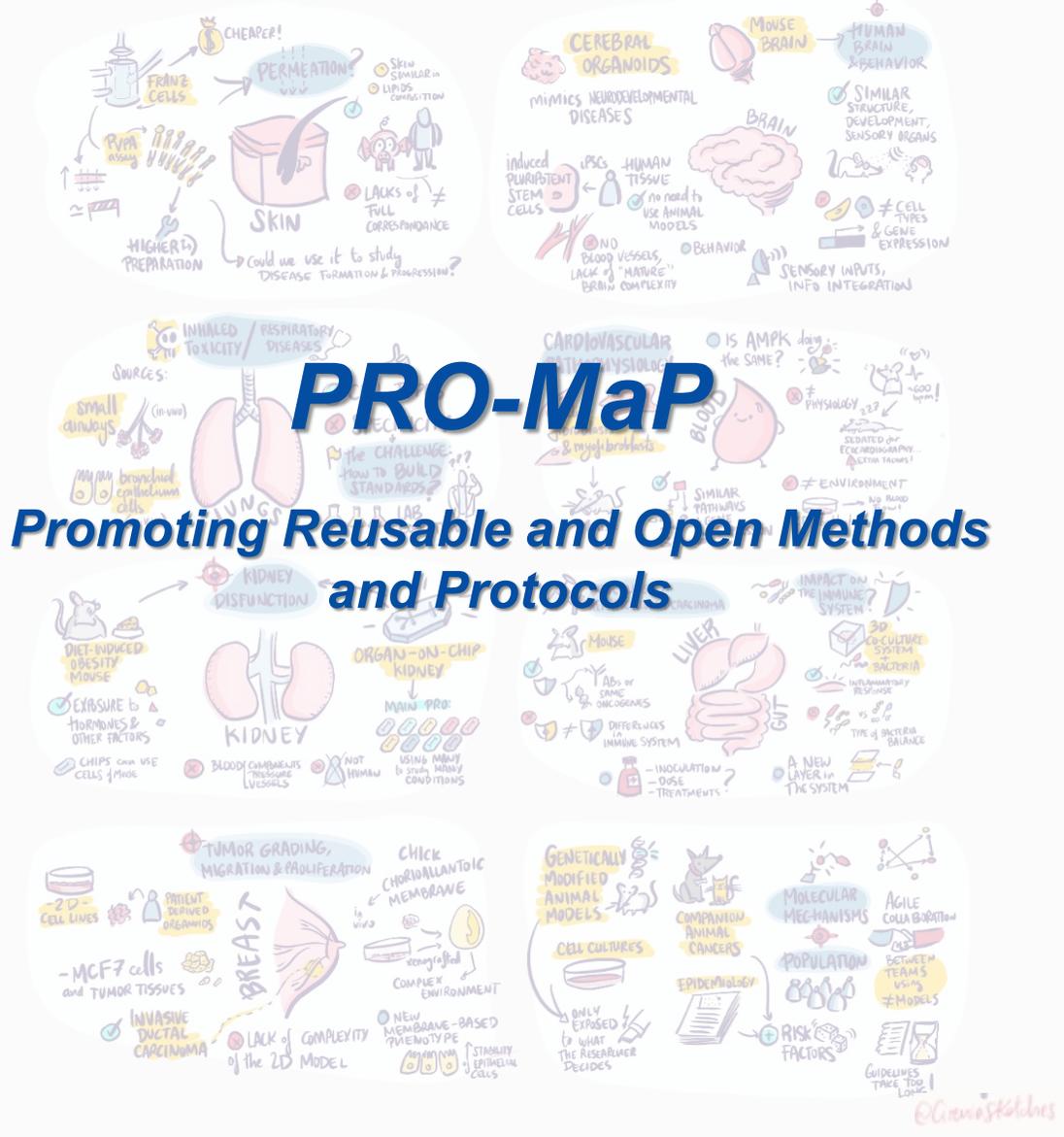




European Commission



PRO-MaP

Promoting Reusable and Open Methods and Protocols

Sofia Batista Leite

European Commission Joint Research Centre
Alternative Methods and Chemical Safety Unit

Pierre Decœurinck (EC - JRC)

Tracey Weissgerber (QUEST Center for Responsible Research)

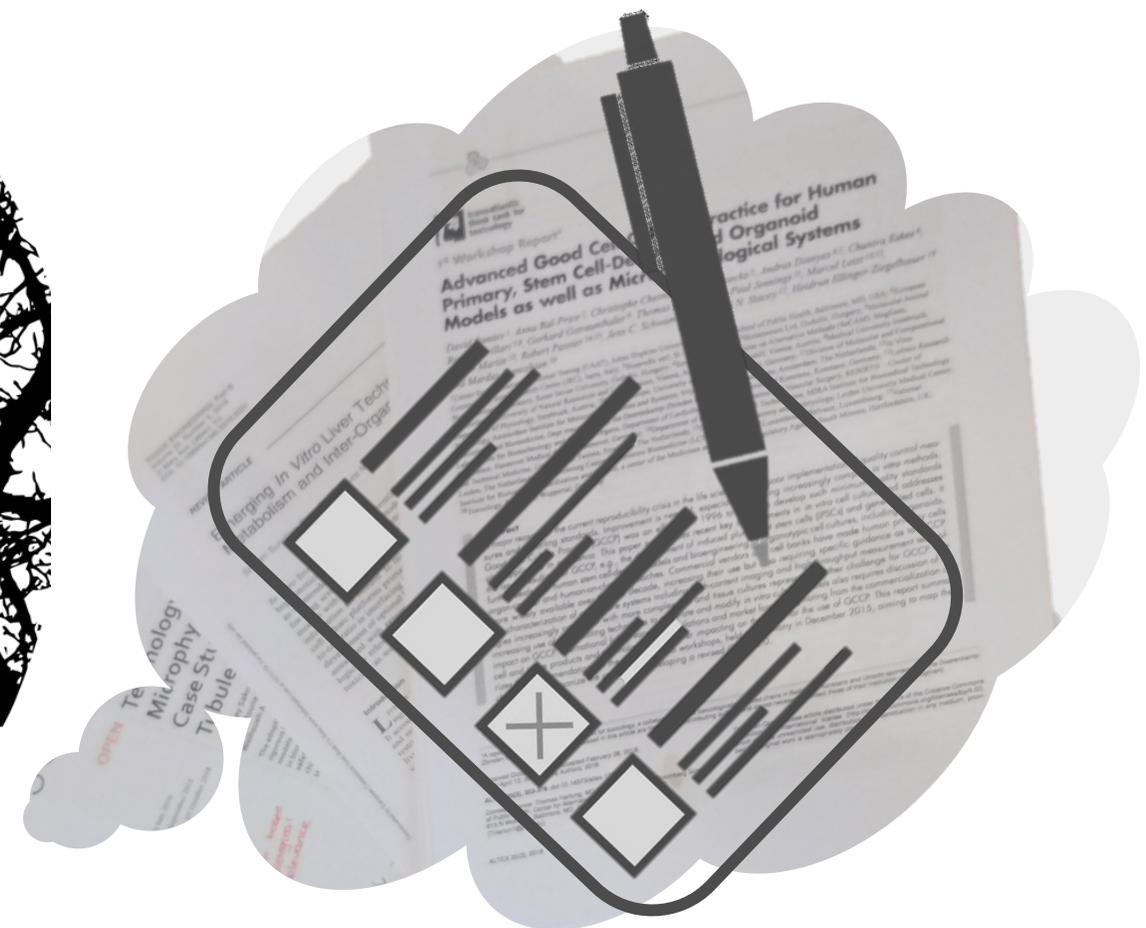
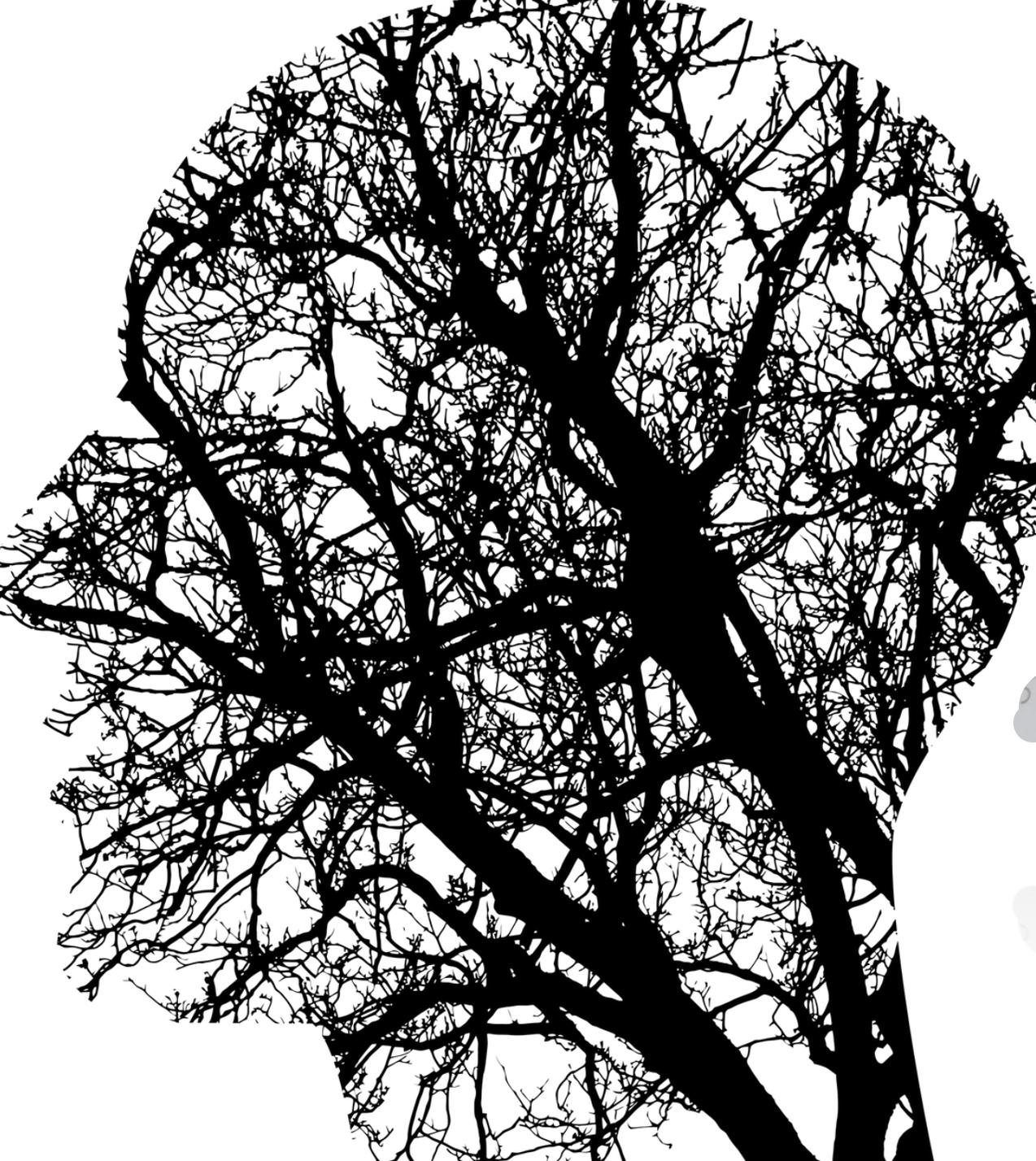
Bernd Pulverer (Editor in chief of EMBO publishers)

Jean François Dechamp (EC DG RTD)

Annamaria Carusi (InterchangeResearch)

David Pamies (University of Lausanne)

Joint Research Centre



Methods Are Frequently Lost

Kindly provided by Emma Ganley

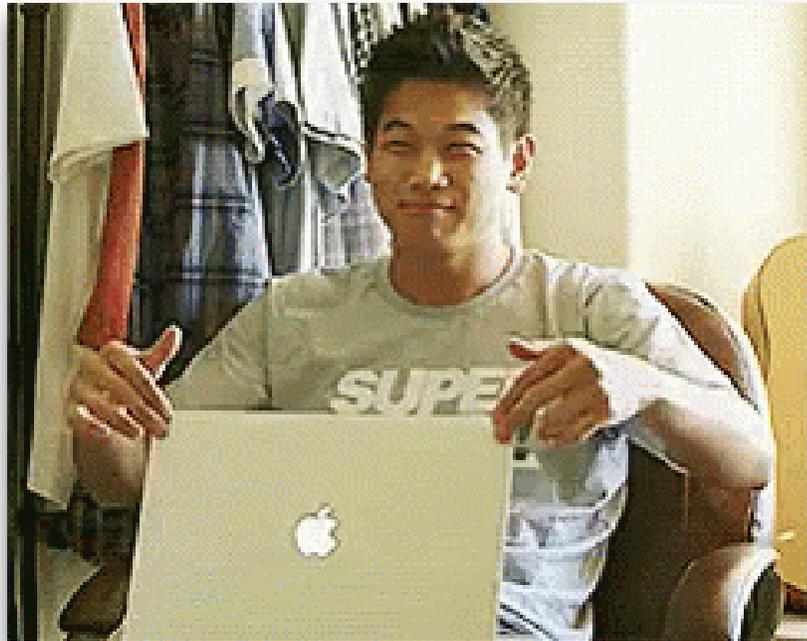


 **Morgan Halane**
@themorgantrail

Folge ich

Looking for protocol in 1997 paper: "as described in (x) et al '96". Finds '96 paper: "as described in (x) '87." Finds '87 paper: Paywall.

 Tweet übersetzen



21:20 - 1. Nov. 2017 aus **대한민국 포항시**

34 Retweets 96 „Gefällt mir“-Angaben



 **Daniel Gonzales**
@dgonzales1990

Folge ich

2017: “Devices were fabricated as previously described [ref 8]”

[ref 8] 2015: “Devices were fabricated as previously described [ref 4]”

[ref 4] 2013: “Devices were fabricated as previously described [ref 2]”

[ref 2] 2009: “Devices were fabricated with conventional methods”

 Tweet übersetzen

13:16 - 17. Jan. 2018

230 Retweets 798 „Gefällt mir“-Angaben



 28  230  798 

The European Union Reference Laboratory for alternatives to animal testing



- Research
- **Validation**
- Dissemination
- Promotion

TRUST

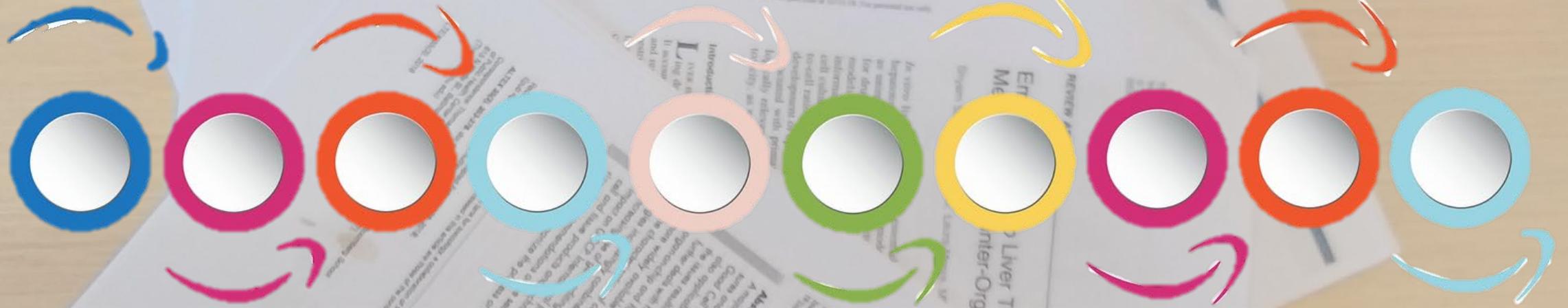


Show 5 entries Search:

	Document type	Title	No.	Topic area	Models and Strategies	Biological endpoints	Experimental systems	EUProject
	All	All	/	All	All	All	All	All
	Method summary	Steroidogenesis assay using H295R cell line	456	Effects on Endocrine System	Cell Lines Human Origin TESTING STRATEGIES	Cell viability Estrogen production Hormone production Steroidogenesis Testosterone production	H295R - human adrenocortical carcinoma cell line	
	Method summary	Transactivation Assays to Detect Estrogen Receptor Agonists and Antagonists In Vitro with Stably Transfected Human Cell Lines	455	Effects on Endocrine System	Genetically Engineered Cells	Anti-estrogenic activity Cell proliferation Cell viability Estrogenic activity (Estrogenicity) Receptor activity: Estrogen Receptor (ER) Receptor activity: Estrogen Receptor (ER) Reporter gene expression: Luciferase (Luc)	(h)ERα-HeLa-9903 - Engineered human cervix carcinoma cell line BG1Luc-4E2 - Engineered human ovarian adenocarcinoma cell line	



Promoting of non-guideline methods

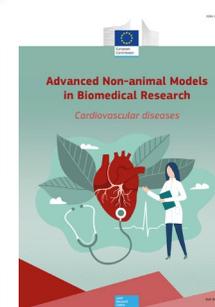
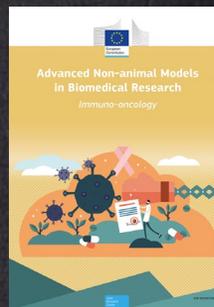
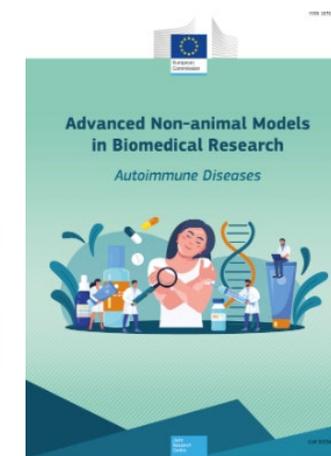
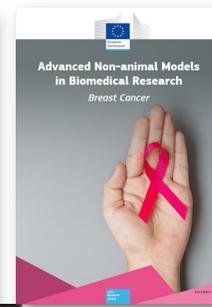
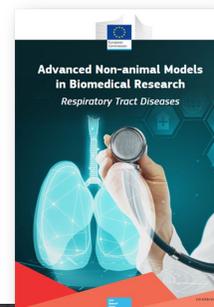


Methods & Protocols in Peer Review Publications

working with the community

Conclusions of our research..

1. Majority of publications do not value the methods section enough



Published: 16 March 2012

Neutrinos not faster than light

Half of top cancer studies fail high-profile reproducibility effort

Barriers to reproducing preclinical results included unhelpful author communication, but critics argue that one-time replication attempts don't tell the whole story.

Asher Mullard



Vague experimental protocols was one barrier to replication that researchers encountered. Credit: Patrick Hertzog/AFP/Getty

NEWS | BIOLOGY

Sleuthing sheds light on STAP cell fiasco

Researchers describe artifacts that could have misled authors and prompted sensational reprogramming claims



DAVIDE BONAZZI

Plan to replicate 50 high-impact cancer papers shrinks to just 18

Science

By Jocelyn Kaiser | Jul. 31, 2018, 5:45 PM

makes possible to

udies lack proper reporting



DAVIDE BONAZZI

Plan to replicate 50 high-impact cancer papers shrinks to just 18
Science
By Jocelyn Kaiser | Jul. 31, 2018, 5:45 PM



2%

experiments with open data

70%

of experiments required asking for key reagents

69%

of experiments needing a key reagent original authors were willing to share

0%

of protocols completely described

32%

of experiments the original authors were not helpful (or unresponsive)

41%

of experiments the original authors were very helpful

nature physics

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[nature](#) > [nature physics](#) > [perspectives](#) > article

Perspective | [Open Access](#) | [Published: 15 November 2018](#)

Open is not enough

DATA

METHODS

'open access' and 'open data' do not guarantee reproducibility

Reproducibility of scientific results in the EU : scoping report



WHY sharing Protocols and Methods?

TRUST

Transparency

Advance in Science

Transferability of Science

Reproducibility is CORE to science

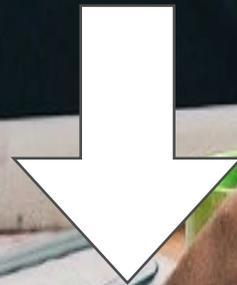
Translation of Science (impact citizens)

adapted from pixabay

Conclusions of our research..

- 1. Majority of publications do not value the methods section enough*
- 2. (Part of the) Community is aware of this and some initiatives trying to tackle it!*

Community Work



Phase 0:
Workshop with Key representatives

Publishers

Funders

Researchers

Platform
Managers

NINDS workshop - 2012

PERSPECTIVE

doi:10.1038/nature11556

A call for transparent reporting to optimize the predictive value of preclinical research

Story C. Landis¹, Susan G. Amara², Khusru Asadullah³, Chris P. Austin⁴, Robi Blumenstein⁵, Eileen W. Bradley⁶, Ronald G. Crystal⁷, Robert B. Darnell⁸, Robert J. Ferrante⁹, Howard Fillit¹⁰, Robert Finkelstein¹, Marc Fisher¹¹, Howard E. Gendelman¹², Robert M. Golub¹³, John L. Goudreau¹⁴, Robert A. Gross¹⁵, Amelie K. Gubitzi¹, Sharon E. Hesterlee¹⁶, David W. Howells¹⁷, John Huguenard¹⁸, Katrina Kelner¹⁹, Walter Koroshetz¹, Dimitri Krainc²⁰, Stanley E. Lazic²¹, Michael S. Levine²², Malcolm R. Macleod²³, John M. McCall²⁴, Richard T. Moxley III²⁵, Kalyani Narasimhan²⁶, Linda J. Noble²⁷, Steve Perrin²⁸, John D. Porter¹, Oswald Steward²⁹, Ellis Unger³⁰, Ursula Utz¹ & Shai D. Silberberg¹

The US National Institute of Neurological Disorders and Stroke convened major stakeholders in June 2012 to discuss how to improve the methodological reporting of animal studies in grant applications and publications. The main workshop recommendation is that at a minimum studies should report on sample-size estimation, whether and how animals were randomized, whether investigators were blind to the treatment, and the handling of data. We recognize that achieving a meaningful improvement in the quality of reporting will require a concerted effort by investigators, reviewers, funding agencies and journal editors. Requiring better reporting of animal studies will raise awareness of the importance of rigorous study design to accelerate scientific progress.

Methods Matter for Open & Reproducible Research



IF Cookies == Data

Analysis of

Size / Thickness / Texture / Flavour etc.

Can ***ONLY*** be interpreted in the context of the method tweaks

too much flour / incorrect ingredient

amount of butter / bake time etc.)



These were all made by tweaking the same recipe. Rachel Askinasi/Insider

Kindly provided by Emma Ganley

Cell Press launched STAR Protocols in 2019 to fulfill this need

Author perspective

As an author, I want to...

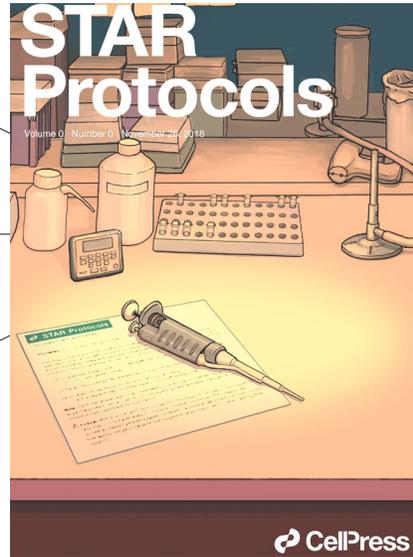
- Be accurate in my reporting
- Showcase my technical expertise
- Get credit for my work
- Update my protocol as needed



Peer review
and editorial
curation

Structured
formatting
based on
researcher
feedback

Credit &
Showcasing



Troubleshooting
&
User feedback

Visualization &
'At bench'
usability

Content
evolvability

User perspective

As a user, I want to...

- Find and choose the right method
- Reproduce a method step-by-step
- Troubleshoot
- Get expert advice



Benefits to authors

- Increase the reach and use of the original research article
- Gain another publication in an open access, indexed and peer reviewed journal
- Author template simplifies the process of converting lab protocols to a STAR Protocol
- Innovative, timely peer review and publication process
- Quick turnaround time (50 days from submission to accept)
- Improve lab record keeping to preserve institutional knowledge
- Contribute to open science and help encourage reproducibility

Kindly provided by Elisa De Ranieri

Study reporting checklist, based on GIVIMP

Kindly provided by Ingrid Langezaal



→ Used GIVIMP guidance and SciRap tool to establish the following reporting checklist:

Apparatus, materials and reagents

1. The **apparatus was described**.
2. The **limit of detection or limit of quantitation** of the apparatus was indicated.
3. The **materials and reagents** were described.
4. The **culture dimensions** were described (mm² or ml).
5. The **use of animal-derived materials or reagents** (e.g. Trypsin, antibodies, collagen, Matrigel etc.) was described.
6. The **use of fully animal-free materials and reagents** was described.

Test item treatment

1. The **test item concentrations/dose levels** were stated.
2. **Biological fluid characterisation** was described (quantification of proteins and cells/tissue present).
3. **Binding to biological fluid material** was described.
4. **Binding to culture material** was described.
5. **Test system number, density, dimension, quantity used during treatment** was described.
6. The **duration of treatment** was stated.
7. The **number of replicates per concentration/dose** was stated.
8. The **number of times the experiment was repeated** (independent biological runs) was stated.

Data collection and analysis

1. The **experimental design** and relevant **acceptance criteria** were described.
2. The **experimental layout**, e.g. plate layout was described.
3. The **time points for data collection** were stated.
4. It was stated that the effect of the test item on **cytotoxicity was measured**.
5. **Other observations that may impact the results** (e.g. autofluorescence, absorbance by the test system) are reported.
6. Details on **calculation of results** were given.
7. All **results were clearly presented**, including **negative and failed runs**.
8. The **statistical methods & software used** were described.
9. A clear **description on how to interpret read outs and criteria for decision-making** were given. OR Evaluation/data interpretation criteria were given.

Funding and competing interests

1. The **funding sources** for the study were stated.
2. Any **competing interests** were disclosed or it was explicitly stated that the authors did not have any competing interests.
3. Information on the **overall availability of the IPR protected components**, including whether they are commercially available or require a Material Transfer Agreement or other licensing agreements, was given.

Methods &
Protocols



**Importance in
Peer-review**



Publishers

Funders

Researchers

Platform
Managers

Affiliation	
eLife	Andy COLLINGS
InterChange Research	Annamaria CARUSI
EMBO	Bernd PULVERER
Springer Nature	Bronwen DEKKER
Bio-protocol and Harvard Medical School	Caroline SHAMU
University Lausanne	David PAMIES
F1000	David SADLER
Cell Press	Elisa De RANIERI
protocols.io	Emma GANLEY
Bio-protocol	Fanglian HE
EC-JRC	Ingrid LANGEZAAL
Science Europe	James MORRIS
EC-RTD	Jean-Francois DECHAMP
PLOS	Marcel LaFLAMME
FRESCI	Marco STRACCIA
NC3Rs	Matthew BROOKE
EC-JRC	Monica PIERGIOVANNI
EC-JRC	Pierre DECEUNINCK
EC-JRC	Sofia BATISTA LEITE
QUEST Center for Responsible Research	Tracey WISSGERBER
Bio-protocol and MIT	Vivian SIEGEL



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Ideally....



**Detailed, Clear,
Complete,
Transferable,
Reusable,
Dynamic,
Transparent,
Reliable, Reproducible
and Open**



Recommendations to Key Groups

AIM

- 1. Increasing awareness**
- 2. HOW to achieve good methods and protocols reporting**
- 3. Developing better means and tools to share and publish protocols**
- 4. Increasing funding and Investing in education on good reporting**

**Researchers
& their
Institutions**

**Editors
/Publishers**

**Funding
Agencies**

RECOMMENDATIONS

for

Researchers & their Institutions



- ✓ **Embed in the culture**
- ✓ Use of protocols
- ✓ Relevant guidelines
- ✗ Shortcut citations
- ✓ Method section linked to dynamic protocols
- ✓ Training
- ✓ Reward: CV, Prizes, awards..
- ✓ Embed on PhD thesis structure

RECOMMENDATIONS

for

Editors & Publishers

- ✓ **Promote access to detailed protocols**
- ✓ Ensure and allow enough detail – no word limit or copyright, include material reference
- ✓ Structured methods
- ✓ Link to protocols that are versioned, fork and not duplicate or supplementary
- ✗ Shortcut citations
- ✓ Update guides for authors and reviewers accordingly

RECOMMENDATIONS

for

Funding Agencies



- ✓ **Support open protocols**
- ✓ Request availability of study protocols
- ✓ Reward good practices
- ✓ Focus on Early Career researchers
- ✓ Fund dedicated actions and development of tools
- ✓ Fund training

WHY IS THIS RELEVANT FOR Non-ANIMAL METHODS?

Methods in the Regulatory arena

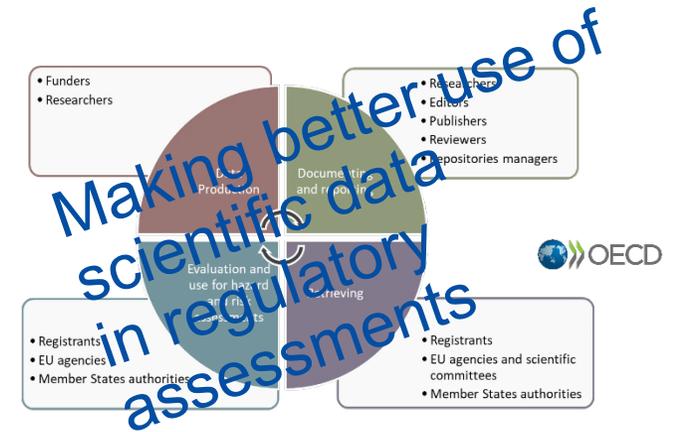
Regulatory Testing for Endocrine Disruptors; Need for Validated Methods and Integrated Approaches

Elise Grignard*, Kelly de Jesus and Philippe Hubert

PEPPER, Paris, France

Another aspect to take into account when considering the revision of the information requirements is the need of methods able to fulfil the three aspects of the criteria for the identification of EDs, as laid out in the Pesticides and Biocides Regulations, i.e., the

Identifying methods with a potential for validation and use in regulatory-relevant ED characterisation is a tricky issue for many reasons. For example, the published literature is mainly presenting toxicological properties of substances, and rarely describes methods in an extensive or transparent way. A list of data collection on methods was compiled by a group developing a case



Animal methods better covered for transparency

- ✓ Ethics
- ✓ Mandate by funding entities
- ✓ Guidelines enforced by journals
- ✓ Compulsory training
- ✓ More scrutinized at the facilities

Important to invest in the same type standards for non-animal methods



Phase 0

Workshop

Identification of the problem and possible actions.

Phase 1

Commitment and Actions Document

Working in separate working groups

Phase 2

YOU ARE HERE

Engaging with Key players

Open the document to consultation/feedback from others.

Phase 3

Final document and implementation of the actions

The document open to all and further engagement.



Improve Reporting of Protocols and Methods to

Increase Transparency

Increase Reproducibility

Increase trust in methods & data

Advance in Science

adapted from pixabay

Acknowledgments

PRO-MaPs

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Evangelos DASKALOPOULOS, EC-JRC

Francesca PISTOLATTO, EC-JRC

Ivana CAMPIS, EC-JRC

Thank you

JRC SUMMER SCHOOL ON NON-ANIMAL APPROACHES IN SCIENCE

Towards Sustainable Innovation

23-26 MAY 2023
JRC ISPRA



Sofia.BATISTA-LEITE@ec.europa.eu;



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EU Science Hub -
Joint Research Centre



Joint Research Centre



EU Science Hub



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