Quality Assurance in non-regulated research of the pharmaceutical industry

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The views expressed in this presentation are solely those of the individual authors, and do not necessarily reflect the views of their employers.
Industry and academia facing the same issues

Pharmaceutical Industry

• Bring new products to market
• Be a trustworthy source of efficacious and safe products
• Short timelines to next decision
• Limited development costs
• Increased outsourcing
• Responsible expenditure of company budget & other resources
• Patients
• Society / Stakeholders
• Animals (3Rs)

Risk

Portfolio

Reputation

Operations

Finance

Ethics

Academia

• Publish new findings in top journal
• Be a trustworthy source of robust and reliable scientific findings
• Short timelines to next grant appl.
  • Limited study costs
  • Increased collaborations
• Responsible expenditure of research grants & other resources
• Patients
  • Society / Stakeholders
  • Animals (3Rs)
The additional challenge of Pharma

In response to declining productivity of traditional approaches, Pharma:

- Embraces open innovation programs to access external ideas
- Sources preclinical drug discovery projects from academia
- Uses CRO’s in performing fundamental phases of R&D

→ Great potential for the development of innovative approaches
→ Increased flexibility to optimally source projects with the right expertise

→ Increased risk related to decentralized/globalized outsourcing activities
The drug development process

Non-regulated

Regulated (GLP, GCLP, GCP, PV)

A variety of business models: Diagnostics co-development, Lab Services, internal and external Partnerships

10 - 15 years / $ 2.6 billion

Quality in Discovery

Quality in Decision Making

Quality Molecules Moving Forward
Risks in a non-regulated environment

- Decision making
- IP rights
- Reputation
- Public trust
- Patient safety
Despite what many people believe: Non-regulated ≠ GLP or ISO!

Finding the Balance...
Non-regulated quality management system implementation

NR quality management cycle...

- **Gap analysis**
  - Assess “as is” situation / integrate lessons learned

- **Plan**
  - Agree with business on best practices

- **Measure success**
  - Check quality metrics/compliance

- **Implement**
  - Tackle gaps

...must be fit-for-purpose

- **Target selection**
  - Hit identification

- **Hit to lead**
  - Lead optimization

- **Preclinical development & safety**

- **Innovation**

- **Oversight**
Non-regulated quality management system implementation

NR quality management cycle... ...is a collaborative approach

- **Gap analysis**
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Joint effort by QA and (discovery) scientists

Senior leaders sponsorship and support

Multidisciplinary teams to leverage best practices and tackle gaps
Janssen’s non-regulated quality program

**Training**
- Data quality introduction training for all scientists
- Ad hoc refresher trainings
- Phase transition package guideline training to project leads
- On-line training

**Data quality culture**
- Data quality champions community
- Data quality awareness activities (newsflashes, posters, ...)
- Data quality guidelines
- Pulse checks on and updates of data quality guidelines

**Internal Science**
- Risk based audits to measure success of program, focus on phase transition decision making data
- Lessons learned sessions
- Follow up to observations, no formal CAPA process

**External Science**
- Data quality contract language
- Janssen guidelines for collaborators
- L&A support
- Audits on high risk collaborators (in discussion with BPs)
- Moving to more proactive approach: education of collaborators before data generation
Data has to be complete, accurate, and consistent through its entire lifecycle

- Accurate
- Traceable
- Recon-structable
- Unbiased
# Accuracy

## What?

- All data generated in drug Discovery and Preclinical research, internal and external
- Validated materials, tests/assays, reliable methods, robust procedures, standardization where possible
- Appropriate controls/baseline

## Why?

- Only “healthy data lead to healthy patients”
- Reported results must accurately reflect the raw data
- Impacts decision making, IP rights, reputation, public trust, patient safety

## How?

- Advise, support, training
- Automation where possible
- Traceability and reconstructability are key
- QC and QA
Traceability and reconstructability

What?
- All data must be retrievable and reconstructable
- Documentation of methods and of any deviations (with rationale)

Why?
- Impacts IP rights, reputation, public trust

How?
- Advise, support, training
- Safe storage: use of ELN or another authorized archival system / central storage
  (also allows central data sharing for teams, projects etc.)
- Good reporting practices, reference to source data
- Transparency / full disclosure is key
- QC and QA
Unbiased reporting

What?

• All data must be reported, including negative data and invalid data

Why?

• Impacts decision making, IP rights, reputation, public trust, patient safety

How?

• Advise, support, training
• Full disclosure of all data
• Pre-defined criteria: in- and exclusion criteria, start- and endpoints, outlier criteria
• Pre-specified analytic / statistical methods (biostatistical support!)
• No cherry-picking, p-hacking etc.
• QC and QA
What is the role of QC and QA?

**Research Organization**
- **Executes** studies
- **Reports**/documents outcomes
- **Signs and dates**

**Quality Control** / monitoring
- Reviews the product (data, reports), checks for consistency
- **Peer review** process
- **Countersigns and dates**

**Quality Assurance**
- (independent quality organization)
- Ensures the process is adequate for the research to meet its objectives
- **Risk-based audits**
  - Study-specific audits (data spot checks = measures of success)
  - System audits (assessment of processes)
  - Feedback on good practices & gaps (not a formal CAPA process)
- **Guidelines and Documentation**
  - SOPs
  - Questionnaires
  - Templates (e.g. for reporting)
- **Training** (mandatory)
- **Metrics** (trending)
Example guidance

Important in the complex research environment of Janssen R&D
- 36,000 employees
- 150+ countries
- 30 manufacturing sites
- 30 R&D centers
- Target: BALANCE BETWEEN INTERNAL AND EXTERNAL SCIENCE

Record keeping
Data storage
External collaborations
Phase transition
Example trending categories

- Risk for bias
- Data Consistency
- Review/Sign off/IP
- Easy Reconstruction
- Easy Retrieval
- Safe storage
- Full Disclosure
External influencing
Towards a common quality system for non regulated research in both industry and academia!
What is the relevance?
The IP example

Dates determine who may be entitled to a patent

Europe: “first to file” (the date on the application counts)
USA: “first inventor to file” (the date of the invention counts)

Lack of properly dated, signed and countersigned documentation in a lab notebook may lead to a patent not being granted!
May also lead to internal disputes on inventorship, remuneration,...

Disclosure / Information determines whether a patent is valid

Europe: non-disclosure of part of an invention in the patent application may be acceptable upon filing, if plausible
USA: lack of written disclosure can result in a patent becoming void

Invalid / fraudulent data or lack of full transparency on ALL valid data may lead to a patent not being granted / invalidated!
Issues with data integrity can be found in both academic and industrial research environments.
Key success factors for a non-regulated QMS at Janssen

- **Role Models**
  - Senior leaders sponsorship & support
  - “Talking the talk, walking the walk”

- **Mandatory education**
  - All staff

- **Awareness campaigns**

- **Partnerships**
  - QA, IT, Biostatisticians, Communications, ...

- **Simple, sustainable solutions and “fit for purpose” guidance**
  - By scientists, for scientists

- **Transparency**
  - Central data sharing for teams, projects etc.

- **Spot check program**
  - (= measure of success)

- **Speak up culture**
  - (hotline)
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