International Supply Chain: How are we handling globalisation? GCP oversight

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Non compliance in bioequivalence
Non compliance in bioequivalence

- Several historical cases
- Recent referrals
  - Case I:
    - Outcome: 700 MA suspended (33 INNs)
    - EU referral scope approx. 0.5% of generic MA in the EU
      - 1 product = multiple MAs, in several MS
      - large proportion of the affected MAs were not active, (products were not marketed)
    - Two other high profile cases after this

It can affect credibility of the industry
What can we do to prevent this?

Workshop on risk based quality management in clinical trials (12/2013)

- “GCP inspectors are of the opinion that sponsors currently too often take a reactive, fire-fighting approach to tackle problems in clinical development projects instead of avoid problems by adequate planning”
Reflection paper on risk based quality management in clinical trials

- (Adopted by GCP Inspectors Working Group Sep/2013)
- Risk assessment
- Risk control
- Risk review and quality reporting
- Objective: focus resources where risk is higher

Risk management

Risk management in GXP

- GMP
- Pharmacovigilance: risk management plan
- GLP
- GCP
  - Quality management
  - Monitoring

Challenges to implementation

- Risk assessment is complex: what are the risks?
- Requires careful planning
- Will it be accepted by everyone? (Harmonisation!?)
- Is it worth it?
GCP compliance in BE trials

EMA Workshop
April 2015

BE trials
(including licensed dossiers)

Common practice required!

- CRO qualification (before 1st trial is conducted)
- CRO requalification (routinely after collaboration with CRO starts)
- Monitoring
- Auditing
- Including due diligence in licensed dossiers
- Including bioanalytical
Monitoring

• On and/or off site visits to each trial
• Both clinical and bioanalytical part

“Off site only might not be sufficient”

Licensing in dossiers

• Due diligence may need to be extended in some cases, as required, to actual on site auditing by licensee

Licensing contract
CRO contracts
...
## Comparison GMP vs. GCP

**GMP**
- **Inspection results**: Non-compliance and GMP certificates published on EudraGMP.
- **Compliance certificates**: are issued
- **International cooperation**: International recognition of inspections to some extent
- **Audits**: Focus on molecule/product.

**GCP**
- **Inspection results**: Inspection results are collected but not made publically available.
- **Compliance certificates**: are not issued
- **International cooperation**: EMA-EU MSs-FDA initiative on inspections for Generic Applications
- **Audits**: Focus on specific study.

## Inspections vs. audits

- Inspectors have immediate authority to access study data vs.
- Sponsors cannot see actual study data until the first study is performed

- Early information from inspectorate on serious non-compliance would be welcome!
  (warning letters?)
Expectations from the industry

• Inspection Transparency
• Fast communication of results (time from signal to communication of information!)
• Warning letter system leading to
• GCP certification

EGA Bioequivalence Working Group

• Common practice document
  • Internal circulation
  • External circulation
  • Endorsement
• Not only for Medicines for Europe members!
• Continued dialogue with agencies/EMA to ensure alignment between expectations and practice
• Sharing of auditing results/joint audits among companies currently under analysis (benefits and risks)
Steps

- Vendor qualification and requalification
- Monitoring (minimum standards for clinical and bioanalytical)
- Auditing
- Licensed dossiers

Critical aspects

- Definition of expectations from authorities
- Communication of expectations to industry
- Implementation of a common approach
- Faster and more effective implementation

Keep in mind:

Dossiers that will be presented in two or three years are being built NOW
Thank you!

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