EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

QbD/PAT – The Benefits and Challenges – a European Overview

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Presented by: **Riccardo Luigetti**
Senior Scientific Administrator

The views presented here are those of the author and should not be understood or quoted as being made on behalf of the European Medicines Agency

Content of the Presentation

Regulatory Tools

QbD: Benefits

QbD: Remaining Challenges

Conclusion

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Regulatory Tools – ICH finalised

ICH Q8 R2 – Pharmaceutical Development

ICH Q9 – Quality risk Management

ICH Q10 – Pharmaceutical Quality system

ICH Q8-9-10 Implementation Working Group Q/As clarifying concepts in the guidelines such as Pharmaceutical Quality System, Knowledge Management, Design Space, Real Time Release Testing, Control Strategy

ICH Q8-9-10 IWG training material

Regulatory Tools – ICH ongoing

ICH Q11 – Development and Manufacture of Drug Substances (step 3 – Public consultation ended on 30th September)

ICH Q8-9-10 Points to Consider

- Finalised
  - Criticality of Quality Attributes and Process Parameters
  - Control Strategy
  - Level of Documentation in Enhanced (QbD) Regulatory Submissions
- To be finalised by the end of 2011
  - Role of Modelling in QbD and associated level of documentation
  - Design Space and associated level of documentation
  - Process Validation/Continuous Process Verification

EU Specific Ongoing Regulatory Activities Related to QbD Implementation

Revision of NIR Guideline (next step: 2nd public consultation)

Revision of the Parametric Release Guideline to take into account RTRt concepts (next step: finalisation after external consultation)

Revision of the Process Validation Guideline to include continuous process verification (next step: public consultation)

Revision of GMP guide annexes 15 (Qualification and Validation) and 17 (Parametric Release) to align them with revised quality guidelines above (next step: start of work)

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QbD: Benefits for Industry

Better understanding of the processes

Less batch failure

More effective and efficient control of change

Return of investment/cost savings

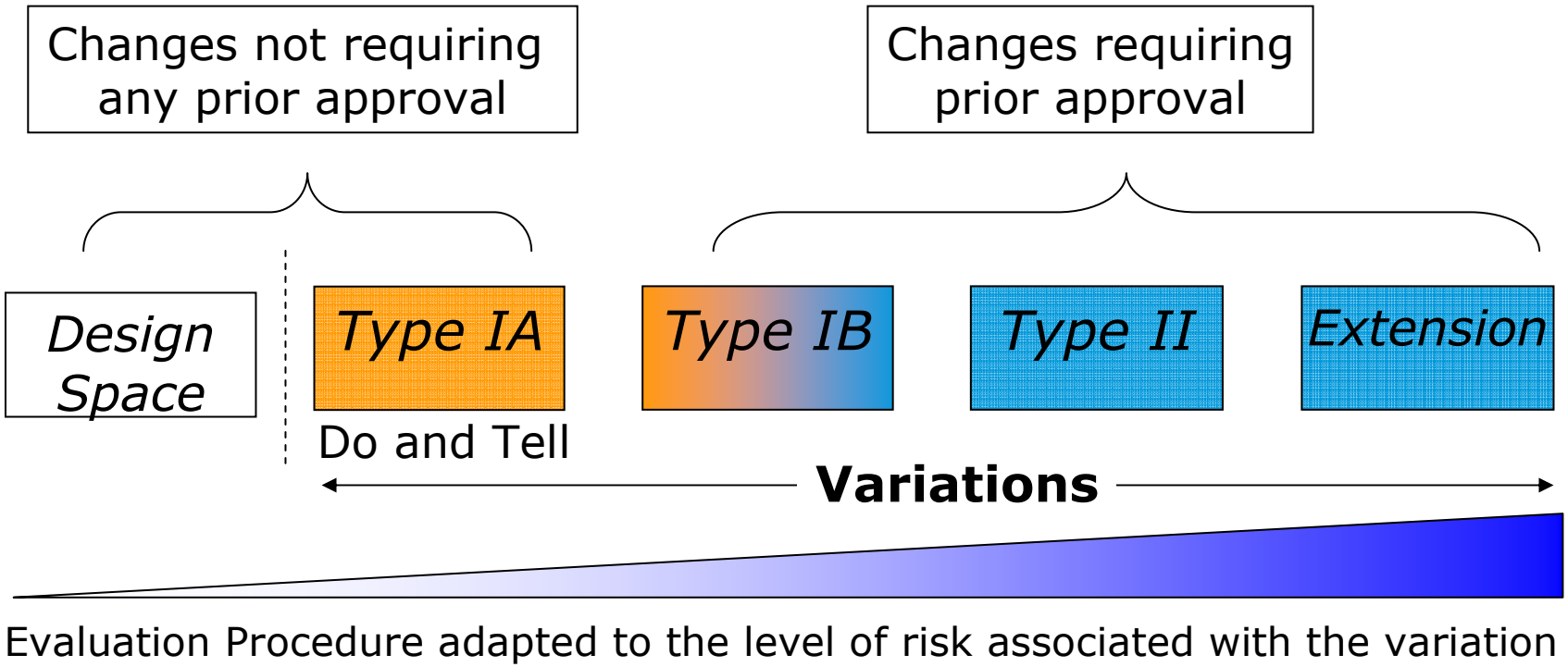
More flexible regulatory approach

QbD: Opportunities Offered by EU Regulators

The possibility of having more flexible regulatory approaches for the assessment of applications and inspections when an enhanced (QbD) approach is applied to development and manufacture is accepted by EU regulators, examples are:

- Real Time Release testing
- Continuous Process Verification
- Risk-based regulatory decisions
- Changes within the DS without regulatory review
- Post Approval Change Management Protocols
- Parallel assessment EMA-FDA
- Scientific dialogue

Variation Regulation: Regulatory Oversight Level



Post Approval Change Management Protocols

Step-wise approach to assessment of changes post-approval

- Early assessment of a change protocol (down to studies to be carried out, methods and acceptance criteria for the tests to be performed)
- Later (fast) assessment of the data produced according to the pre-approved protocol

Expected to lead to faster and more predictable implementation of complex changes post-approval (e.g. introduction of QbD/PAT elements)

Draft Q/AS:

http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2010/11/WC500098524.pdf

EMA-FDA Pilot Project for Parallel Assessment of QbD Applications

Started in April 2011 for a 3 years period

Objectives:

- Ensure consistent implementation of QbD between EMA and FDA
- Increase assessors/inspectors awareness of QbD concepts
- Sharing of information
- Facilitate the existing collaboration on inspections (joint EMA-FDA inspections are envisaged)
- Better define cooperation between assessors and inspectors
- Harmonise regulatory decisions

http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2009/10/WC500004147.pdf

Scientific Dialogue: EMA PAT Team

Formed by quality assessors (chemical and biological products) and GMP inspectors

Aim is to prepare a harmonised approach in the EU for QbD and PAT

Pharmaceutical companies are welcome to participate in order to discuss specific applications involving QbD/PAT as well as general strategies

Contact with the team at any stage (including very early stage of development) is possible

Meetings with the PAT Team are complementary to Scientific Advice

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Some Challenges for Industry

Investments

Application of QbD/PAT in existing products

Wider use of QbD/PAT by smaller companies (e.g. generics)

Align terminology used to regulatory documents

Some Challenges for Regulators

Cooperation between assessors and inspectors

Harmonisation of requirements between agencies

Need for further guidance (or may be increase awareness of the existing one!)

Clarification of need for inspection for QbD/PAT applications (e.g. when RTRt is applied for)

Level of details (amount of data) required in applications

Scientific dialogue with pharmaceutical companies

'Regulatory Flexibility'

Challenges for Industry and Regulators

Cultural change

'Common understanding' of QbD and PAT concepts and associated scientific and regulatory requirements

Possible Ways Forward

Joint industry/regulators conferences/workshops/trainings in order to develop the 'common understanding'

Provide further guidance, to be developed at ICH level instead of regional guidance (harmonisation, 'common understanding')

Increase cooperation and exchange of information between agencies on e.g. assessment, scientific advice and joint inspections

Increase opportunities for scientific dialogue with pharmaceutical companies

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Summary of Experience with QbD at EMA

In the last years, the number of 'QbD' applications received in the centralised system has substantially increased

Application of QbD and PAT to biological products is now relatively common (in particular for antibodies)

Request for scientific dialogue with the PAT Team and for scientific advice related to QbD/PAT are now common

All the applications received so far in the centralised system are from big Pharma companies

The PAT Team has met with some smaller companies, but application of QbD to e.g. generics seems to be still not common

Conclusion (1)

The new concepts introduced with Q8 and the other related ICH guidelines are fully accepted by regulators (this includes RTRt)

Recently introduced legislation e.g. Post-Approval Management Protocols, should further help with the implementation of QbD in the EU

Although some challenges remain, applicability of QbD to both chemical and biological products is well established, wider application of QbD and PAT concepts e.g. to generics would be desirable

Conclusion (2)

Several programs for cooperation between international agencies are in place e.g. EMA-FDA pilot for parallel assessment of QbD applications, joint inspection programs; further harmonisation among agencies should be envisaged whenever possible; guidance on QbD should be developed through the ICH process; awareness of the existing ICH documents should be increased

Opportunities for companies for scientific dialogue with regulators in the context of QbD are provided by EMA e.g. PAT Team; regulators and the pharmaceutical industry should continue to work together in order to reach the 'common understanding' through e.g. conferences, workshops, joint training

Further Information

EU legislation

http://ec.europa.eu/health/documents/eudralex/index_en.htm

EMA website

http://www.ema.europa.eu/

Questions?

Riccardo.luigetti@ema.europa.eu

European Medicines Agency (EMA)

Thank you for your attention!