PREMIER

A tool for structured quality assurance measures in academic preclinical biomedical research

QUEST Seminar on Responsible Research

June 07th 2022

Claudia Kurreck

BIH QUEST Center for Responsible Research

Charité Experimental Neurology Berlin

VolkswagenStiftung

BIH Berlin Institute of Health @Charité

QUEST structure and work within the BIH and Charité

Charité

BIH

QUEST
Board of directors
IT, office and project management

Scientific advisory board

SERVICES	**RESEARCH**
Education and training	Translational bioethics
Open data and research data management	Quality in research
Bibliometric data analysis	Quality in preclinical research
Incentives and indicators	Automated tools
Patient and stakeholder Engagement (PSE)	CAMARADES
Program evaluation	METRIC Berlin
Tools and other services	PSE
	Program evaluation
	Research data management

Visiting fellows

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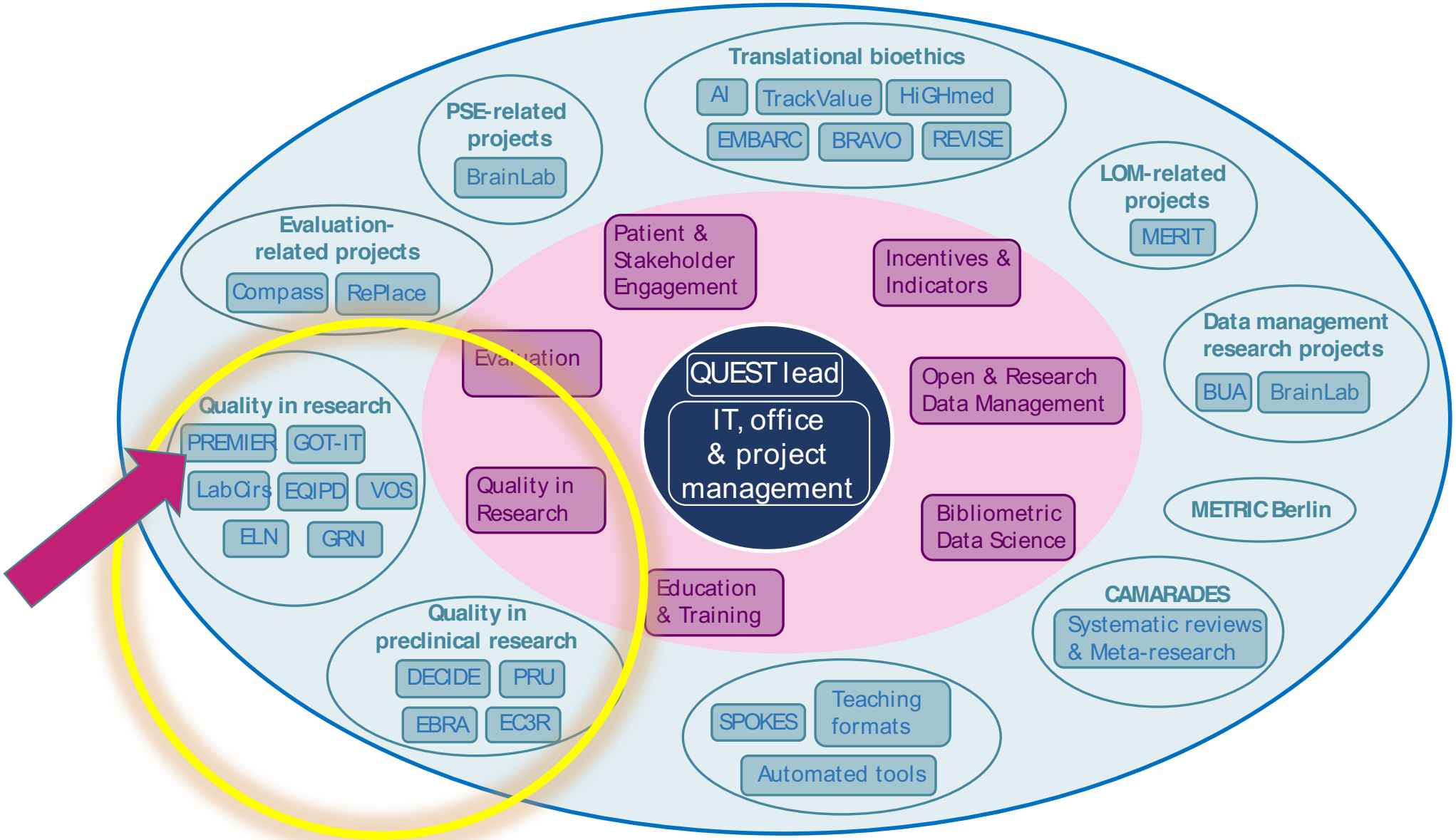
QUEST internal structure



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Lack of reproducibility: Replication crisis

The lack of reproducibility published in highly respected journals has given rise to the term "replication crisis" and is probably at least partly responsible for the low success rate in translating often spectacular findings from preclinical research into clinically effective therapies.

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Objective: Improving quality in basic research

Strategies are need to fill the gaps

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Is it possible to establish structured measures for quality assurance in research?

Quality Management (QM) in the Department of Experimental Neurology

- QM keeps us busy since 2013
- there are various QM systems on the market, but none specifically for research institutions
- we have introduced and applied ISO 9001 for three years (2014 - 2017) (certification by TÜV Süd) in the Exp. Neuro
- The ISO is a general standard for QM certification: it should be usable for all organizations (industry, companies, service providers).

ISO in daily laboratory routine

Result after three years ISO in the Exp. Neuro:

Positive Aspects	Negative Aspects
- Structural elements very useful -> PDCA (plan-do-check-act) cycle - Standardization of methods (SOPs) - better documentation - better communication within the team - better laboratory organization	- technical, partly not understandable language - TÜV audits (core processes were not checked, only the formal structure)
Handling of errors regulated	high administrative effort
Compliance with GSP and legal requirements improved	partly overregulated
Control of data archiving	
Moving towards Open Access /Open Data	

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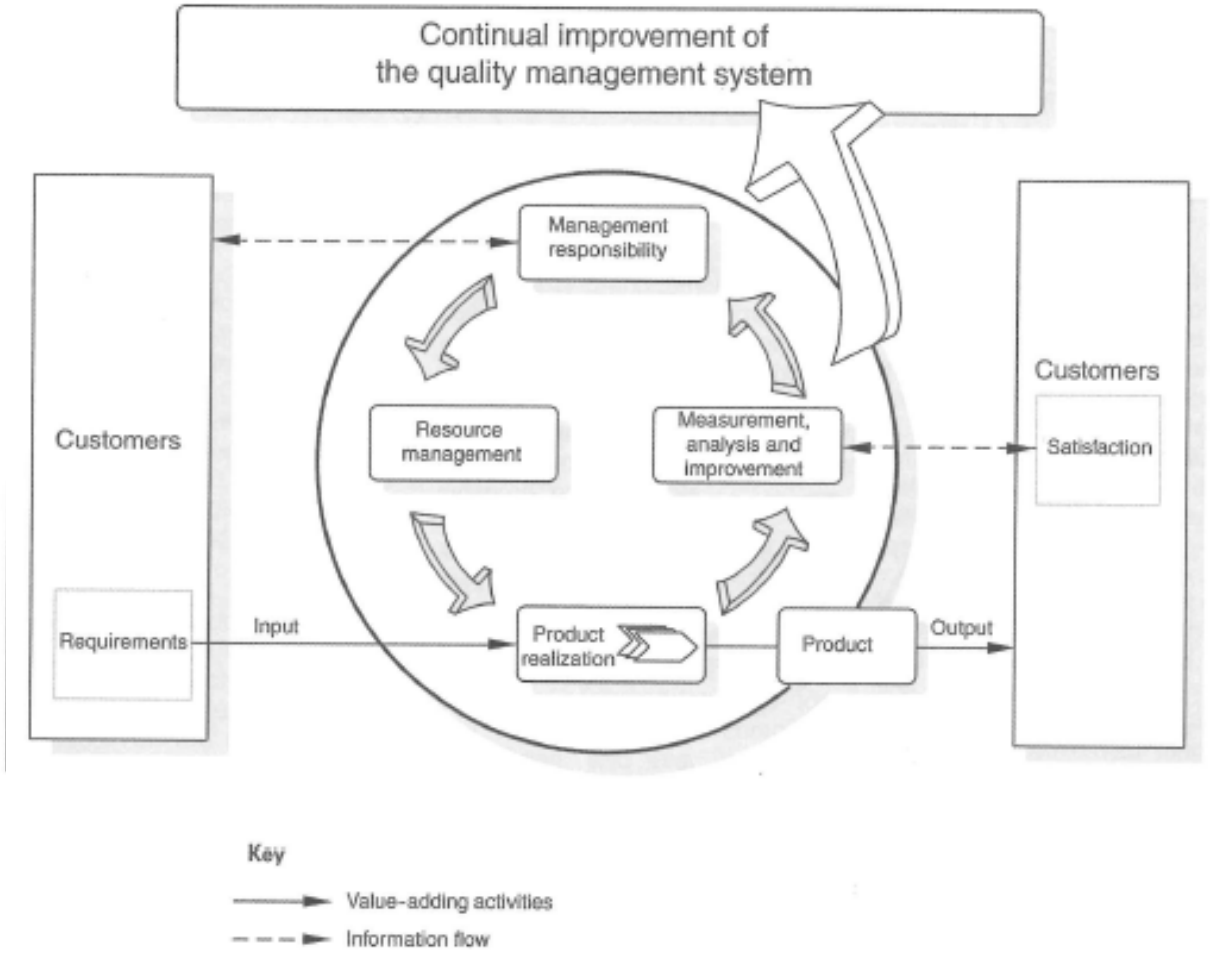
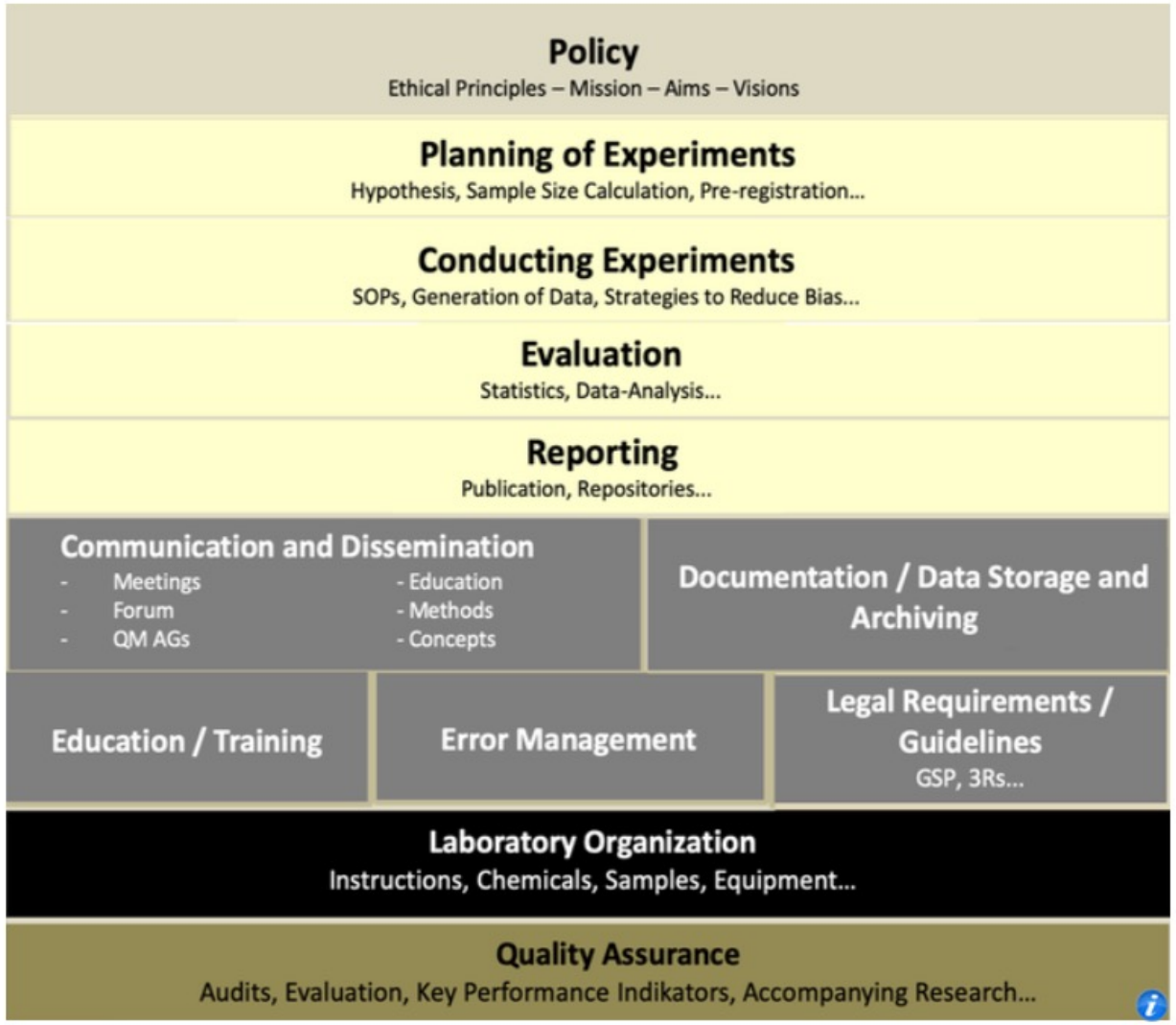
Concept ISO 9001:2008



Concept PREMIER



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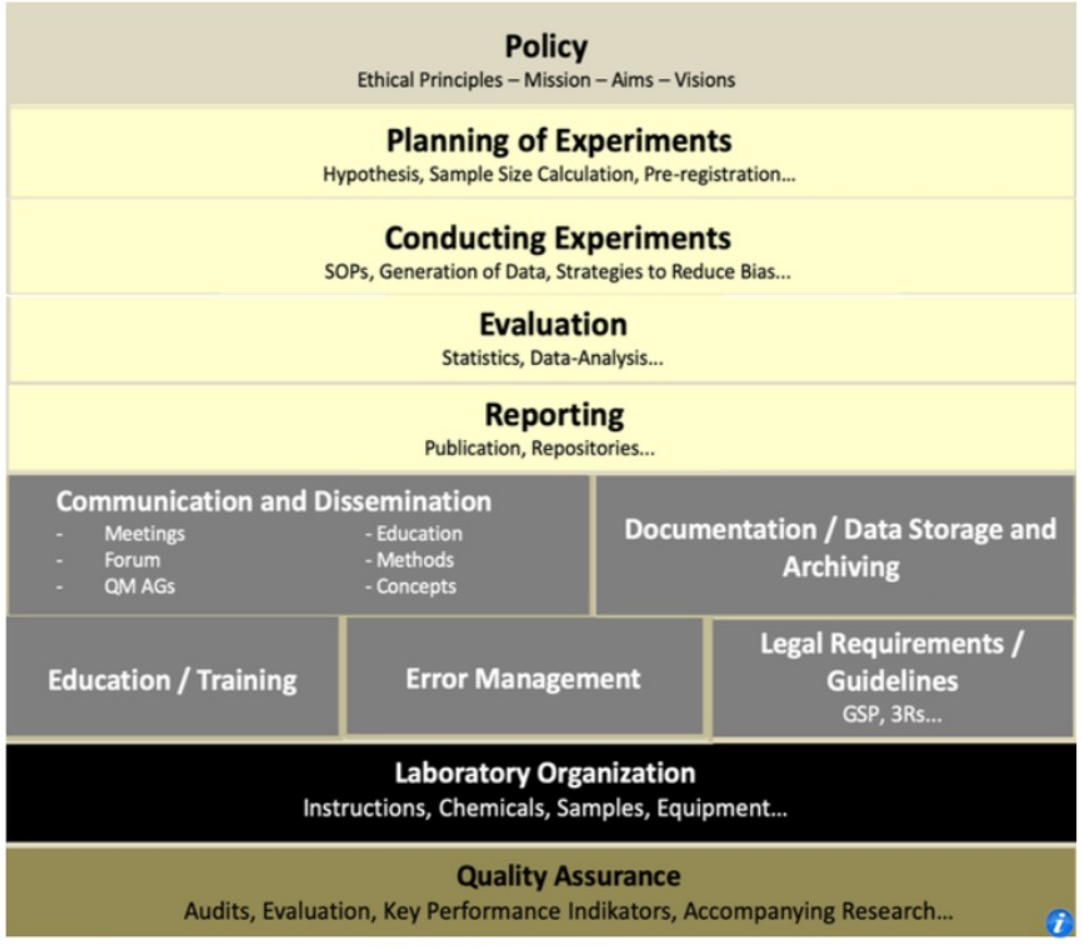
PREMIER (Predictiveness and Robustness through Modular Improvement of Experimental Research)

PREMIER is a Quality Management System (QMS) which was developed by researchers for researchers in the Department of Experimental Neurology in response to ISO 9001.

PREMIER is specifically tailored to the requirements of basic research and has a modular structure so that it can be used by both small laboratories and large institutions.

PREMIER can be used as a complete QM system and also modularly, which is especially useful for smaller laboratories.

Depending on your needs and quality objectives, you can select individual modules and implement them step by step.



Responsibility of Management

Core-(Research-) Processes

Support Processes

measuring, analyzing, improving

The PREMIER concept is pre-registered at OSF under: https://osf.io/xw75z/

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PREMIER

How is PREMIER used in a laboratory like the Experimental Neurology?

It is stored in the Wiki (in German and English) and accessible for everyone in the lab via a password.

Modules can be clicked on individually; behind them are corresponding research-specific contents.

PREMIER / QM House

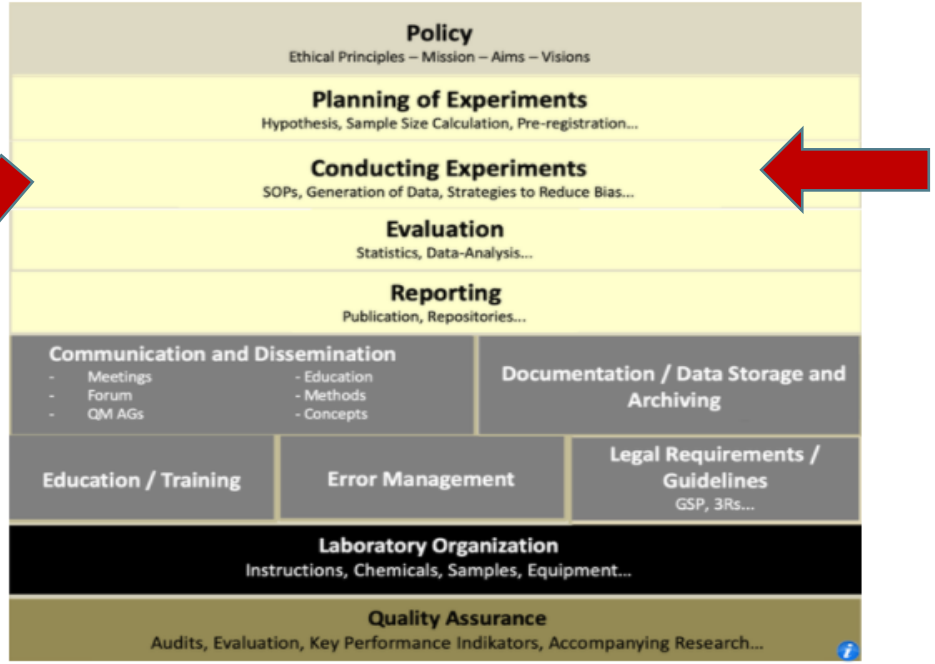
German Version

[1]

This structure is the basis and visualization of our new research QM. Officially, the QM House is called PREMIER (Productiveness and Robustness through Modular I

The aim of PREMIER is the development of a structured quality assurance, consisting of modular elements, in which high-quality preclinical research is feasible and p the effectiveness of the measures and lay a foundation for the scientific community to further develop and improve such an open system.

The individual modules of the QM House can be clicked on and lead to further information.



The PREMIER concept (QM House) is pre-registered with OSF at https://osf.io/xw75z/

You can find detailed information on the PREMIER Website.

The PREMIER Explainer Video describes the objectives of such quality assurance and why PREMIER should be used as a basis for biomedical research.

Example of usage

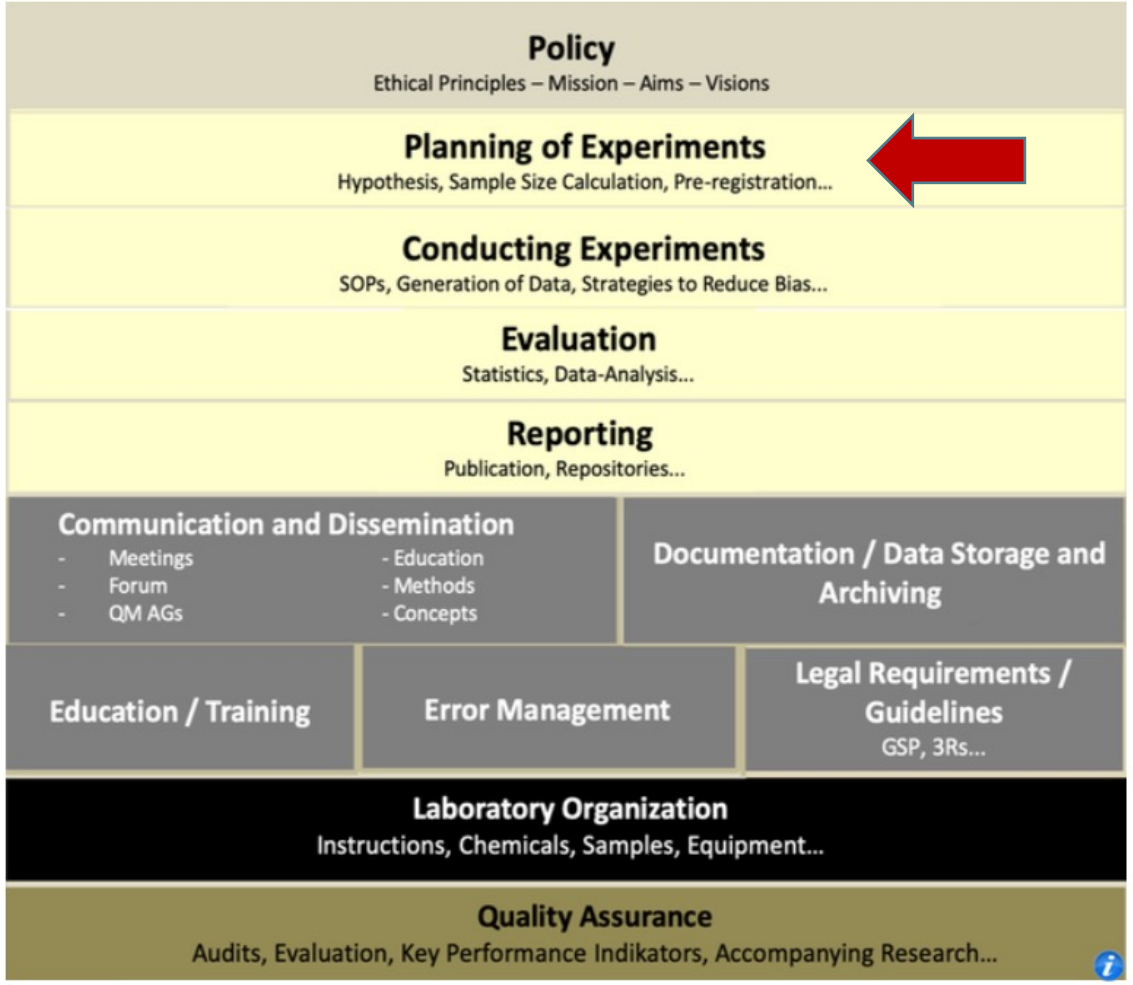


Table. Suggested Differences Between Exploratory and Confirmatory Preclinical Study Designs

	Exploratory (Discovery)	Confirmatory
Hypothesis	(+)	(+++)
Establish pathophysiology	(+++)	(+)
Sequence and details of experiments established at onset	(+)	(+++)
Defined primary end point	(-)	(++)
Sample size calculation	(+)	(+++)
Blinding	(+++)	(+++)
Randomization	(+++)	(+++)
External validity (aging, comorbidities, etc)	(-)	(++)
Predefined inclusion/exclusion criteria	(++)	(+++)
Test statistics	(+)	(+++)
Preregistration	(-)	(++)
High sensitivity (high type I error rate, low type II error rate): find what might work	(+++)	(+)
High specificity (low type I error rate, high type II error rate): weed out false-positives	(+)	(+++)

Modified from: Dirnagl U. Thomas Willis Lecture: Stroke.2016;47-2148-2153 (ref. 4)

Process of Experimental Design [Bearbeiten | Quelltext bearbeiten]

Depending on the type of project, the following steps must be considered and answered for a comprehensive and complete design of experiments:

1. Search
2. Hypothesis / Counter (null)-Hypothesis
3. Target Parameters
4. Sample Size Calculation
5. Model Planning / Study Design
6. Feasibility Study
7. Nesting and Pseudoreplication
8. Randomisation and Blinding
9. Resource Plan (financing, capacities, personnel)
10. Schedule
11. Accompanying Training and Courses
12. Planning of Data Preparation / Analysis
13. Data Storage
14. Clarification of Authorship
15. Pre-registration

Template Experimental Design [Bearbeiten | Quelltext bearbeiten]

In addition to this background information, a template was created for the design of experiments, which is available to all Exp. Neuro members in the l according to the GSP guidelines. In addition, a PDF with help and contact persons is linked in the template.

A video tutorial on the use of templates for design of experiments and the export as PDF can be found under Template Design of Experiments in labfo

Changes [Bearbeiten | Quelltext bearbeiten]

Changes that have occurred during the design of the experiment and during the project must always be documented and explained in the ELN, e.g. if necessary and mandatory in order to generate robust and reliable results.

Sustainability [Bearbeiten | Quelltext bearbeiten]

Every researcher should finally think about how and with what means the project can achieve sustainability. Are there factors that could affect the proj

labfolder ● Vorlagen

NOTIZBUCH | VERWALTEN | DASHBOARD

+ Hinzufügen

	Besitzer	zuletzt geändert:	erstellt:
Gruppen-Vorlagen: Exp Neuro			
QM	Ingo Przesdzing	21.11.2018 16:40	04.07.2018 15:44
QM Haus Versuchsplanung	Claudia Kurreck	22.01.2019 11:14	21.11.2018 15:25
QM House Experimental Planning	Claudia Kurreck	25.01.2019 10:01	21.11.2018 16:40

Claudia Kurreck

erstellt: 21.11.2018
geändert: 25.01.2019

Keine Tags verwendet

Hypothesis / Counterhypothesis

support

Set up hypothesis / counter hypothesis: Have you formulated your hypothesis and the corresponding counter and/or null hypothesis?

Counterhypothesis: Have you searched for literature that argues against the hypothesis?

Ein Bild einfügen
oder
+ Datei oder Bild hochladen

Target Parameter

support

Contact person for:
In vivo questions: André Rex
In vitro questions: Dorette Freyer

Definition of the target parameters: Which primary and secondary target parameters have you defined?

Ein Bild einfügen
oder
+ Datei oder Bild hochladen

Sample Size Calculation

support

Need for experimental units: How was the need for experimental units (number of animals, organs, organ sections or cultured cells) determined?

Which reference was used for the estimation? groups and units: Name the experimental groups with the exact number of units and identify test and control groups.

Ein Bild einfügen
oder
+ Datei oder Bild hochladen

Experimental Design / Model Planning

support

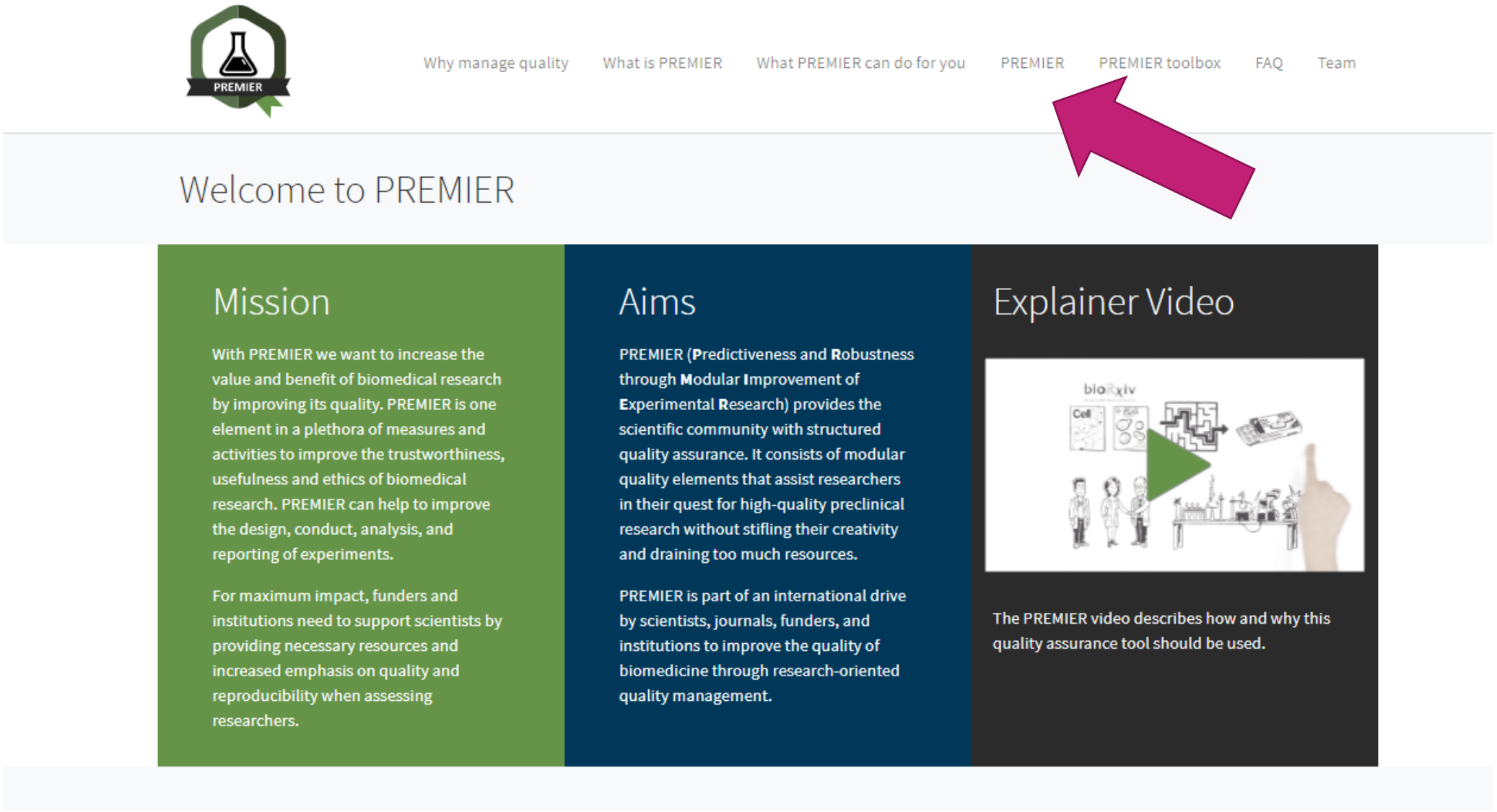
Definition of criteria: Have you defined the following criteria for your project: - method selection - influencing factors - requirements - control groups - validations?

PREMIER

The QM house was rewritten and formulated in a general way so that it can be used by any research laboratory.

The content of PREMIER is transparent and free of charge for the scientific community as an independent website: https://premier-qms.org/

PREMIER Webpage: www.premier-qms.org



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PREMIER

Why manage quality | What is PREMIER | What PREMIER can do for you | PREMIER | PREMIER toolbox | FAQ | Team

The clickable PREMIER "House"

Policy
Ethical Principles (GWP) - Mission – Aims - Visions

Planning of Experiments
Hypothesis, Sample Size Calculation, Pre-registration…

Conducting Experiments
SOPs, Generation of Data, Strategies for Reduction of Bias…

Evaluation
Statistics, Data-Analysis…

Reporting
Publication, Repositories…

Communication and Dissemination
Meetings, Wiki, QM AGs, Education, Methods, Concepts

Documentation / Data Storage and Archiv

Education / Training

Error Management

Legal Requirements / Guidelines
GSP, 3Rs

Laboratory Organization
Introductions, Chemicals, Samples, Equipment…

Quality Assurance
Audits, Evaluation, Key Performance Indicators, Accompanying Research…

How to use PREMIER

- Click on the individual modules of PREMIER and find out about the contents of the quality blocks.

- Think about which contents are currently most important for your laboratory/organization.

- Contact the PREMIER team for an assessment to determine the status quo in your laboratory/organization.

- Define your quality goals after the assessment.

- Select one to all PREMIER modules [illegible]ement them in your laboratory/organization using the quality tools provided. The implementation of each individual module helps to increase the quality of your research. When you have implemented all modules, you have implemented a complete QM system that is specifically tailored to basic research.

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Home / PREMIER / Documentation / Data Storage and Archiving

NEW! Discuss at premier forum

- Policy
- Planning of Experiments
- Conducting Experiments
- Evaluating Experiments
- Reporting Results
- Communication and Dissemination
- Documentation / Data Storage and Archiving
- Education / Training
- Risk- and Error Management
- Legal Requirements and Guidelines
- Laboratory Maintenance
- Quality Assurance

PREMIER Documentation and Data Storage

Objectives

The aim is to ensure the traceability and integrity of the research data so that the reported results can be documented and verified.

Background

To ensure experimental recording, experiments should be documented. The entries should include all data and relevant details in a way that other researchers can trace and, if needed, repeat the experiment.

To ensure the traceability, the source of the data (primary and secondary), including the identity of the scientist involved in the generation of the information should be available to authorized personnel, ensuring the personal data protection rights of the people involved.

Tasks / Actions

In order to create a lab specific action plan, the first step is an assessment, which will be carried out by the PREMIER team. The assessment will determine the status quo of the laboratory in regard to existing quality tools. Here you find the general tasks / actions that are necessary to implement the module.

- Data Collection +
- Documentation +
- Electronic Lab Notebooks +
- Traceability of Data +
- Data Storage +
- References +

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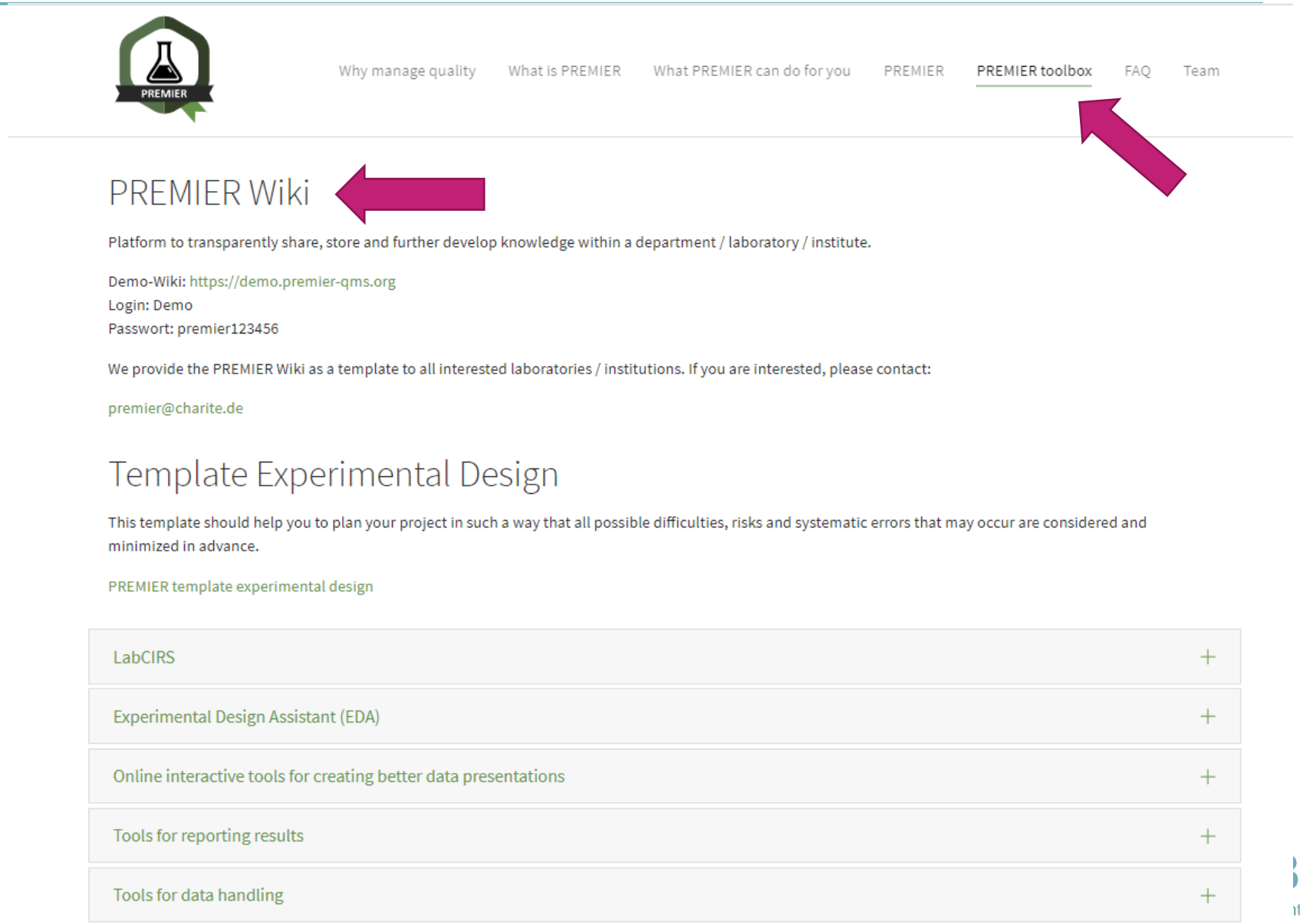
PREMIER Toolbox



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PREMIER Wiki

Full text searchable

Ckurreck Dis… Einstellungen Beobachtungsliste Beiträge Abmelden

Seite | Diskussion | Lesen | Bearbeiten | Quelltext bearbeiten | Versionsgeschichte | Als PDF-Datei ausgeben | Mehr | ExpNeuropedia durchsuchen

CHARITÉ EXPERIMENTAL NEUROLOGY BERLIN

Hauptseite
Letzte Änderungen
Zufällige Seite
Hilfe

Werkzeuge
Links auf diese Seite
Änderungen an verlinkten Seiten
Datei hochladen
Spezialseiten
Druckversion
Permanenter Link
Seiteninformationen
Seite zitieren

Neue Seite erstellen
Neue Seite erstellen (ohne SOP und WI)
Neue (M)SOP erstellen
Neue WI erstellen

Kategorien
Seiten nach Kategorien
Alle Seiten

Links
Abenddienst
Abenddienst-Kalender
Abwesenheits-kalender
Das QM Haus
Dokumentenliste
Einstellung neuer Mitarbeiter
Transponderformular
Exp Neuro Homepage
Fachbereiche
Forum
LabCIRS
Labfolder
Labmeeting
Organigramm
Schulung und Training
Sicherheits-

SOP Steriles Arbeiten Zellkultur

English Version

All changes traceable

Revision	Stand	Autor
03	08.10.2021	DFRE

Version control

Inhaltsverzeichnis [Verbergen]

Änderungen gegenüber der vorherigen Version [Bearbeiten | Quelltext bearbeiten]

5.3.	Abfall und Reinigung aktualisiert

Ziel [Bearbeiten | Quelltext bearbeiten]

Eine Grundvoraussetzung für erfolgreiches Arbeiten in der Zellkultur ist es, Kontaminationen der Kulturen mit Bakterien, Hefen, Mykoplasmen oder Fremdzellen zu vermeiden.

Hintergrund [Bearbeiten | Quelltext bearbeiten]

Alle Maßnahmen zur Vermeidung der o.g. Kontaminationen werden unter dem Begriff „steriles Arbeiten" zusammengefasst. Die Anforderungen an steriles Arbeiten sind für jedes Forschungslabor etwas anders und unterscheiden sich außerdem von denen im klinischen Bereich.

Geltungsbereich [Bearbeiten | Quelltext bearbeiten]

Fachbereich Zellkultur

Prozessbeschreibung, Handlungsabläufe [Bearbeiten | Quelltext bearbeiten]

Die im Folgenden aufgeführten Handlungsanweisungen stellen keine Reihenfolge dar, sind aber beim sterilen Arbeiten in der Zellkultur grundsätzlich einzuhalten.

Zusätzliche Schutzmassnahmen (Kittel, Handschuhe, Abflammen der Flaschenöffnungen,

Abwischen mit Descosept u.a.) sind aber jederzeit nach eigenem Ermessen möglich.

Material [Bearbeiten | Quelltext bearbeiten]

PREMIER Toolbox

Why manage quality | What is PREMIER | What PREMIER can do for you | PREMIER | PREMIER toolbox | FAQ | Team

PREMIER Wiki

Platform to transparently share, store and further develop knowledge within a department / laboratory / institute.

Demo-Wiki: https://demo.premier-qms.org
Login: Demo
Passwort: premier123456

We provide the PREMIER Wiki as a template to all interested laboratories / institutions. If you are interested, please contact:

premier@charite.de

Template Experimental Design

This template should help you to plan your project in such a way that all possible difficulties, risks and systematic errors that may occur are considered and minimized in advance.

PREMIER template experimental design

- LabCIRS +
- Experimental Design Assistant (EDA) +
- Online interactive tools for creating better data presentations +
- Tools for reporting results +
- Tools for data handling +

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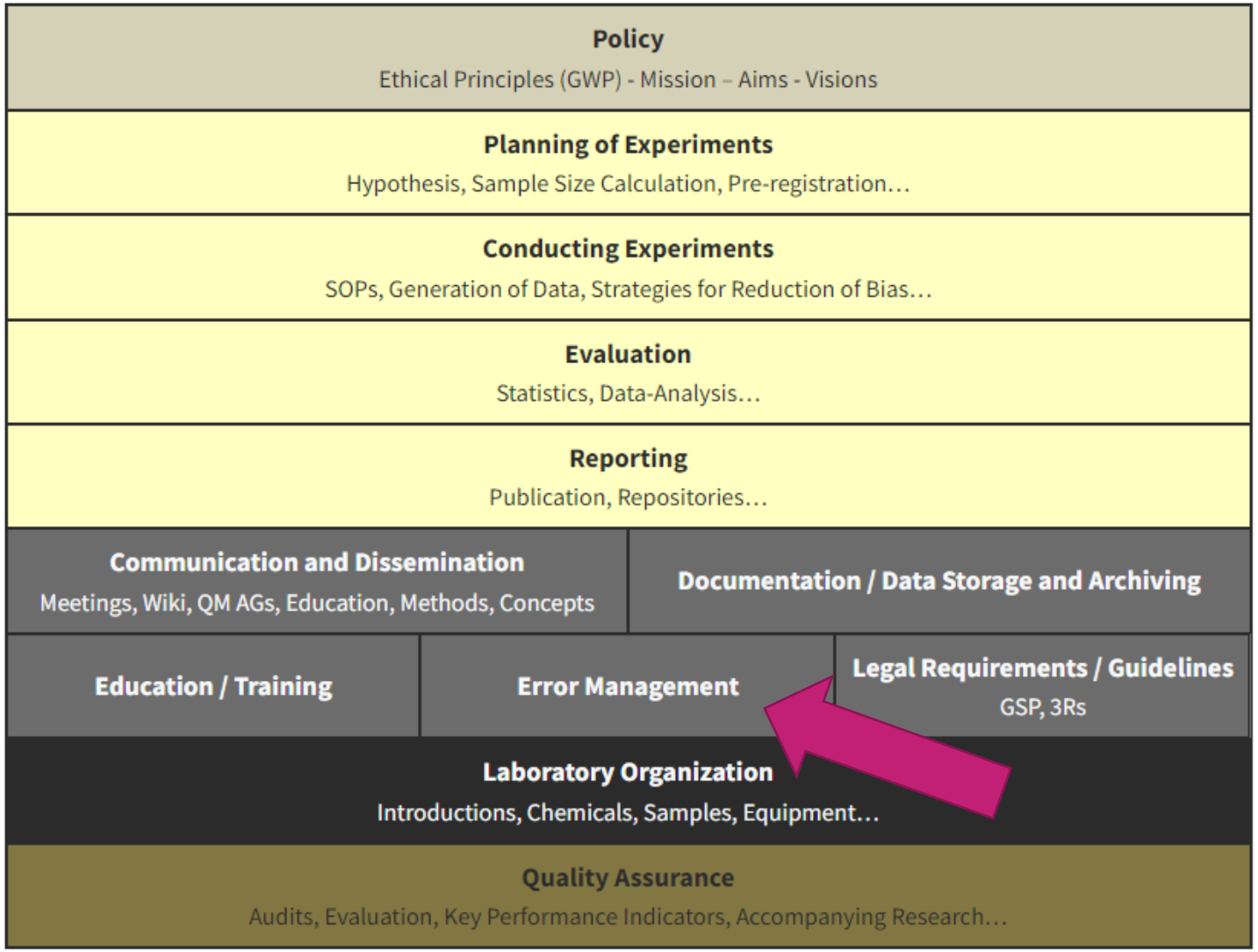

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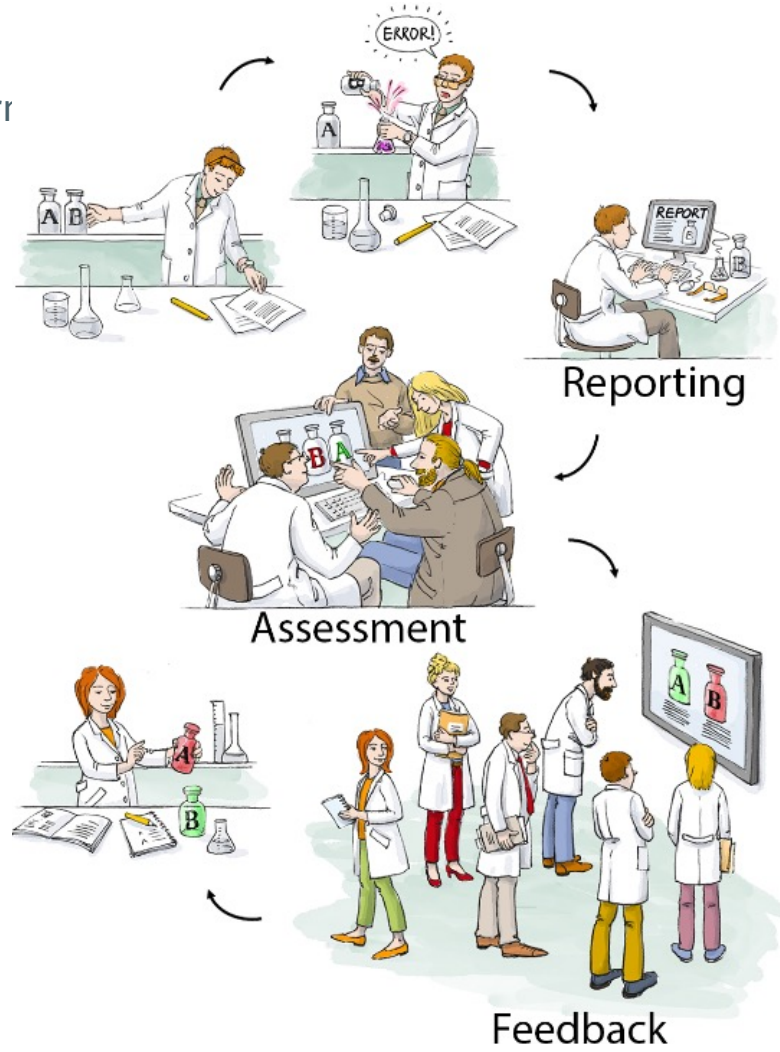
LabCIRS

LabCIRS (Laboratory Critical Incident Reporting System)

is an anonymous error reporting system developed by the Department of Experimental Neurology.

- This structured error management is intended to make it easier to learn how to deal with errors and to create a positive error culture.
- Aim is to prevent re-occurrence and identification of risk areas.
- If we want to learn from errors and critical incidents, these errors must be reported, analyzed and improved.
- It is an open-source software and can be used by every laboratory.
- The source code is available on GitHub.
- LabCIRS access for Charité members can be requested through QUEST Center.

  Contact: labcirs-admin@charite.de



Publication:
https://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.2000705

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Overview PREMIER

PREMIER	
Goals	• to improve the quality of academic preclinical biomedicine through structured quality-ensuring measures • help to improve the design, conduct, analysis, and reporting of experiments • to ensure robust and reliable research results
User	academic basic research
Structure	modular structure: 12 modules with minimum requirements
Implementation	as a complete QM system or as a modular approach (individual, freely choosable modules) with a low implementation threshold
Access to content	Via a freely accessible website: www.premier-qms.de; Support through an initial assessment by the PREMIER team to determine the goal and needs of the laboratory.
Certification	none
Audits	internal and external (peer-) audits; ringaudits are planned

Which requirements have to be fulfilled to implement quality assurance measures?

Requirements for Quality Assurance Measures

What have we learned in many years of QM use and implementation regarding the requirements?

Personnel and financial resources

- QM is always teamwork, so all employees must always be involved.
- At least one person is needed to manage the processes and keep them running.

Time resources

- Employees must be allowed to invest time in using quality tools.

The leadership must definitely support the QM.

- Without the support of the leadership, no quality assurance measures can be implemented. A QM mindset is needed.

-> If only one of these requirements is not fulfilled, it is very difficult to ensure an active QM.

Challenges of PREMIER

- **The aim now in the second phase is to roll out PREMIER to other laboratories and see if this model works everywhere or needs to be modified.**
- **The search for partner laboratories has begun for implementing either individual modules or the entire system.**

What do I need to do if I am interested in introducing PREMIER modules in my laboratory?
- Use cases -

Introducing PREMIER: Use Case 1

Small lab with 10 researcher; no extra financial und human resources; want to introduce one module

The following steps should be taken:

1. The leadership should consider what goals should be achieved with the selected PREMIER module.
2. Communicate the added value of such a quality measure to the laboratory team, since broad acceptance of the staff is important for implementation.
3. Contact the PREMIER team: claudia.kurreck@charite.de
4. Make an appointment for an assessment to determine your status quo.

All further steps will be coordinated together.

Introducing PREMIER: Use Case 2

Lab with 30 researcher; want to introduce three modules

The following steps should be taken:

1. The leadership should consider what goals should be achieved with the selected PREMIER modules.
2. Communicate the added value of such quality measures to the laboratory team, since broad acceptance of the staff is important for implementation.
3. Contact the PREMIER team: claudia.kurreck@charite.de
4. Make an appointment for an assessment to determine your status quo.

All further steps will be coordinated together.

Introducing PREMIER: Use Case 3

Big lab with 50 researcher; a half position for QM (scientist in the team) can be financed; want to introduce PREMIER as a wohle system (all modules)

The following steps should be taken:

1. The leadership should consider what goals should be achieved with a QM system in the laboratory.
2. Communicate the added value of such a system to the laboratory team, since broad acceptance of the staff is important for implementation.
3. Contact the PREMIER team: claudia.kurreck@charite.de
4. Make an appointment for an assessment to determine your QM status quo.

All further steps will be coordinated together.

Conclusion

- **Is it possible to establish structured measures for quality assurance in research?**
  - Yes, a QM system like PREMIER could be one possibility.
- **Which requirements have to be fulfilled to implement quality assurance measures?**
  - personnel and financial resources
  - time resources
  - leadership must support quality assurance measures
- **What needs to be done to implement PREMIER quality assurance measures in the laboratory?**
  - Think about the goals you want to achieve and contact the PREMIER team for further information and guidance.

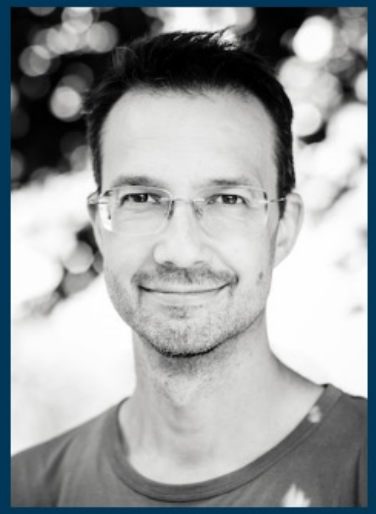
PREMIER Team

Prof. Dr. Ulrich Dirnagl

Director Department of Experimental Neurology, Charité - Universitätsmedizin Berlin
Director of QUEST Center, Berlin Institute of Health (BIH)
PREMIER Project Leader
Concept and Development

Dipl. Biochem. Claudia Kurreck

Quality Manager
PREMIER Project Coordinator
Concept and Implementation, Management of Documents, Key Performance Indicators, Audits and Assessments, Wiki, LabCIRS, Training

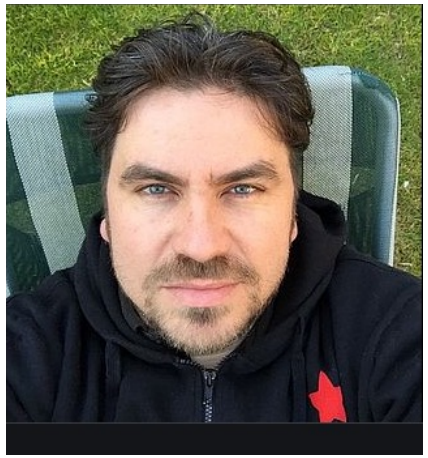


Dr. René Bernard

Scientist
PREMIER Scientific Support
Open Access, Open Data, Randomizing, Blinding, Nesting, Audits and Assessments, Training

Dipl. Ing. Ingo Przesdzing

IT-Administrator
PREMIER IT Development
Electronic Laboratory Notebook, Wiki, LabCIRS, Databases, Data Archiving, Training



Dipl. Phys. Göran Bodenschatz

Freelancer / Webdesigner
Development PREMIER Webpage and PREMIER Wiki,
Technical Support

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PREMIER Publications

- The PREMIER concept is pre-registered at OSF: **PREMIER: Structured Quality Assurance from and for Academic Preclinical Biomedicine**: https://osf.io/xw75z/
- **Quality management for academic laboratories: burden or boon?** published in the EMBO Journal.
- We investigate practicable options for auditing which have the potential to improve quality of preclinical research in academia. Preprint**: Improving quality of preclinical academic research through auditing: A feasibility study**: published at Plos One
- **A Laboratory Critical Incident and Error Reporting System for Experimental Biomedicine**: LabCIRS at Plos Biology
- **A pocket guide to electronic laboratory notebooks in the academic life sciences:**F1000Research
- **Rethinking research reproducibility**. EMBO Journal
- **Resolving the Tension Between Exploration and Confirmation in Preclinical Biomedical Research.** Handb Exp Pharmacol. Springer
- **Preregistration of exploratory research: Learning from the golden age of discovery.** Plos Biology

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Thank you!

June 07th 2022

Contact:
claudia.kurreck@charite.de

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Charité Experimental Neurology Berlin

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BIH Berlin Institute of Health @Charité