Implementation group
Q8, Q9 and Q10

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Brief history

A long story of concepts and theories …. Starting with this nice sentence expressed in Brussels in May 2003

"Develop a harmonised pharmaceutical quality system applicable across the **life cycle** of the product emphasizing an integrated approach to quality risk management and science"

Main message : science is no more isolated and is living across the lifecycle of the product

Brief history

Since these days, we have elaborate :

- Q8,
- Q8 R (under development with expected step 4 in November 08),
- Q9,
- Q10,
- Q11 (step 1).

You can see works accomplished in 5 years and I can tell you that I was not so optimistic when we started with ….

Brief history

To start with practical understanding, different initiatives have been created :

- EMEA and US FDA PAT teams,
- Many conferences and workshops throughout the world,
- And now, we have activities performed in the framework of ICH Q8, 9 and 10 implementation group.

I really hope that perspectives will be clearer for both industry and regulators (including for GMP inspectors ….).

Brief history

My first understanding came with explanations from Susane Keitel (Head of the EDQM) :

Design Space …. Quality by Design ….

It sounds like good old “Common Sense“!

I was happy with these words (common sense) as they are really an intelligible concept for a traditional GMP inspector !!

Why an implementation group ?

After ICH Q10 raised step 4, it has been obvious for all participants that there is a need for developing a common approach and implementation of the 3 guidelines (Q8 and derivatives, Q9 and Q10) in the 3 concerned ICH regions.

A proposal was made to the ICH Steering Committee in Portland last June which agreed.

All the participants working into this implementation group were previously involved in drafting one of these ICH documents.

First steps

* First meeting in Portland (USA) in June 2008

* Second meeting in Brussels (Belgium) in November 2008

* Third meeting in Yokohama (Japan) in June 2009

First steps

During the first meeting, it has been decided to work following 2 different timetables :

- Short term using questions & answers (Q&A) system for clarifying some urgent issues,
- Long term using other Q&A but also defining training materials and collaboration with professional structures (as PICS, ISPE, PDA …..) for disseminating agreed approaches between ICH regions and also outside for interested parties.

First steps

At the same period of time and during meetings, seminars, conferences, training courses, many questions have been raised on :

- Knowledge Management (KM),
- Quality by Design (QbD),
- Design Space (DS),
- Real Time Release Testing (RTRT),
- Control Strategy (CS),
- Pharmaceutical Quality System (PQS),
- ICH new quality guidelines impact on GMP inspection practices,
- Software solutions.

First steps

For facilitating the work, all questions have been shared between the 3 ICH regions for drafting answers, as followed :

- Japan (MHLW + JPMA) : Knowledge Management,
- USA (US FDA + PhRMA: Design Space, Real Time Release Testing, Control Strategy, Criticality,
- EU (EC + EFPIA) : PQS and inspection, assessor-inspector collaboration.

First steps

Between Portland and Brussels meetings, each region (regulators and industry) worked on dedicated topics and preliminary results were shared during a teleconference.

An agenda was proposed for Brussels meeting dedicated mainly on :

- discussions on different topics and work on Q&A,
- training issues as workshops, set of agreed slides …
- collaboration with other organisations (setting up a procedure for).

Short term action : developing Q&A

Knowledge Management : example of questions

- Does Q10 suggest an ideal way to manage knowledge ?
- What are the potential sources of information for KM ?
- Is an IT system required for the implementation of KM with respect to ICH Q8, Q9 and Q 10 ?
- Will regulatory agencies expect to see a formal KM approach ?

Short term action : developing Q&A

Quality by Design : example of questions related to Design Space

- Is it necessary to study multivariate interactions of all parameters to develop a DS ?
- Can a DS be applicable to a site change ?
- Is there a regulatory expectation to develop a design space for an existing product ?
- Is it possible to develop a DS for existing products ?

Short term action : developing Q&A

Quality by Design : example of questions related to Real Time Release Testing

- What is the difference between "real time release" and real time release testing ?
- How is batch release affected by employing real time release testing ?
- Does real time release testing mean elimination of end product testing ?
- What is the relationship between Control Strategy and RTRT ?

Short term action : developing Q&A

Quality by Design : example of questions related to Control Strategy

- What is the difference in a control strategy for products developed using the traditional approach versus QbD approach ?
- Are GMP requirements different for batch release under QbD ?
- What is the relationship between a Design Space and a Control Strategy ?

Short term action : developing Q&A

Pharmaceutical Quality System : example of questions

- How does a company demonstrate implementation of A PQS in accordance with ICH Q10 ?
- Is it necessary to describe the PQS in a regulatory submission ?
- Will there be ICH Q10 certification ?
- How should the implementation of the DS be evaluated during inspection of the manufacturing site ?

Short term action : developing Q&A

ICH new quality guidelines impact on GMP inspection practices : example of questions

- How will product related inspections differ in an ICH Q8, Q9 and Q10 environment ?
- How will system related inspections differ in an ICH Q8, Q9 and Q10 environment ?

Short term action : developing Q&A

Software solutions : example of questions

☛ With the rapid growth of the new science and risk based quality paradigm coupled with the IWG efforts to facilitate globally consistent implementation of Q8, Q9, and Q10, a number of commercial vendors are now offering products that are being marketed as 'ICH compliant solutions' or ICH Q8, 9 & 10 Implementation software, etc. Is it necessary for a pharmaceutical firm to purchase these products to achieve a successful implementation of these ICH guidelines within their companies ?

Long term actions : training

- Objective

Make sure that the correct and consistent interpretation is presented

- Common training package

Setting up a common set of agreed slides (ass a model: ICH Q9 briefing pack: EWG delegation developed and agreed on a slide set; published at ICH web site)

Long term actions : training

- Workshops
  - Co-sponsorship by Q-IWG,
  - Run one workshop in each region to bring regulators & industry together (as a model: ICH Q7 EWG delegation as committee members for workshops run in each region),
  - Oversight technical contents to be evaluated by Q-IWG,
  - Q-IWG to identify experts and speakers in industry and regulatory authorities outside Q-IWG members,
  - Logistics to be done by the organisers and not by Q-IWG,
  - In and outside ICH regions ?

Long term actions : external collaboration

- General
  - Not-for-profit organisations with a global reach,
  - Only technical and scientific contribution will be considered,
  - Q-IWG endorsement.

- How to liaise ?
  - Evaluate publications e.g. articles, papers, journals,
  - Reference in the next Q&A version, if agreement in Q-IWG,
  - Identify proactively, which case studies could be helpful,
  - Publish request on specific topics at the ICH Website,
  - Reference in the next Q&A version, if agreement in Q-IWG.

Next steps

- Review by the 6 Parties / Observers / Interested parties
  - Regulators and Industry internal consultation with constituencies,
  - Time to be foreseen for translation,
  - Maximum time foreseen: 3 month.

- Discuss on results by teleconference (March 2009) and categorise to :
  - Agreed Q&A for publication before Yokohama,
  - Q&A for editorial changes and publication before Yokohama,
  - Q&A to go back for Q-IWG discussion for adoption in Yokohama.

Next steps

- Collect additional questions through the ICH Secretariat (IFPMA)
  - Filter the questions before,
  - To be looked at by Q-IWG before Yokohama and prioritise there.

Next steps

☛ Referring to relevant case studies, examples, detailed documents and further discussions e.g.

- ⚐ Role of knowledge management approach under Q8, Q9, Q10,
- ⚐ Design Space for multiple unit operations, scale up and site change,
- ⚐ Statistical considerations for sampling and acceptance criteria for Real time release testing,
- ⚐ Inspection practice under the Q8, Q9, Q10 environment.

Next steps

- Collaborations with external parties and organisations : notably defining which to collaborate with

- Publish initial Q&A after endorsement by ICH-SC (written procedure)

Conclusion

We need to match what we defined in the concept paper

"…., it is important that, due primarily to departure from the traditional approaches to quality guidance, proper implementation of these concepts is provided by bringing clarity, further explanation and removing ambiguities and uncertainties."

Conclusion

So, work done into ICH Q8, Q9 and Q10 implementation working group is crucial for :

☛ Right interpretation of all these guidance implemented together,

☛ Common interpretation and implementation at least between the 3 ICH regions and observers.

Thanks

to you for your attention