Implementation of ICH Q8, Q9 and Q10: EMEA Perspective

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Any views expressed are the those of the author and not necessarily those of EMEA and its Scientific Committees

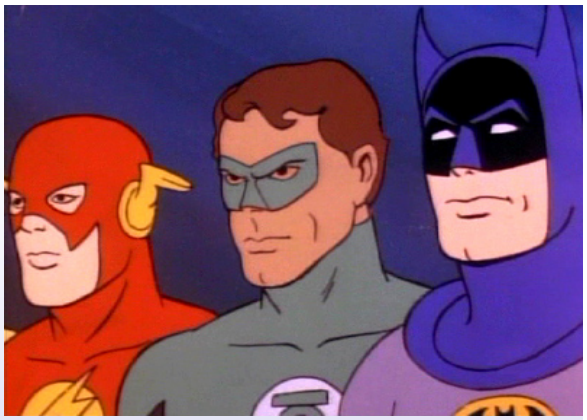
“If you don’t know where you’re going, you may miss it when you get there”

Anon

Agenda

- Q8 implementation and the EMEA PAT Team
- Q9 implementation in the EU
- Q10 implementation in the EU
- ICH Quality Implementation Working Group

EMEA PAT Team



- Mandate (general objective)
  - "A forum for dialogue and understanding…to prepare a harmonised approach in assessment of applications and inspections of products, systems, facilities for Process Analytical Technology, including Quality by Design principles…."
- Composition
  - Chair (UK); 5 quality assessors (chemicals and biologicals); 4 GMP inspectors; chairs of the QWP, BWP and GMP/GDP IWG; observer from EDQM; EMEA secretariat (3).

EMEA PAT Team Activities (1)

- 4 meetings/year
- Liaison with a number of companies, equipment manufacturers and EFPIA
- Participation in workshops
  - e.g. Design Space Workshop (May 2006), Workshop on PAT for Biologicals (March 2007), Seminar on QbD/PAT (April 2008)
- Site visits to manufacturers using PAT/QbD
- Training of assessors and inspectors
  - Upsalla, Sweden (2005), Bradford, UK (2007) and London (2009)

EMEA PAT Team Activities (2)

- Published documents:
  - Q&As: clarifying regulatory requirements
  - Reflection Paper on how information should be presented in the MA dossier
- Discussion with EFPIA on a mock (CTD P.2) submission (Examplain)
  - a similar document outlining a case study for an antibody product “A-Mab is also being developed and has been the subject of initial discussion
- Input to QbD/PAT applications in the Centralised Procedure and in a Work Sharing pilot project
- Pre-submission discussion with applicants and informal advice

EMEA PAT Team: Ongoing Activities

- Continue dialogue with companies on both general and product-related issues
- Develop guidance for assessors, inspectors and applicants on:
  - Impact on batch release
  - Impact on assessment of dossiers
  - Impact on inspection practices
- Further Q&As unlikely unless EU-specific
  - ICH Q-IWG Q&As

Other Ongoing Related Activities

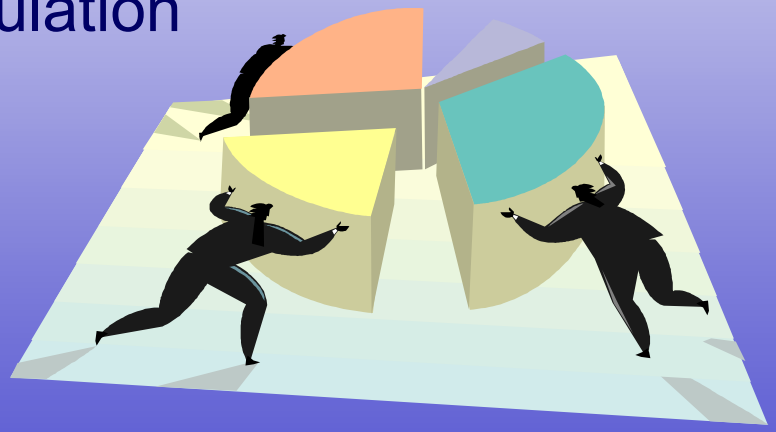
- Revision of the CHMP Guideline on Near Infra Red
- Revision of the CHMP Guideline on Parametric Release (to extend to Real Time Release Testing)
- Anticipated revision of GMP Annex 17

Work Sharing Project

- No harmonised variations process for older nationally authorised products
  - variations at national level perceived by companies as a major barrier to introduction of QbD and/or PAT
- The Work Sharing Project for PAT/QbD variations to nationally authorised products was published in June 2006
  - Draws from the mutual recognition principles behind the EU marketing authorisation procedures
- The procedure is co-ordinated by EMEA through the Quality Working Party and pools the best available expertise in the EU on QbD/PAT
  - The EMEA PAT team plays a monitoring role to ensure consistency
- The project is not legally binding, however, it is supported by the Heads of Medicines Agencies

Work Sharing Project: Results

- 4 applications have been assessed within the project, involving the EMEA PAT Team
- All the applications were successfully finalised
- Real Time Release Testing was authorised in one case
- The project has paved the way to further development of the Work Sharing concept, as foreseen in the current revision of the Variations Regulation



Summary of Q8 Implementation status in EU

- Q8 was adopted as a CHMP guideline in November 2005 (step 5)
  - Q8R was adopted in December 2008
- The QbD approach is compatible with the existing regulatory system
- QbD and PAT elements have been authorised in new applications and in variations using the work-sharing project
- The Design Space concept is specifically recognised in EU legislation (Variations Regulation)
- The EMEA PAT Team has played a key role in the implementation of QbD in the EU

ICH Q9: Quality Risk Management Implementation considerations

- Quality Risk Management was not a new concept at the time Q9 was introduced
  - Its use is implicit in many parts of the EU GMP Guide
- Q9 is optional
- Q9 is aimed at regulators as well as industry
  - the general perception was that the best single location for the document was within the EU GMP Guide
- EU GMP applies equally to human and veterinary medicines
  - Veterinary manufacturers not involved in the ICH process

Q9 implementation solution

- Introduce the principles of Quality Risk Management into Chapter 1 of the GMP Guide (Quality Management)
  - Done in February 2008
  - A concept paper and public consultation invited specific comment from the veterinary industry
  - Similar process underway for the Quality Management chapter of Part II of the GMP Guide (for APIs)
- Add Q9 as an optional Annex (20) to the GMP Guide
  - Done in February 2008
  - Provided as a reference source only
- Examine the impact of Quality Risk Management on other guidelines

The Compilation of Procedures

Legal basis
Art. 3(1) Directive 2003/94

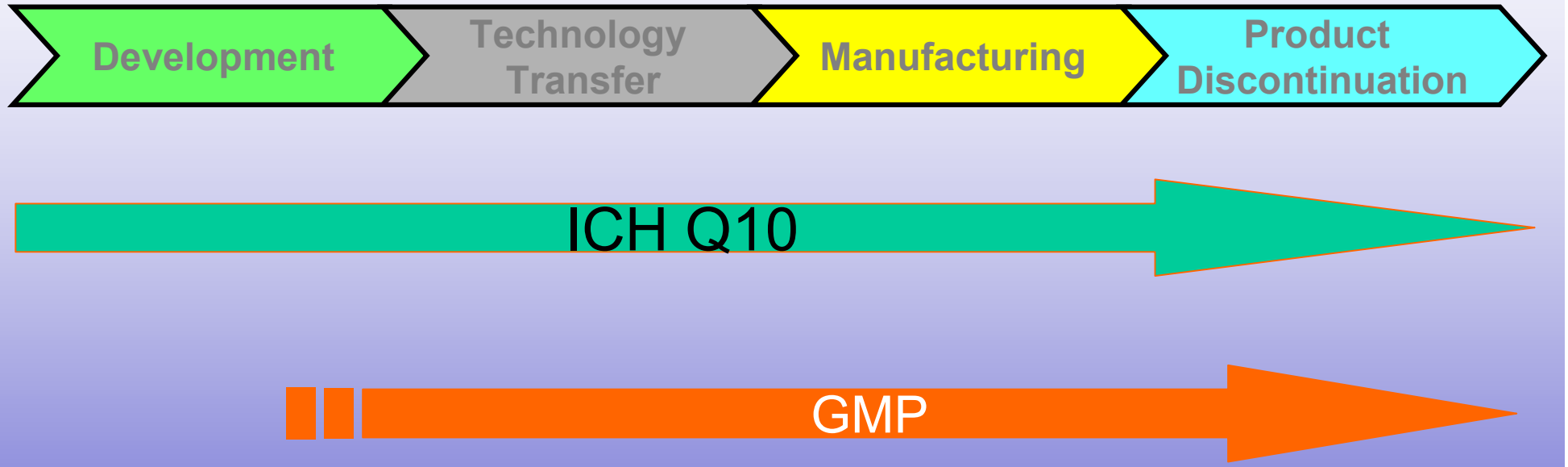
- Quality System for GMP inspectorates
- Handling suspected defects, rapid alerts and non-compliance
- Inspection procedures
- Formats for manufacturing authorisation, GMP certificates and inspection reports
- Exchange of information procedures
- Procedures for centralised inspections
- Verification of GMP in 3rd countries
- Inspection of API manufacturers
- Training and Qualification of Inspectors
- Risk-based inspection planning

Q9 Impact on the Compilation

- The concept of the risk-based approach to inspection is elaborated in the context of preparation and conduct of inspections
- Training on QRM principles and tools is included in the standard training profile for GMP Inspectors
- An elementary approach to risk-based inspection planning is introduced

ICH Q10
Pharmaceutical Quality System: Implementation problem

- EU GMP has always required a Quality System to implement GMP
  - Laid down in Directives 2003/94/EC and 91/412/EEC and elaborated in Chapter 1 of the GMP Guide
    - "The manufacturer shall establish and implement an effective pharmaceutical quality assurance system, involving the active participation of the management and personnel of the different departments."
- Q10 extends the concept of the Pharmaceutical Quality System beyond the scope of GMP
- Q10 is optional
- EU GMP applies equally to human and veterinary medicines
  - Veterinary-only manufacturers not involved in the ICH process


Development
Technology Transfer
Manufacturing
Product Discontinuation
ICH Q10
GMP

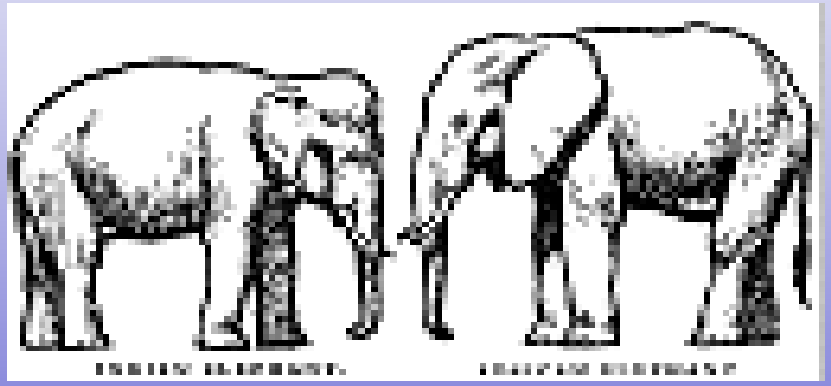
Implementation solution

- Add the text of Q10 as a new Annex (21) of the GMP Guide
  - An introductory text will clarify its optional nature with respect to application in those stages of the product lifecycle outside of the scope of GMP
- Update chapters 1 (Quality Management) and 2 (Personnel) of the GMP Guide
  - The update is intended to introduce the more modern terminology used in Q10 and more fully reflect modern practices and existing expectations which are better stated in Q10
  - Concept Paper published March 2009
  - Draft proposals are ready for public consultation
- A further proposal to update Chapter 7 (Contract Manufacture and Analysis) is under consideration in the light of Q10 but also in the light of the increasing level of outsourcing occurring.
  - To be dealt with as a separate exercise and a new Concept Paper will be published soon

ICH Quality Implementation Working Group

- Established to ensure a harmonised interpretation of ICH Q8, 9 and 10 in the 3 ICH regions
- A major tool is the development, adoption and publication of Q&As
- The group is planning to complement these Q&As with training events in each of the ICH regions and planning to sponsor the development of scientific papers

Thanks for listening.
Any questions?



Well, goodbye, Sidney.
Of course, I will never forget you.