

Conflict of Interest



Use of animal models for the development and approval for medical devices and for education of surgeons

External Advisor/ Trainer and Animal Welfare Officer
(Tierschutzbeauftragte)

@Medizinisches Kompetenzzentrum

c/o HCx Consulting GmbH

[Medizin im Grünen](#)

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Full Membership (*ordentliche Mitgliedschaft*):



GV-SOLAS

Gesellschaft für Versuchstierkunde
Society for Laboratory Animal Science



Pro-Test
Deutschland e.V.

Workshop Academia and industry

Mutual benefits

Natascha Drude, PhD

30.11.2023

BIH QUEST
Center for Responsible Research

BIH Berlin Institute
of Health
@Charité


Aus Forschung wird Gesundheit

Reproducibility crisis -Pharma blew the whistle



Published: 31 August 2011

Believe it or not: how much can we rely on published data on potential drug targets?

Florian Prinz, Thomas Schlange & Khusru Asadullah 

Only 25% out of 67 papers could be validated

Nature Reviews Drug Discovery **10**, 712(2011) | [Cite this article](#)

44k Accesses | **992** Citations | **823** Altmetric | [Metrics](#)



Raise standards for preclinical cancer research

Only 6 out of 53
,landmark' papers could
reproduce results

C. Glenn Begley and Lee M. Ellis propose how methods, publications and incentives must change if patients are to benefit.

→ Not without criticism –"not scientific" –they did not know how...

Different types of reproducibility

1. Methods reproducibility

- Exact same tools, design, outcome
- No additional Evidence

2. Results reproducibility (replication/ confirmation)

- Technically competent repetition (strict or conceptual)

3. Inferential reproducibility

- Do we draw the same conclusions from the same results??

PERSPECTIVE | SCIENTIFIC INTEGRITY

What does research reproducibility mean?

Steven N. Goodman*, Daniele Fanelli and John P. A. Ioannidis

+ See all authors and affiliations

Science Translational Medicine 01 Jun 2016:
Vol. 8, Issue 341, pp. 341ps12
DOI: 10.1126/scitranslmed.aaf5027

What does reproducibility mean?

1. Significance and p-Values

Replication effect against null hypothesis of no effect

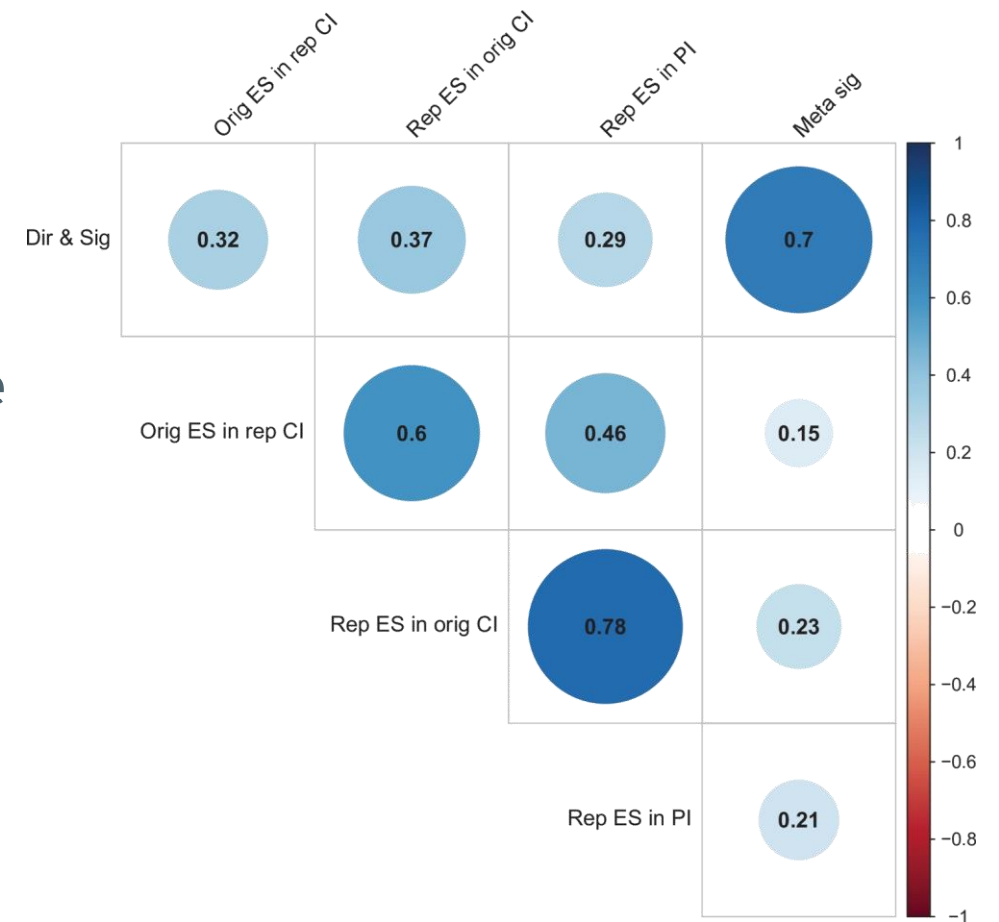
2. Replication effect size versus original effect size

Original effect size within 95% CI of the replicated one

3. Meta-analysis –cumulative evidence

4. Subjective assessment

Did it replicate??



Rethinking research reproducibility

Ulrich Dirnagl^{1,2} 

Replication versus non-replication

What does it mean if you do not replicate?

Original results false positive?

Replication false negative?

Does successful replication mean that the original results were correct?

Could both results be false positives?

Was the study technically competent?

Hidden moderators

Why look at Industry?



HHS Public Access

Author manuscript

Trends Pharmacol Sci. Author manuscript; available in PMC 2018 December 01.

Published in final edited form as:

Trends Pharmacol Sci. 2017 December ; 38(12): 1052–1060. doi:10.1016/j.tips.2017.10.003.

The Academic-Industrial Complexity: Failure to Launch

Leonard A. Levin, MD, PhD^{1,2,*} and Francine Behar-Cohen, MD, PhD^{3,4}

Seyhan *Translational Medicine Communications* (2019) 4:18
<https://doi.org/10.1186/s41231-019-0050-7>

Translational Medicine
Communications

REVIEW

Open Access

Lost in translation: the valley of death across preclinical and clinical divide – identification of problems and overcoming obstacles



Attila A. Seyhan^{1,2}

POLICY FORUM

RESEARCH INTEGRITY

Fostering reproducibility in industry-academia research

Sharing can pose challenges for collaborations

By B. R. Jasny,¹ N. Wigginton,² M. McNutt,^{3*} T. Bubela,⁴ S. Buck,⁵ R. Cook-Deegan,⁶ T. Gardner,⁷ B. Hanson,⁸ C. Hustad,⁹ V. Kiermer,¹⁰ D. Lazer,¹¹ A. Lupia,² A. Manrai,¹² L. McConnell,¹³ K. Noonan,¹⁴ E. Phimister,¹⁵ B. Simon,¹⁶ K. Strandburg,¹⁷ Z. Summers,¹⁸ D. Watts¹⁹

Cell Metabolism

Crosstalk

CellPress

Pharma and Academia: What We Have Here Is a Failure to Communicate

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<http://dx.doi.org/10.1016/j.cmet.2016.08.026>

In recent years, there has been substantial interest in the potential value of collaboration between academia and the pharmaceutical industry. In this Crosstalk, I discuss obstacles to these relationships being optimally productive.

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Different pathways –different language

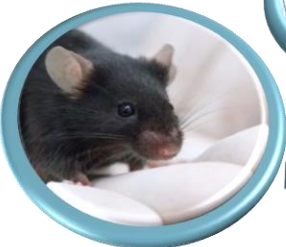
Approval Process



Research & Development
(Basic research)



In vitro testing



In vivo testing



Approval Process

–What Does that Mean?



1. Final Indication

To demonstrate safety and efficacy

2. (Non) GLP/ manufacturing (GMP)

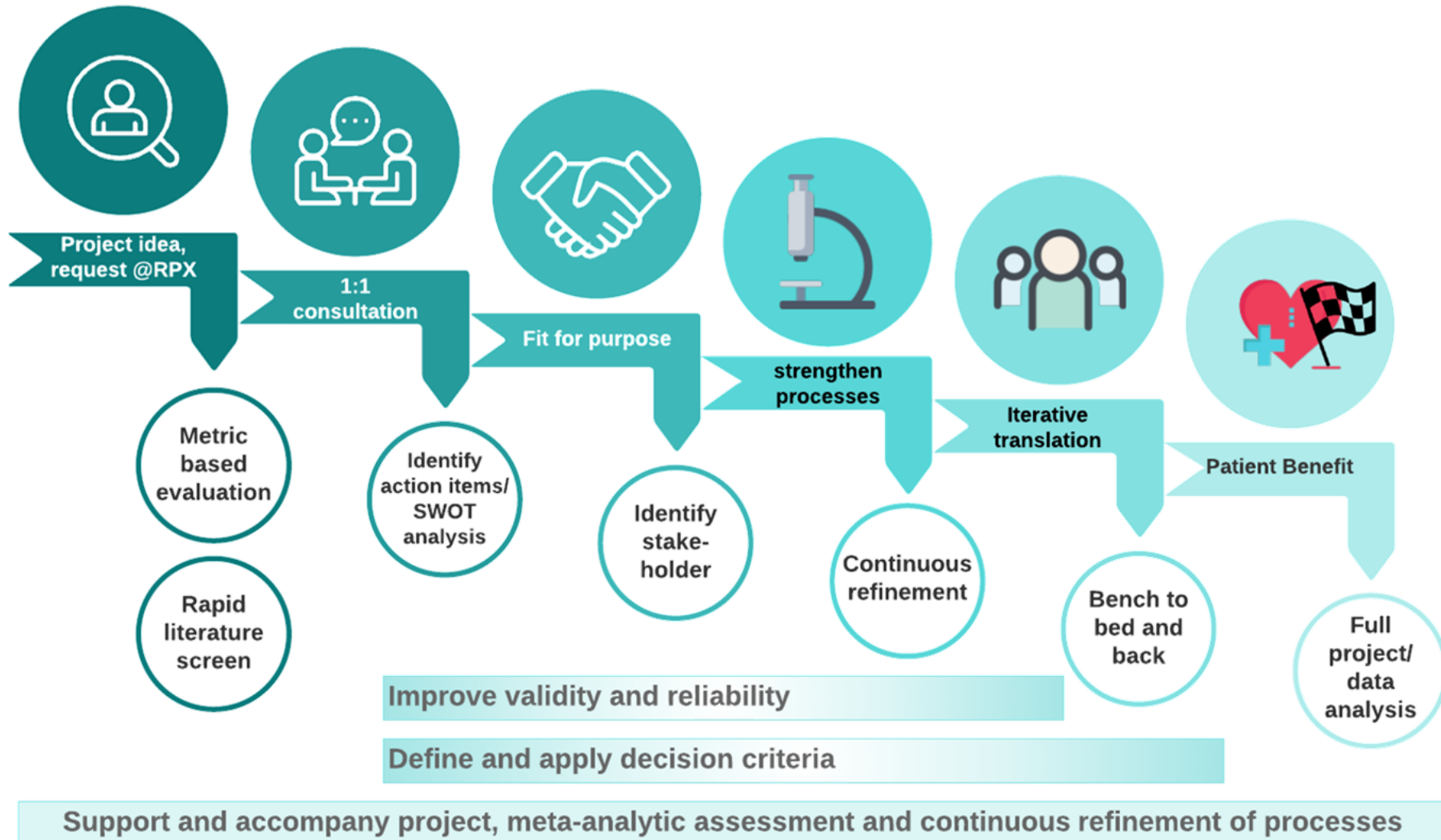
Good Laboratory Practices (GLP) refers to a system where non-clinical health and safety studies are carried out, planned, monitored, recorded, archived and reported.

3. Regulatory acceptance/ requirements

e.g., biocompatibility testing of medical devices (ISO 10993)

Safety and Efficacy testing according to ISO 10993 under recommendation of Notified Body (EU) or FDA (US)

Responsible PreclinIX –institutional initiative to foster reproducibility



How to plan preclinical trials for success (or failure)?

Aim of this meeting?

Where/when/how can we benefit from one another?



Minimum set of
information/ evidence?



Open innovation/
market



Exploration in
academia



Regulatory processes

- ⇒ **Build a network/ scientific communication platform for better industry-academia collaborations**
- ⇒ **Create templates for e.g., minimum sets of information**

Thank you!

Please do not hesitate to contact us!
QUEST Center for Responsible Research



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SPARK
— BIH —



berliner
fortbildungen

BIH Charité (Junior) Clinician Scientist
Programm



GEFÖRDERT VOM



Bundesministerium
für Bildung
und Forschung



Empirical Evidence 2018/19 pioneering BMBF Call: *Confirmatory Preclinical Studies and Systematic Reviews*

<https://www.gesundheitsforschung-bmbf.de/de/8344.php>

Drude et al.
Translational Medicine Communications (2022) 7:24
<https://doi.org/10.1186/s41231-022-00130-8>

Translational Medicine
Communications

REVIEW

Open Access



Planning preclinical confirmatory multicenter trials to strengthen translation from basic to clinical research – a multi-stakeholder workshop report

Natascha Ingrid Drude^{1*}, Lorena Martinez-Gamboa¹, Meggie Danziger¹, Anja Collazo¹, Silke Kniffert¹, Janine Wiebach^{1,2}, Gustav Nilsson^{1,3,4}, Frank Konietschke², Sophie K. Piper², Samuel Pawel⁵, Charlotte Micheloud⁵, Leonhard Held⁵, Florian Frommlet⁶, Daniel Segelcke⁷, Esther M. Pogatzki-Zahn⁷, Bernhard Voelkl⁸, Tim Friede⁹, Edgar Brunner⁹, Astrid Dempfle¹⁰, Bernhard Haller¹¹, Marie Juliane Jung¹², Lars Björn Riecken¹², Hans-Georg Kuhn^{13,14}, Matthias Tenbusch¹⁵, Lina Maria Serna Higuaita¹⁶, Edmond J. Remarque¹⁷, Servan Luciano Grüninger-Egli¹⁸, Katrin Manske¹⁹, Sebastian Kobold^{19,20}, Marion Rivalan²¹, Lisa Wedekind²², Juliane C. Wilcke²³, Anne-Laure Boulesteix²³, Marcus W. Meinhardt^{24,25}, Rainer Spanagel²⁵, Simone Hettmer²⁶, Irene von Lüttichau²⁷, Carla Regina²⁸, Ulrich Dirnagl¹ and Ulf Toelch^{1*}

COMMENTARY

Open Access



Finding the best fit for improving reproducibility: reflections from the QUEST Center for Responsible Research

Natascha Drude¹, Lorena Martinez-Gamboa¹, Tamarinde Haven¹, Constance Holman¹, Martin Holst^{1,2}, Silke Kniffert¹, Sarah McCann¹, Torsten Rackoll¹, Robert Schulz¹ and Sarah Weschke¹

Magazine | Feature Article
Medicine



Science Forum: Improving preclinical studies through replications

Natascha I Drude, Lorena Martinez Gamboa, Meggie Danziger, Ulrich Dirnagl, Ulf Toelch

Balancing sensitivity and specificity in preclinical research

Meggie Danziger, Anja Collazo, Ulrich Dirnagl, Ulf Toelch

doi: <https://doi.org/10.1101/2022.01.17.476585>

This article is a preprint and has not been certified by peer review [what does this mean?].

Science & Society



EMBO
reports

Introducing quality measures in an academic research consortium

Lessons and recommendation from implementing an ad hoc quality management system for organ model research

Maren Hülsemann^{1*}, Janine Wiebach¹, Natascha Ingrid Drude¹, Silke Kniffert¹, Laura Behm², Katja Hönzke³, Morris Baumgardt³, Stefan Hippenstiel³, Andreas C Hocke³, Ulrich Dirnagl¹ & Ulf Tölch¹

Internal Validity

confidence that the cause- and effect relationship (e.g. treatment and outcome) being tested is trustworthy and not influenced or explained by other factors or variables. The internal validity largely depends on the experimental design and can be improved by reducing known sources of experimental confounders, especially selection bias.

Reliability

consistency of a measure under repeated testing. Testing more experimental units will reduce the uncertainty about an effect resulting in higher reliability of an estimated treatment effect.

External Validity

refers to how well the outcome of a study can be expected to apply to other settings, such as other study conditions, animal strains/species.

Translational Validity

refers to the similarity of the studied model system to human disease conditions. Even though this transfer is the most difficult step, some indicators may help predict translational success.