Making Medicines Affordable

Quality by Design for Generic medicines:

Regulatory Challenges Ahead

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European Generic medicines Association -27 Sept 2012

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EGA & ISPE COLLABORATION

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EGA: Who are We?

Making Medicines Affordable

- The EGA is the official representative body of the European generic and biosimilar pharmaceutical industry, which is at the forefront of providing high-quality affordable medicines to millions of Europeans and stimulating competitiveness and innovation in the pharmaceutical sector.

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ISPE: Who we are?

- Founded in 1980
- Not-for-profit, non-lobbying global professional society
- 22,000 individual Members from more than 90 countries
- ISPE is a Society of pharmaceutical professionals who use expert knowledge to create high-quality, cost-effective GMP solutions
- Provides technological knowledge, education, and guidance documents
- Provides forums for exchange among manufacturing and development, global regulators, academia and students, and consultants and supply chain

EGA

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ISPE

Why get together?

1. SYNERGY
2. CLARITY
3. GENERIC MEDs SPECIFICITIES
4. HARMONISATION

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1 SYNERGY

- ISPE brings a technical background to QbD
- The EGA brings experts in generic medicines development and EU regulatory background

2 CLARITY

- Reports about significant business benefits when using QbD
  - e.g. reduced product & manufacturing variability, increased efficiency, enhanced post-approval change management
- But also…
- Many practical questions regarding implementation (particularly: regulatory & compliance)

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3 GENERIC MEDs SPECIFICITIES

- Numerous events dedicated to QbD
  - Unfortunately, none focused on the specificities of the generic medicines sector
    - i.e.:
    - Highly competitive,
    - Fast paced,
    - Timing of submission = key to success

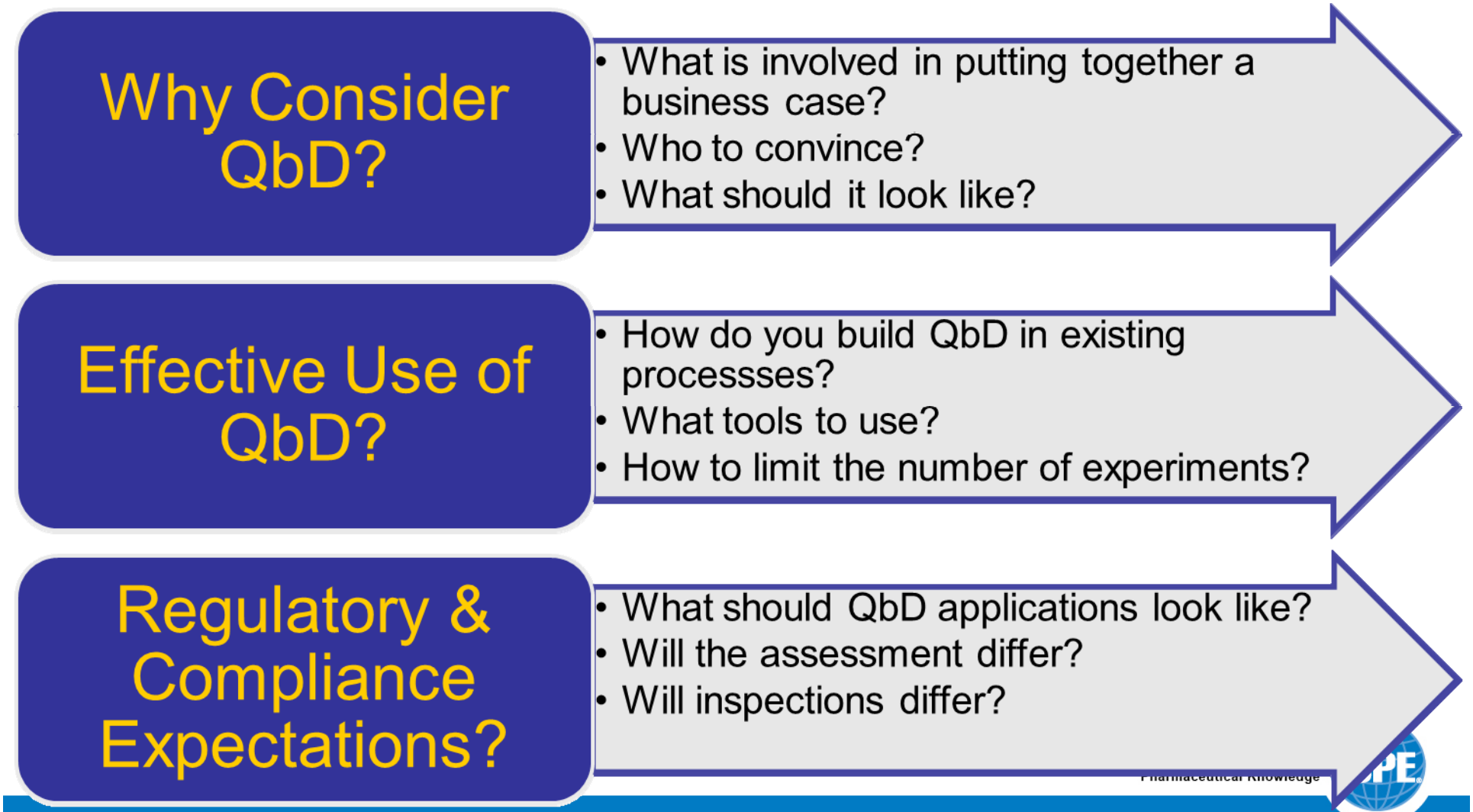
4 HARMONISATION

- US FDA announcement on ‘mandatory QbD’ ANDAs from Jan 2013
  - Companies operate globally
  - Need for a common approach to implementing QbD in ICH regions

EGA-ISPE Conference on QbD for the Generic medicines Industry

GETTING STARTED

Key Aspects of the Workshops



Regulatory & Compliance Expectations?

Conclusions of EGA-ISPE Conference – Workshop C

FOCUS ON THE REGULATORY CHALLENGES AHEAD

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‘QbD Dossier’ | What are we talking about?

- All and nothing:
  - Dossier following CHMP guideline on Development Pharmaceutics
  - Dossiers including RTRT
  - Dossiers including a Design Space

HETEROGENEOUS REALITY
Imprecise terminology:
to avoid !

QbD Dossier' | Filing QbD Elements into the CTD

- CTD structure can suitably accomodate elements of QbD - P.2 (& S.2.6)
- Sub-sections cover all necessary aspects
- Cross-references needed between development aspects and selected controls

‘QbD’ Dossier | Getting Right the Key Elements

Scientific Rationale

- Most important element of the submission
- Tell a story !
- Huge amounts of data might not be needed

Quality Risk Management

- Make sure to address what can go wrong and what needs to be done to mitigate and control?

Control Strategy

- Monitoring and controls rather than solely on measurements

‘QbD’ Dossier | Improving Submissions: Next Steps?

- Industry in favour of more detailed guidance on how to present / how to document the QbD elements in applications
- Regulators not in favour
  - Referred to the numerous ICH documents (PtC), to the EFPIA Mock Applications, the US FDA examples

Industry & Regulators to consider other approaches

Review Approach to ‘QbD’ Dossiers | General

- Assessors will want a good and transparent story
  - Data is important but not in quantity!
  - Structure of the approach to appear early
- Key Elements of Focus for Reviewers
  - Quality risk management
  - Understanding variability (relationships)
  - Control strategy

Review Approach to ‘QbD’ Dossiers | Design Space

- Design Space elaboration at lab scale
- Verification needed for the commercial scale
  - EU: verification protocol at time of submission
    scope still under discussion in the EU
  - US: inspectors will look at the ability to pick up failure

Review Approach to ‘QbD’ | Handling Changes

- Changes need to be documented in the Change Control Programme
- Changes within the Design Space
  - Need to be assessed
  - Are not subject to RA notification if claimed in the file
  - ‘Documentation’ (e.g. SOP) needed during inspection
- Changes outside the DS: Type II

Compliance Approach to ‘QbD’ Dossiers

- No real difference in inspections
- Focus on good company communication on critical parameters
- Pre-Approval Inspections
  - Collaborative approach assessors/inspectors
- Post Approval Inspections
  - Verification of expectation during development
    e.g. Verification protocols

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TIPS FROM THE REGULATORS

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Tips from the regulators

- Multi-functional approach and reviews
  - Getting to an understandable story line
- Quality Risk Management
- Accurate Terminology (glossary) – no new terms please!
- Just do it!

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OVERALL CONCLUSIONS

Conclusions (1/2)

- QbD (although ICH) is probably a term that leads to misunderstandings
- QbD is feasible and makes sense for the generic medicines sector
- A harmonised approach between ICH regions in practice is fundamental
  - Industry should be vigilant as to the evolution of philosophies

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Conclusions (2/2)

- High interest for generic medicines producers to engage in more dialogue with regulators
- A joint industry associations initiative is being developed in view of a Workshop with regulators (Spring 2013)
  - Main Objective: to review experience so far and identify remaining gaps

Thank you for your attention !

QUESTIONS?

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EUROPEAN GENERIC MEDICINES ASSOCIATION

Making Medicines Affordable

| www.egagenerics.com |

EGA ANNOUNCES

6th EGA PHARMACOVIGILANCE DISCUSSION FORUM

16 January 2013

RADISSON BLU PORTMAN HOTEL | LONDON | UK

12th EGA REGULATORY AND SCIENTIFIC AFFAIRS CONFERENCE

17 - 18 January 2013

RADISSON BLU PORTMAN HOTEL | LONDON | UK

9th EGA LEGAL AFFAIRS FORUM

19 - 20 March 2013

THON HOTEL EU | BRUSSELS | BELGIUM

11th EGA INTERNATIONAL SYMPOSIUM ON BIOSIMILAR MEDICINES

25 - 26 April 2013

THE GUOMAN TOWER HOTEL | LONDON | UK

4th EGA SYMPOSIUM ON BIOEQUIVALENCE

DATES AND VENUE TO BE CONFIRMED

focused on the new guideline for Modified Release products

19th EGA ANNUAL CONFERENCE

12 - 14 June 2013

HILTON HOTEL | ATHENS | GREECE

FOR FURTHER INFORMATION

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Upcoming ISPE events

- Online ISPE Global Event Calendar
- http://www.ispe.org/index.php/ci_id/6434/la_id/1/date/2013-01/view/calendar.htm