EQPA Forum 2014

- eine Zusammenfassung

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19. März 2015

Programm

2x ½ Tage zur Themenvertiefung:

- Risk Management in the Supply Chain
- OOS and OOT: What's important for QPs

1 Tag zum Thema "IMP"

2 Tage QP Konferenz

Themenübersicht

- The QP in a Global Environment
- Current and future Activities of the FDA
- The Role of the QP in Product Recalls
- What the QP needs to know about Quality by Design
- Law and Order
- What the QP needs to know about Excipient Quality
- The Written Confirmation and the QP: What Inspectors expect

Themenübersicht II

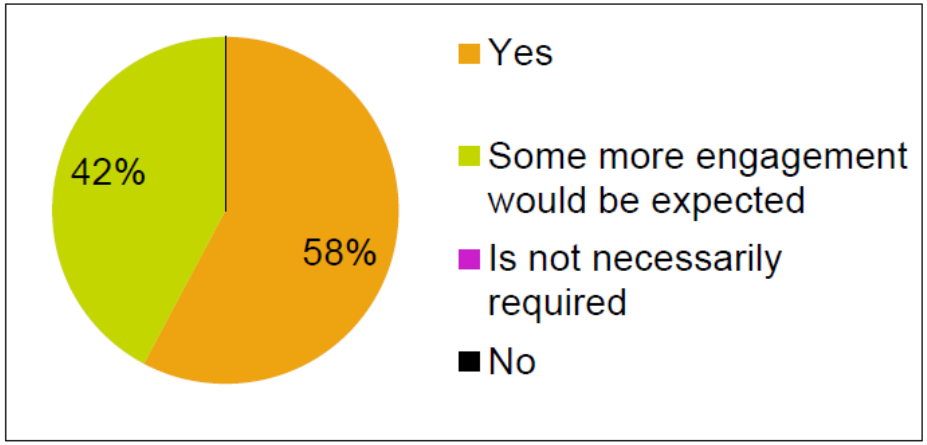
Parallelveranstaltungen

- Update on GMP-relevant topics and what QPs are expected to do
- Annex 16 – how to live with it
- QP Scenarios: Would you know what to do?
- The Role of the QP in an R&D Environment
- How to interpret the PQR
- How to deal with Time Pressure

The QP in a Global Environment

Umfrage an der 50 Mitglieder der GQPA am 17.03. 2014 teilgenommen haben.

- Acting as a QP: In general, in the future QPs should take a more active role and influence the future more proactively!



Current and future Activities of the FDA - Global Regulatory Policy

Human Drug GMP Inspections-Most Inspected Countries (2014):

- India 111
- China 111
- Germany 71
- Canada 46
- France 43
- Italy 49
- Japan 47
- Switzerland 36
- United Kingdom 33

Current and future Activities of the FDA - Global Regulatory Policy

FDA as a Global Regulator

- Need to do more foreign inspections in high-risk areas
- Efficient use of finite resources
- Compelling case for regulator-to regulator work sharing and reliance

Current and future Activities of the FDA - Global Regulatory Policy

Mutual Reliance Initiative

- Strategic collaboration between the US/FDA and EU for drug inspections
- “Comparable public health protection” is the threshold
- Goal: To rely on each other’s GMP inspections

Role of the QP in Product Recalls

(Zusammenfassung von Ines Janssen/Baxter AG)

- **EU-GMP Guide part I Chapter 8 *Complaints, Quality Defects & Product Recalls***
  totally revised – came into force March 2015
  Much more detailed description of expectations on investigations
  → Quality Risk Management tools have to be applied
- ***Old***: Principle / Complaints / Recalls
  New: Principle / Personnel and Organization (QP awareness, inter-disciplinary teams, responsibilities defined) / Procedure for handling and investigating complaints including possible quality defects / Investigations and Decision Making / Root Cause Analysis and Corrective and Preventive Actions / Product Recalls and other potential risk-reducing actions

Role of the QP in Product Recalls II
(Zusammenfassung von Ines Janssen/Baxter AG)

Rapid Alert and Communication between National Authorities and the QP

- Direct personal contacts are important, especially with the person making the report, the person co-ordinating action for the company (usually the QP), (…)
- It is often helpful in detailed discussions if communications are between professional equivalents, e.g. medical assessor with medical staff of the company, inspectors with QPs or production staff, analytical assessors with QC staff, etc.
- All information obtained verbally should be confirmed in writing.

Samples

- Wherever possible the sample involved in the defect report should be obtained by the Competent Authority. It should normally be examined by an Official Medicines Control Laboratory as agreed by the Competent Authority. In certain cases samples should be provided to the company for examination under full supervision of the Competent Authority. Results should always be made available to the company.

Role of QP in R&D Environment –Workshop (Zusammenfassung von Ines Janssen/Baxter AG)

aqpa Austrian Qualified Person Association

APIs for IMPs

- ***Own APIs*** – GMP concept manufacturing & control:
  - GMP should start 1 step back where the molecule is changed the 1st time = defined starting material
  - Supplier qualification of defined starting material has to start in clinical phase I
  - procedure based on requirements of EU GMP Guide part II sec.19 „APIs for use in clinical trials“
- ***External APIs*** / GMP certificate
  - Certificate of Suitability with the EP (CEP) or Drug Master File (DMF) preferable
  - Supplier qualification → proposal of supplier assessment questionaire attached

Role of QP in R&D Environment –Workshop (Zusammenfassung von Ines Janssen/Baxter AG)

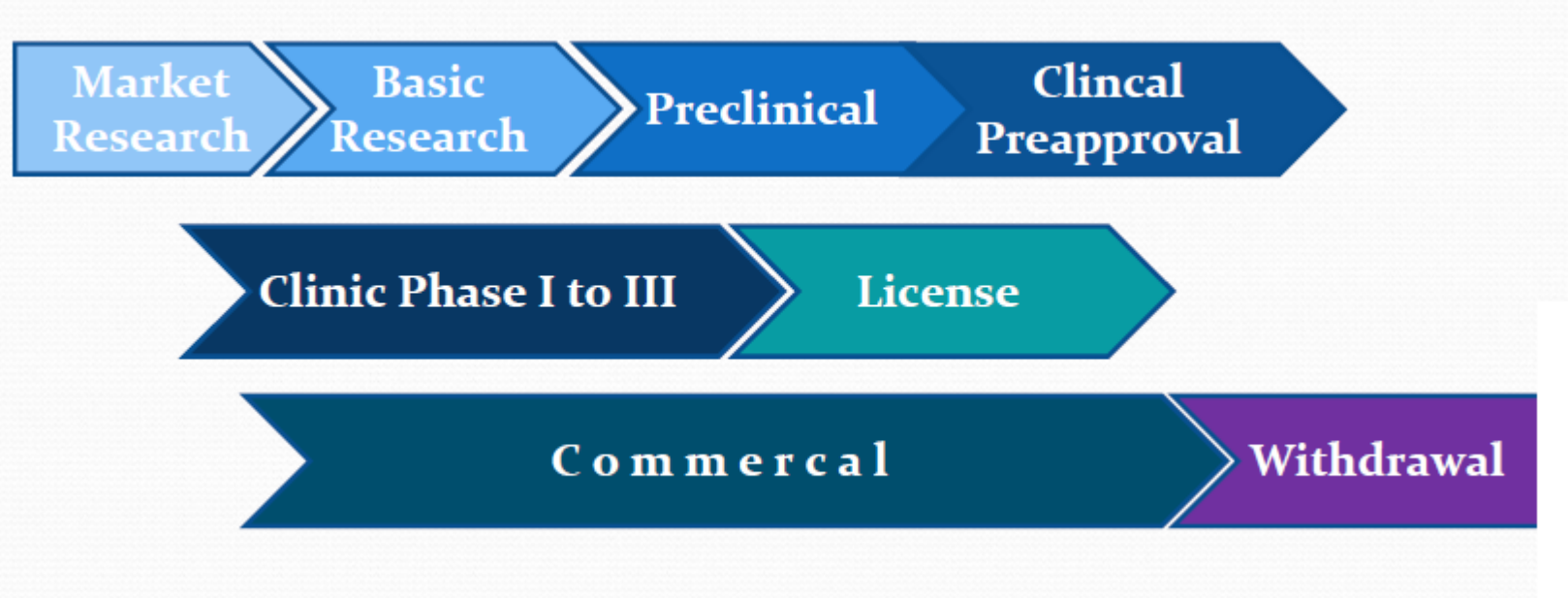
APIs for IMPs

- ***External APIs*** / GMP certificate (cont'd)
  - GMP certificate / batch
  - Certification of GMP at least equivalent to Q7A/ EU GMP Guide Part II
  - Certification of regulatory compliance (challenge)

- ***APIs manufactured in non-EEA*** for IMPs in EU clinical trials
  - „Written confirmation" for import of APIs not required (Exception Germany), but applicable for IMPs for Clinical Phase IV from March 2015

Quality by Design

Pharmaceutical Product Life Cycle



Quality by Design

What is Quality by Design (QbD) and how has it to be implemented

- QbD is a scientific, risk-based, holistic and proactive approach to pharmaceutical development.
- QbD leads to a full understanding of how product attributes and process relate to product performance. (Design Space)
- QbD should be implemented during the basic research, leading to a process development for a new drug.

Quality by Design

Where are the benefits ?

- Robust manufacturing processes ensuring product supply (reduce e.g. CAPA, NCR, recall)
- Effective Technology Transfer: less development work / issues at manufacturing level due to greater process knowledge
- Manufacturing products optimally fullfilling customer needs: Development is systematically linked to initially set „target product profile“
- Decreased risk of critical findings during inspections (expectations are described in ICH 8,9,10 and 11draft)

Excipient Quality

- European Commission (SANCO/D/6/SF/mg/ddg1.d.6(2013)179263) Draft Guideline of the formalized risk assessment for ascertaining the appropriate good manufacturing practice for excipients of medicinal products for human use, draft submitted for public consultation.

- The control of the supply chain of excipients is a must for QPs.

Written Confirmation and QP:
What inspectors expect - Duties of QP

Now:

- *„Written confirmation from the competent authority of the exporting third country "* (Directive 2011/62/EU Art. 46b (2))

► Issuance of WC is part authority responsibility (authority API GMP-statement)

► Issuance of WC can ´t be influenced from QP !?

- But:

- WC is about GMP of API-manufacturer

- Only GMP-compliant manufacturers will receive WC from authority

► QP can influence availlability of WC by only contracting GMP-compliant suppliers

- QP-Part: Supplier qualification- and a audit-system !

Annex 16

(Zusammenfassung von Renate Steurer/Baxter AG)

Status :

- Publication of the (current) draft – July 2013
- Consultation period – 5 November 2013
- Adoption by EMA GMDP IWG probably in Dec. 2014

Sollte nach der Publikation in den nächsten 6 Monaten in Kraft treten!!!!

OOS and OOT:
What is important for QPs

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Austrian Qualified Person Association

Key Points:

- FDA-Guidance (Oct 2006): also for internal Specs or IPC!
- MHRA-Guidance (Feb 2014): ppt only !
  - Includes MIBI tests as well (FDA does not)
  - Addresses OOS, OOT and atypical/aberrant/anomalous results
- SOP of ECA‘s „Analytical QC Working Group“ available
- Never include samples from already released batches into OOS investigation retesting for reference only
- Both FDA and MHRA guidances NOT directly intended for bioassays
- Do not continue testing when you already know an obvious error
- Confirmed lab-error requires corrective action be taken
- Decision to reject a batch CANNOT be reversed as result of further tests
- In case of Retesting: ALL results have to be used in batch evaluation

How to interpret the PQR

Key Points:

- QP has to have an overview of QMS
- QP has to be involved in Quality decisions
- QP has to understand product and process thoroughly
- EU-inspectors expect QP has been to the manufacturing site to know the process
- PQR should be part of Quality Risk Management Plan of the company
- PQR should have intensive discussion of deviations, changes, trends, etc.; not only short statement „everything under control“
- Link PQR to ongoing validation program
- Many PQRs miss CAPA-effectiveness
- Marketing Authorisation Holder has to evaluate PQR (manufacturer is „CMO“)