IT STARTS WITH ONE

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Disclosures – Thomas Steckler

• Employee of Janssen Pharmaceutica / Johnson & Johnson
• EFPIA Project Lead EQIPD IMI consortium
• Co-chair ECNP Preclinical Data Forum
• AAALAC ad-hoc specialist
• BMJ Open Science Associated Editor
Data Quality and Reproducibility in Neurosciences Research An Industry Perspective

Thomas Steckler
Janssen Pharmaceutica NV

The views expressed in this presentation are solely those of the individual author, and do not necessarily reflect the views of his employer.
A “Typical” Scenario

Exciting finding → Enthusiasm in the field → Sobering news
Why Alzheimer's Drugs Keep Failing

Drug candidates have a 99.6 percent failure rate, and poor early detection methods make clinical trials difficult and costly.

By Maria Burke, Chemistry World on July 14, 2014

Challenges

- Understand disease pathophysiology and disease heterogeneity
- Diagnose early
- Get timing of treatment right
- Generalizability / translatability of animal models
- Robustness and reliability of preclinical data
Growing External Investment by Pharmaceutical Industry...

CROs and academic organizations
primary outsourcing partners for pharmaceutical companies and biotech

$19.2bn
spent by pharmaceutical industry in 2016 for outsourcing the discovery of pharmaceutical drugs

$43.7bn
expected rise by 2026 due to outsourcing in drug discovery

News Medical, Feb 2018

...Could Translate in Large Costs for Non-Reproducible R&D

Point estimate of cumulative irreproducibility rate: 53.3%

$28 billion spent on preclinical research that is not reproducible in the US

Approx. $10 billion spent on outsourcing discovery work that was not reproducible in 2016?
Could more than double by 2026
Risks Related to Discovery Data

Key risks:
- Patients, Regulators
- Strategic decisions, $$$
- Intellectual property
- Public trust/reputation
- Ethics - Credo
- Regulators

Quality data = Quality decisions = best assets to patients

Data used in patent filings

- Critical decision making data (efficacy & safety)

Screening
- Lead Identification
- Initial patent filing
- NME Declaration
- IND IB v.1

Target Selection
- Hit ID & Hit-to-Lead
- Lead Optimization
- Preclinical development & safety
- Clinical development

GCP and Human tissue regulations for human samples

Animal welfare

Publications
### FACTS AND FIGURES

<table>
<thead>
<tr>
<th><strong>Full project title:</strong></th>
<th>European Quality In Preclinical Data</th>
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<tbody>
<tr>
<td><strong>Start date:</strong></td>
<td>01 Oct 2017</td>
</tr>
<tr>
<td><strong>Duration:</strong></td>
<td>3 years</td>
</tr>
<tr>
<td><strong>Participants:</strong></td>
<td>29 institutions from 8 different countries</td>
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<tr>
<td><strong>IMI funding:</strong></td>
<td>4.5 million € (4,495,523.00 €)</td>
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[https://quality-preclinical-data.eu/](https://quality-preclinical-data.eu/)
What is EQIPD?

First IMI consortium completely dedicated to improving preclinical data quality

Joint undertaking by Big Pharma, CROs, Academia and Scientific Associations

Proof of concept in Neuroscience and Safety, facilitated by a Quality Management System

Expand R&D-wide if successful
The EQIPD Consortium

29 Institutions from 8 different countries
11 EFPIA companies
10 Universities
7 CROs
1 Scientific society

6 External advisors
8 Associated collaborators
~100 Stakeholders
Our Vision

Robust data and scientific rigor in preclinical studies will enhance the pace of knowledge gain, shorten the time needed to make new drug treatments available to patients and impact on the 3Rs.
Our Objectives

- Within animal study design and data analysis, define the variables that influence the outcome of preclinical research conducted in industry and academia.
- Validate the feasibility of the quality management system in prospective animal studies conducted by our partners.
- Define the components that will make up the EQIPD Quality Management System and formulate consensus quality recommendations.
- Deliver an online educational platform providing certified education and training in the principles of quality management and rigor.
Progress Today

Systematic Review on Alzheimer’s Disease animal models under way

• Systematic search of 3 online database completed
• 265,258 hits detected, 4,000 studies screened, 347 studies included
• To be complemented with historical data from consortium partners

First version of Quality Management System for non-regulated R&D developed

• Roll out for beta-testing May 2019

Guiding Research Principles identified through systematic review of existing guidelines

• Informed development of the QMS and planning for the harmonisation stage of prospective studies

Preliminary scope for E-learning program determined

• E-learning materials have been gathered
Key to Success

- Strong collaborative effort
- Broad buy-in and support
- Very systematic approach, wide coverage
- Evidence based, from scientists for scientists
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Backups
Historical Data Analysis

**Aim:** Define variables of internal and external validity in experimental design, conduct and data analysis that are determinants of outcome in preclinical studies

Consortium data
(3 commonly used in vivo tests)

- Sample size
- Blinding
- Randomization
- ...
- ...

Literature
Public databases
Research Guidelines

**Aim:** Develop guiding principles and criteria governing rigor in experimental design, conduct and analysis of preclinical studies (using animals)

- 13,863 papers screened
- 62 papers finally included
- 58 items extracted
- 2 Delphi rounds
- Consensus meeting
- 33 items finally included
- Recommendations for prospective studies

Evidence from WP4
Cross-site Validation

**Aim:** Validate the principles and research models that improve robustness and data quality in preclinical studies

**Stage 1: Localization**

- Partner 1
- Partner 2
- Partner 3
- Partner ...

**Stage 2: Harmonization**

- Partner 1
- Partner 2
- Partner 3
- Partner ...

Effect of reduced inter-lab variability?
**Aim:** Validate the principles and research models that improve robustness and data quality in preclinical studies

**Stage 2: Harmonization**

**Stage 3: Ring testing**

Effect of blinding of test item
Quality Management System for Emerging and Classical Technologies

**Aim:** Support the essential processes, procedures, responsibilities and cultural aspects relevant to implement the guiding principles that improve robustness of preclinical studies

- Analysis of the current use of research quality principles, best practices and challenges
- Identification of key principles using a Delphi process
- Fine-tuning following stakeholder feedback (ongoing)
QMS Maintenance and Assessment

**Aim:** Generate critical, high-level processes to ensure efficient governance of the new quality system

- **Internal governance:** Develop tools for self-assessment
- **External governance:** Can we learn from AAALAC?
- On-site or remote assessments (e.g. questionnaires)
- Establish an accreditation system?
- Review of existing quality systems

**Quality Systems Evaluated**
- ISOx3
- AAALAC
- RQA
- BBSRC
- ASQ
- GLP
- Janssen
- Novartis

**Governance Building Blocks**
- Roles and responsibilities
- Management of resources
- Conflict of interest
- Control and improvement
- Auditing
- Certification
- Sustainability
- Training
Training Platform

Aim: Maximize sustainability and impact of the EQIPD Quality System by development of an engaging learning environment to ensure research community wide expansion of knowledge about the EQIPD principles

- Evaluation of existing training modules
- User requirements identified
- Potential service providers to host the platform contacted