvements difficult to make – however Industry did also help drive itself into a mindset of 'blind compliance' during the late 1990s/early 2000s. Studies published by PricewaterhouseCoopers and IBM concluded that pharmaceutical manufacturing was highly inefficient, operating 2.5 sigma processes with a heavy emphasis on inspection and QC to provide suitable products to the market place.

Wall Street Journal 2003

"The Pharmaceutical Industry has a little secret: Even as it invents new drugs its manufacturing techniques lag far behind those of potato chip and laundry soap makers."

So – there were, and still are, strong drivers for change. It was clear that the then current regulatory processes and GMPs required significant overhaul and a culture change to facilitate the changes required.

THE 'QUALITY JOURNEY'

The FDA's 'cGMP for the 21st Century' initiative in the early 2000s led the way and catalysed the subsequent development of the ICH Quality Vision in 2003 that then led to the ICH Guidelines ICH Q8/ Q8R (Pharmaceutical Development), ICH Q9 (Quality

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Risk Management) and ICH Q10 (Pharmaceutical Quality System).

Additionally, more recently, Q11 (Development and Manufacture of Drug Substances) and revisions to the variations and post-approval changes regulations in the EU and US are also now actively being progressed – so we are still on the journey.

Note that all the above Guidelines are strongly inter-related, with Q10 providing the 'umbrella' Pharmaceutical Quality System (PQS) to sit above and glue it all together.

THE KEY MESSAGES ON Q10

Remember – Q10 is heavily inter-related with Q8, Q9 (and now Q11).

It has the full endorsement of the regulators as being an acceptable approach to satisfying expectations for a modern Pharmaceutical Quality System. In the eyes of the Regulators – having a Quality System is mandatory, having a Q10 PQS is 'strongly recommended'. The use of alternates will have to be justified.

In order to learn from approaches to Quality Management used in other Industries, Q10 takes the framework of ISO 9001 – and adds a pharmaceutical context. So what are the major aspects to consider in Q10?

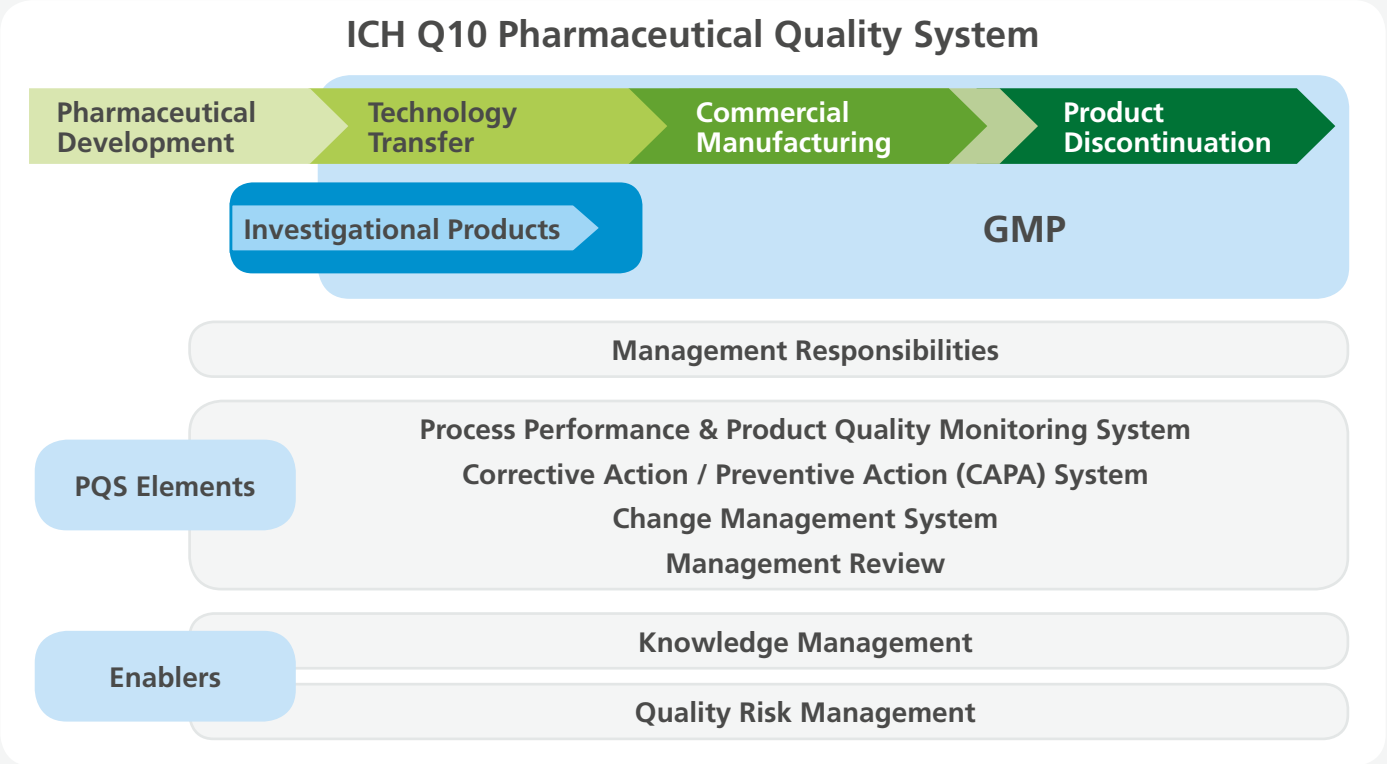
AIM OF Q10

Its aim is to promote a 'paradigm shift' away from just applying GMP at discrete stages of the product lifecycle, to having a comprehensive Quality System approach 'over the lifecycle' of the product. A Q10 PQS will therefore link together the different stages of the product lifecycle and strengthen links between development and manufacturing organisations, including the highly important management of and use of product knowledge.

SCOPE

Q10 is applicable to the development and manufacture of drug substances (API) and drug products, including biotechnology and biological products through the product lifecycle – so it goes beyond the GMPs. Good Manufacturing Practice is the necessary but not sufficient condition for Good Manufacturing Performance.

Annex 2
Diagram of the ICH Q10 Pharmaceutical Quality System Model



It is important to apply Q10 in a manner that is appropriate and proportionate to the stages of the lifecycle, so not to inhibit innovation and improvements. Q10 is applied as a system, and can accommodate both new and existing products.

REGULATORY APPROACHES

The intent of Q10 is that regulatory approaches for a specific product or site should be commensurate with:

- The level of product and process understanding
- The use and results of Quality Risk Management
- The effectiveness of the PQS

The types of opportunities that this may bring are listed in Q10 Annex 1.

ANNEX 1 – POTENTIAL OPPORTUNITIES TO ENHANCE SCIENCE AND RISK-BASED REGULATORY APPROACHES*

*Note: This annex reflects potential opportunities to enhance regulatory approaches. The actual regulatory process will be determined by region.

SCENARIO AND POTENTIAL OPPORTUNITY

1. Comply with GMPs
   - Compliance – status quo
2. Demonstrate effective Pharmaceutical Quality System, including effective use of Quality Risk Management principles (e.g. ICH Q9 and ICH Q10)
   - Opportunity to:
     - Increase use of risk-based approaches forregulatory inspections
3. Demonstrate product and process understanding, including effective use of Quality Risk Management principles (e.g. ICH Q8 and ICH Q9)
   - Opportunity to:
     - Facilitate science-based pharmaceutical quality assessment
     - Enable innovative approaches to process validation
     - Establish real-time release mechanisms
4. Demonstrate effective Pharmaceutical Quality System and product and process understanding, including the use of Quality Risk Management principles (ICH Q8, ICH Q9 and ICH Q10)
   - Opportunity to:
     - Increase use of risk-based approaches for regulatory inspections
     - Facilitate science-based pharmaceutical quality assessment
     - Optimise science and risk-based post-approval change processes to maximise benefits from innovation and continual improvement
     - Enable innovative approaches to process validation
     - Establish real-time release mechanisms

As a result, a more science and risk-based regulatory oversight should result.

CONTINUAL IMPROVEMENT

Q10 seeks to facilitate a culture of continual improvement. This means moving the Industry forward, both organisationally and technically.

Q10 re-enforces a number of very key areas seen within the ISO 9001 approach, and partly in the GMPs. These include:

- Management responsibility
- Monitoring of product quality and process performance
- Corrective and Preventive Action (CAPA)
- Change management
- Management reviews

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To undertake this successfully, the effective use of Quality Risk Management and Knowledge Management need to be embedded/integrated throughout the product lifecycle.

SO WHERE COULD Q10 TAKE US?

A successful implementation of ICH Q10, alongside ICH Q8/Q9, should help move pharmaceutical development and manufacturing and associated regulatory processes towards a much more science and risk-based way of operating. This approach should be consistent across the ICH region and also where observer countries/ regions 'sign up' to the principles.

This all sounds highly desirable, but does it make business sense?

Well, in addition to the above thinking there are seen to be significant business benefits available, which are a perfect fit with today's initiatives driving towards operational excellence, using Six-Sigma and/ or lean thinking.

These include:

- Improved understanding and performance of manufacturing and business processes
- Reductions in the cost of internal failures (rejects, reworks, reprocessing, investigation costs, etc.) and costs of Quality
- Reductions in the costs of holding duplicate stock and operating multiple processes as changes/improvements are more easily made with less 'prior-approval' changes
- Reductions in the costs and delays of certain regulatory submissions
- Improved relationships between Industry and Regulators focused on science and risk management, allowing Industry and Regulators to focus on the things that matter – not just on 'blind compliance'
- Risk-based regulatory scrutiny – commensurate with a firm's use of ICH Q8/Q9/Q10

So Q10 presented a great opportunity to contribute to modernising and improving the approach to Quality Management within the Pharmaceutical Industry, giving us the opportunity to improve the efficiency and effectiveness of our Industry and better facilitate improvement and innovation.

For more information, contact **pharmamail@nsf.org** or visit **www.nsfpharmabiotech.org**

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NSF INTERNATIONAL | PHARMA BIOTECH

The Georgian House, 22/24 West End, Kirkbymoorside, York, UK YO62 6AF

T +44 (0) 1751 432 999 | **E** pharmamail@nsf.org | www.nsf.org | **www.nsfpharmabiotech.org**

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