Quality Assurance in non-regulated research of the pharmaceutical industry

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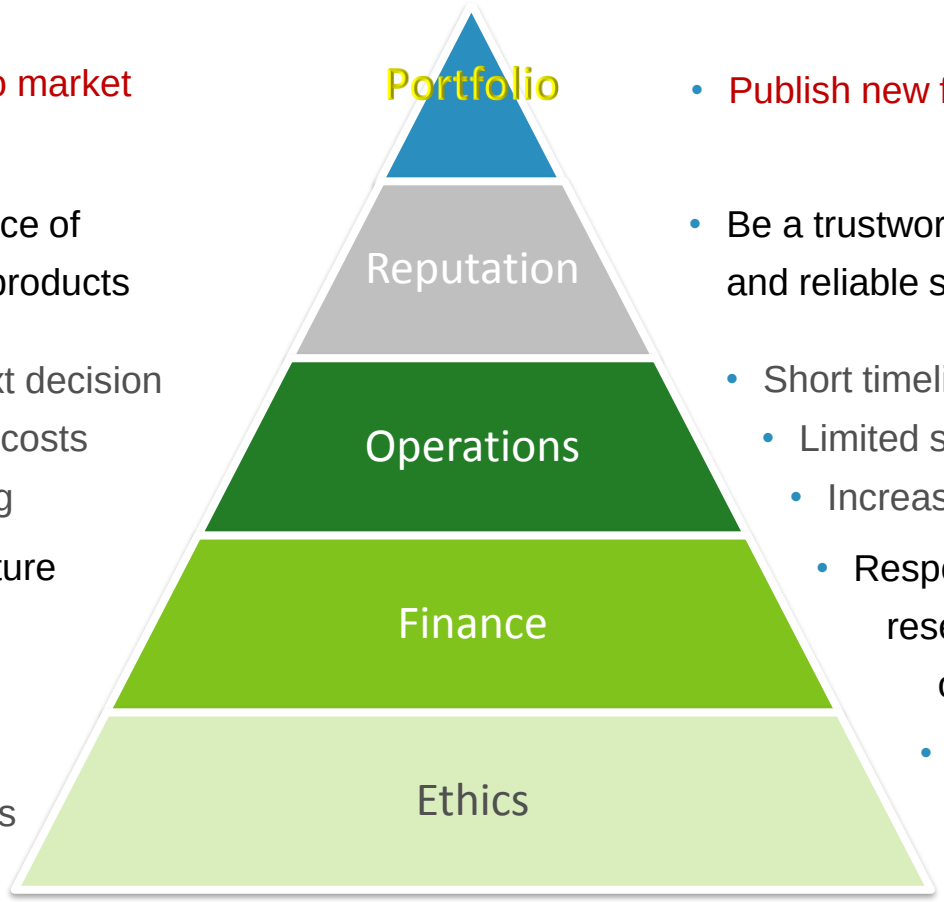
janssen | PHARMACEUTICAL COMPANIES OF Johnson&Johnson

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



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:

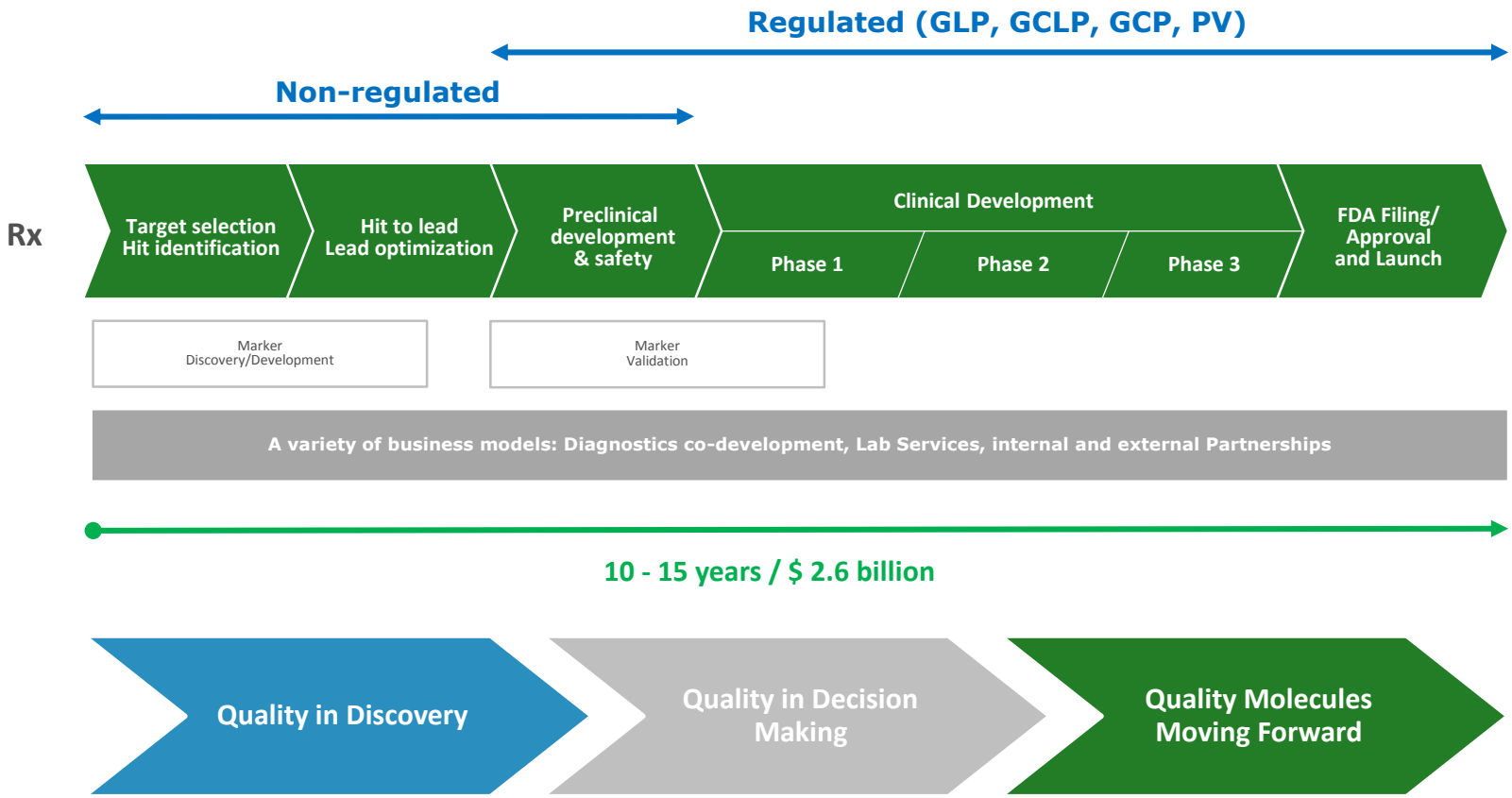
- Embraces open innovation programs to access external ideas
- Sources preclinical drug discovery projects from academia
- Uses CRO‘s in performing fundamental phases of R&D

→ Great potential for the development of innovative approaches

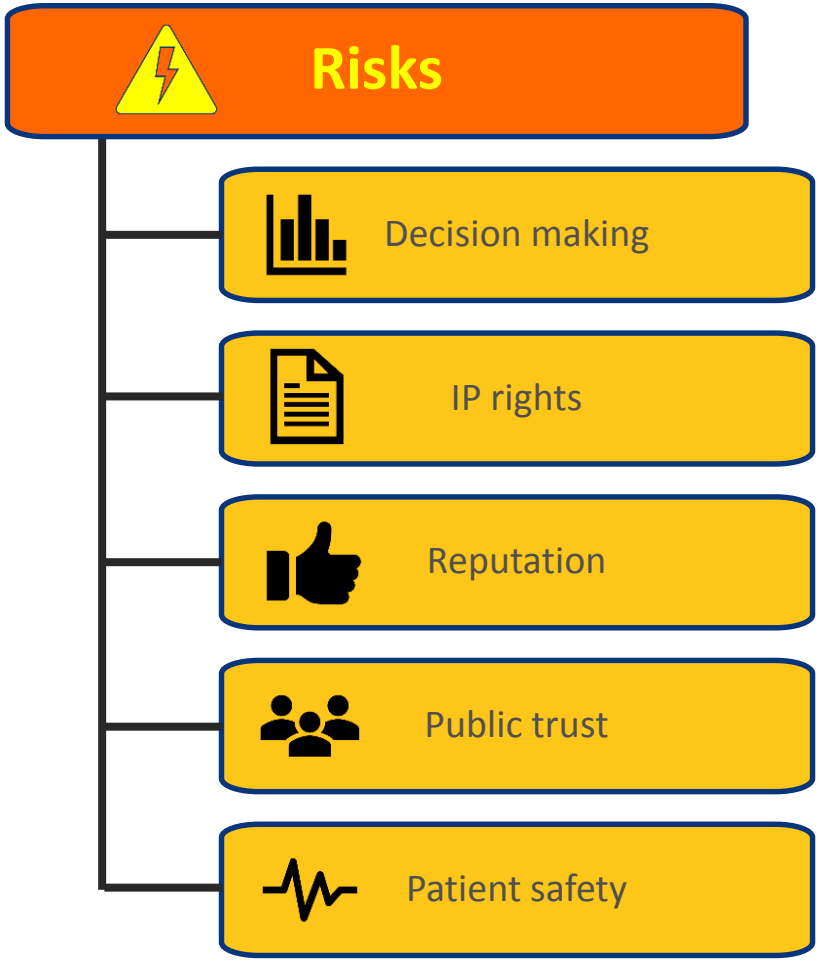
→ Increased flexibility to optimally source projects with the right expertise

→ Increased risk related to decentralized/globalized outsourcing activities

The drug development process



Risks in a non-regulated environment



Despite what many people believe:
Non-regulated ≠ GLP or ISO !

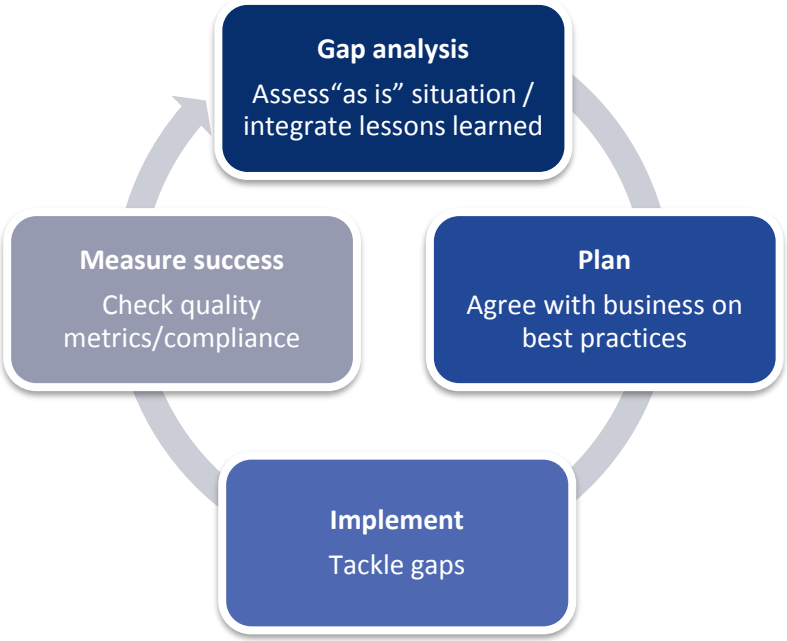
Innovation
Research
Exploration

Integrity
Accuracy
Reconstructability

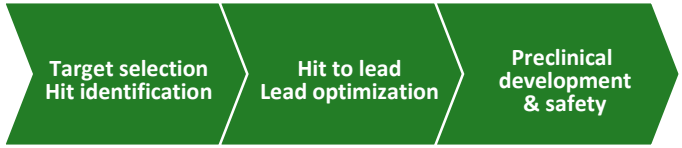
Finding the Balance…

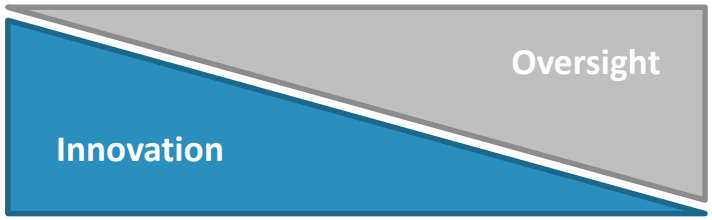
Non-regulated quality management system implementation

NR quality management cycle…



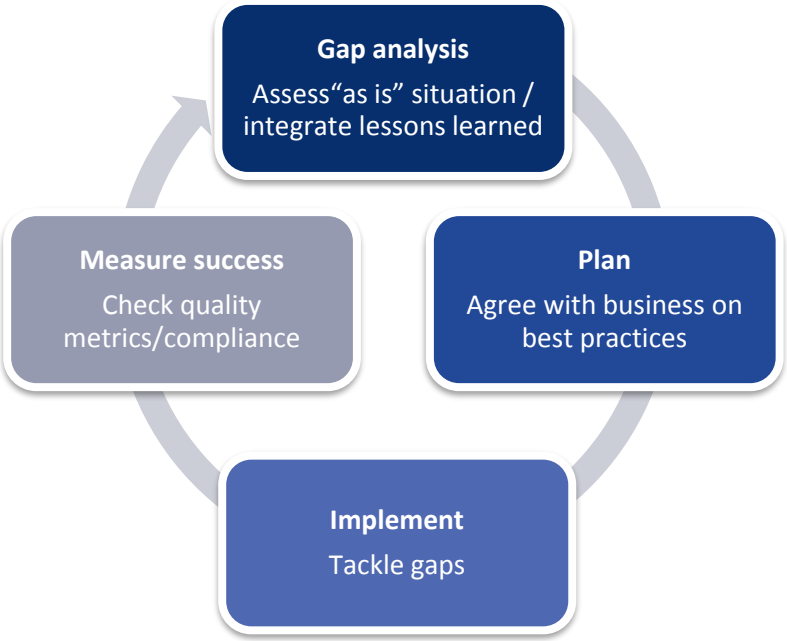
…must be fit-for-purpose





Non-regulated quality management system implementation

NR quality management cycle…



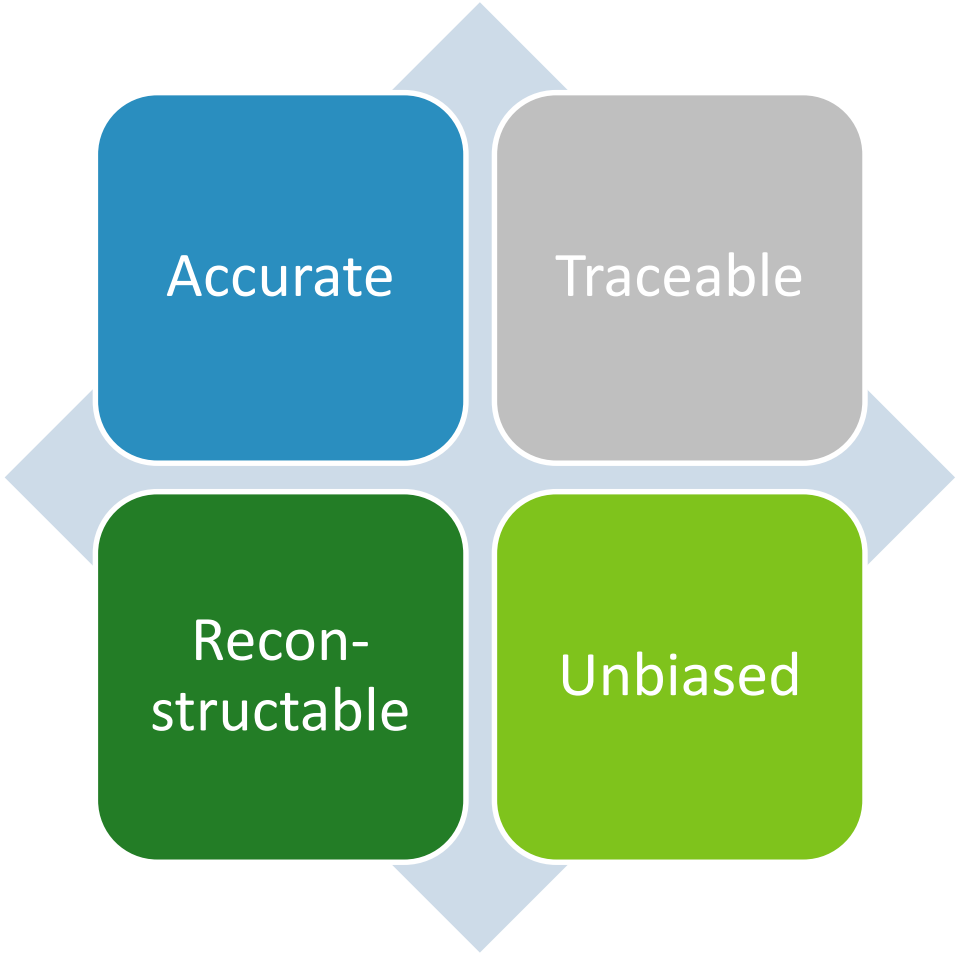
…is a collaborative approach

- 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



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

(including external partners)

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

Quality Control / monitoring

(often within research organization)

- 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

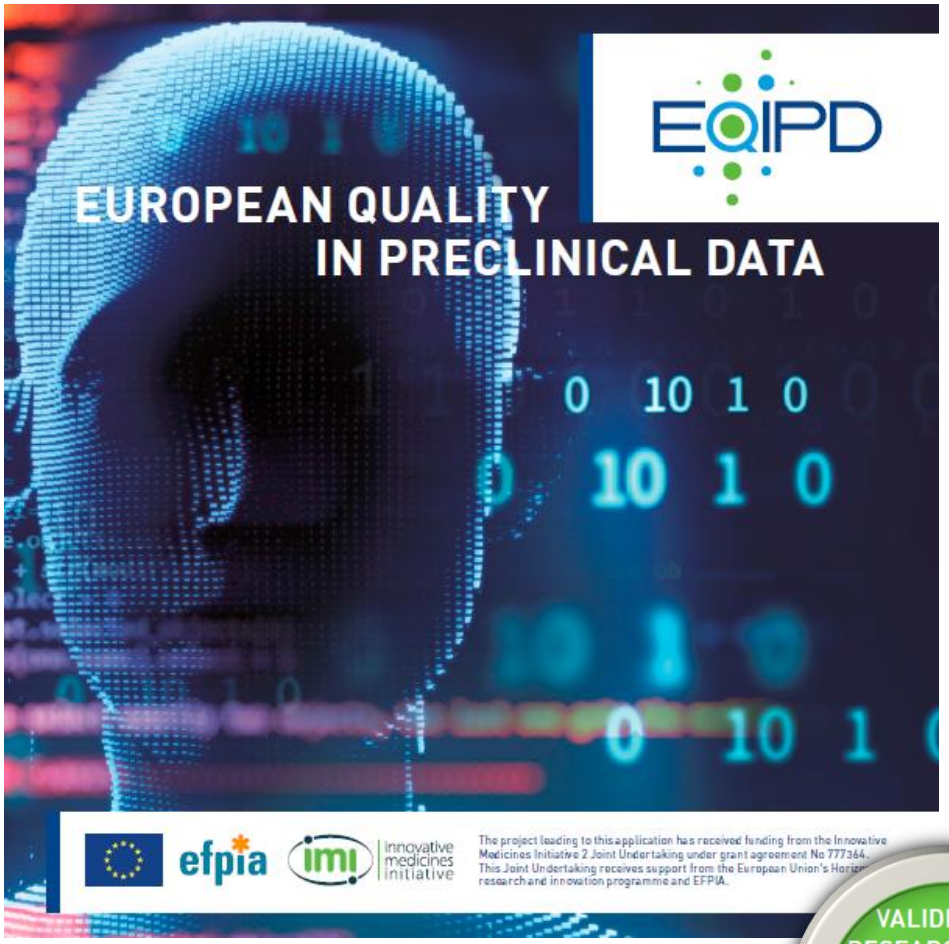
Important in the complex research environment of Janssen R&D

- 36,000 employees
- 150+ countries
- 30 manufacturing sites
- 30 R&D centers
- Target: BALANCE BETWEEN INTERNAL AND EXTERNAL SCIENCE

Example trending categories

External influencing

Towards a common quality system for non regulated research in both industry and academia!



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MEMBERS

EQIPD is an international research project that brings together 29 transdisciplinary institutions from 8 different countries.

VALIDITY OF RESEARCH DATA: A KEY DRIVER FOR DECISION MAKING IN MEDICAL SCIENCES

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

GlaxoSmithKline Fires China R&D Boss for 'Misrepresented' Data

Dan Mangan | @_DanMangan
Tuesday, 11 Jun 2013 | 6:35 PM ET

CNBC

Francois Lo Presti | AFP | Getty Images

http://www.cnbc.com/id/100807468

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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