

Quality, fast, cheap: choose two.

Practical advice on how to conduct better Science

Adrian Smith

adrian.smith@norecopa.no

[@adrian_3r](#)

norecopa.no/quality



<https://norecopa.no>

Norecopa: PREPARE for better Science

norecopa.no : an updated overview of global 3R resources

NORSK ENGLISH

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norecopa.no / More resources / Experimental design and reporting

Design and reporting of animal experiments

This page supplements advice given in [Section 4 of the PREPARE guidelines](#). PREPARE covers all aspects of design (including animal and facility related issues).

[Resources about contingency plans and preparedness](#), relevant to the Covid-19 pandemic

This page contains a collection of links to resources on the more "mathematical" aspects of experimental design and analysis. Direct oversight by a statistician is likely to be more effective than reliance on self-education [websites](#), although many of these are excellent. The following points should be considered

1. A clear hypothesis and descriptions [a priori](#) of primary and secondary outcomes, [to avoid HARKing](#) (see also [Bishop, 2019](#)).
2. Steps to minimise numbers and suffering of animals by [appropriate statistical analysis](#), including [the use of pilot studies](#).
3. Decisions on [the power and significance levels to be used](#).
4. Definition of the [experimental unit](#) and number of animals in each unit
5. Choice of [sample size](#) and gender, age and/or developmental stage
6. Avoidance of bias, including "blinding" and randomisation (the procedure should be specified)
7. Inclusion and exclusion criteria

over 10,000 webpages
approx. 1,000 hits daily
7-8 detailed newsletters per year

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September 2024



- > [Ergonomics and Well-being in the Animal Facility](#), online (Søren Hald), 2 September 2024
- > [The ethical issues related to animal research](#) (COST Action IMPROVE workshop, [programme](#)), Istanbul, 2-3 September 2024
- > [Organ-on-chip-workshop](#), Jena, 2-4 September 2024
- > [Organ-on-chip Summer School](#), Tübingen, 2-6 September 2024
- > [Practical Approaches to Each of the 3Rs](#), webinar series, 4-5 & 11-12 September 2024
- > [Good Research Practices in Biomedical Animal Research](#), Utrecht, 4-6 September 2024
- > [EUROTOX 2024 \(58th Conference of the European Societies of Toxicology\)](#), Copenhagen, 8-11 September 2024
- > [5th Annual Aquatic Life Conference](#), online, 9-10 September 2024
- > [Refining Rodent Oral Administration Protocols: Exploring Advantages, Limitations and Recent Developments](#), webinar (Paulin Jirkof), 10 September 2024
- > [The use of animals in education, teaching and training \(ANZCCART Conference\)](#), Christchurch, 10-12 September 2024
- > [The gut microbiome of research animals - Implications and remedies for reproducibility and translatability](#), webinar (Aaron Ericsson), 11 September 2024
- > [61st Annual Meeting of GV-SOLAS](#), Würzburg, 11-13 September 2024
- > [Developing Coaching and Mentoring skills for First Line Managers](#), hybrid course, 17 September and 3 December 2024
- > [EUSAAT congress](#), Linz, 18-20 September 2024
- > [UK Animal welfare legislation](#), hybrid course, 18 & 25 September 2024
- > [Communicating animal research via social media](#), UAR webinar, 19 September 2024
- > [7th IC-3RS Symposium](#), Brussels, 19 September 2024
- > [GA-rodents: Colony management, breeding strategies and genetic quality control](#), London, 19-20 September 2024
- > [Lab Research Publication School](#), online, 23-26 September 2024
- > [How AWERBs can support Named Persons](#), online RSPCA event, 24 September 2024
- > [Laboratory skills](#), hybrid course, 25 September & 2 October 2024
- > [Die Rolle des Tierpflegepersonals in der Diskussion und Kommunikation über Tierversuche](#), webinar (Roman Stilling), 27 September 2024
- > [Responsible Aquatic Animal Research: Critical, Challenging and Creative Thinking](#), online course, 30 September - 3 October 2024
- > [Anaesthesia for minor procedures](#), online, 30 September - 1 October 2024
- > [11th Annual International Zebrafish Husbandry Course](#), Buguggiate, 30 September - 4 October 2024

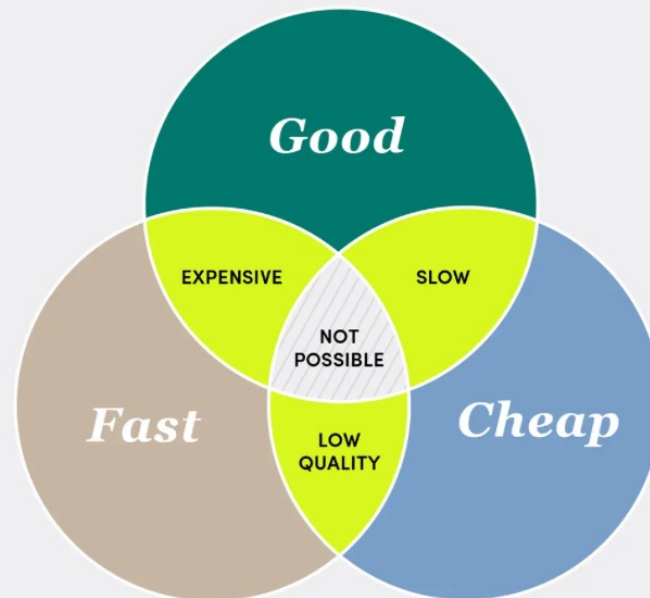
norecopa.no/meetings/meetings-calendar

Fast, Good, or Cheap

.....

The Iron Triangle

Weighing the opposing forces of quality, speed and cost against each other.



b.

Cheap + Fast = low quality
Good + Cheap = too slow
Fast + Good = expensive

Good isn't optional

”what is good quality Science?”

- replacement if possible
- reduction and refinement if not possible to replace
- valid data (a true treatment effect)
- reproducible and translatable experiments
- best possible animal welfare
- health & safety (of animals and people)
- a culture of care at the animal facility
- communication of best practice to others



colourbox.com



Prepare



Care



Share



Flag

Ignorance of ways to achieve these creates bad science

We need to evaluate both the quality and the standard of our research

←  r/Shittyaskflying · 1 yr. ago
DaveWick420

Flying back in the 80s on Hawaiian air looked fun!



<https://boeing.com>



https://www.reddit.com/r/Shittyaskflying/comments/13b67ut/flying_back_in_the_80s_on_hawaiian_air_looked_fun

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Some of the issues scientists may have underestimated:

training in novel procedures (animals and staff)
time spent recording data
extra staff at evenings / weekends

extra protective clothing
additional cages/tanks and equipment

cost of disposal of hazardous waste
cost of decontamination of the animal facility

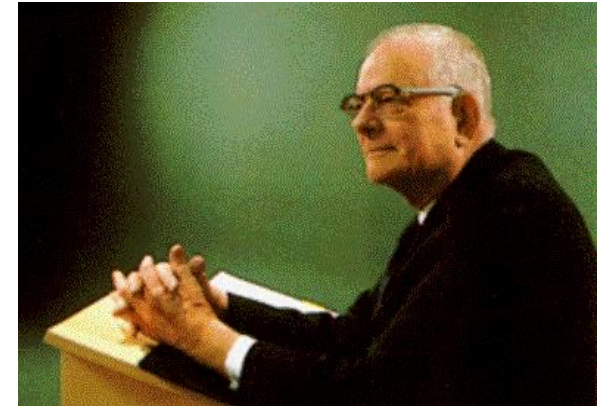
These issues must be factored into the cost of an experiment

How do others achieve success and reproducibility?



<https://www.meonuk.com/runway-markings-explained>

Standard Operating Procedures are the clue



“The use of standards (i.e. SOP’s) frees resources within problem areas that have already been solved and have become a routine, so that these resources can instead be used for creative work in areas where problems still exist”

W. Edwards Deming

without SOP's:



'Our long experience and modern coffee machines are your guarantee of quality' (?)

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SOPs are like aviation checklists

- Reduce risk of **forgetting** to carry out vital actions
- Ensure checks are carried out in the **correct sequence**
- Encourage **cooperation** and **cross-checking** between crew members and ground staff
- Make sure that everyone is "**on the same page**"

10-15 checklists even on short routine flights



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Hudson River, 2009

en.wikipedia.org

All 155 passengers and crew saved



15.25.33	-01.38	Kaptein	Cockpit	V one, rotate
15.25.38	-01.33	Kaptein	Cockpit	positive rate
15.25.39	-01.32	Styrmann	Cockpit	Gear up please
15.25.39	-01.32	Kaptein	Cockpit	Gear up
15.26.37	-00.34	Kaptein	Cockpit	Uh what a view of the Hudson today
15.26.42	-00.29	Styrmann	Cockpit	Yeah
15.27.07	-00.04	Kaptein	Cockpit	After takeoff checklist complete
15.27.10	-00.01	Kaptein	Cockpit	Birds
15.27.11	-00.00	Styrmann	Cockpit	Whoa
15.27.11	00.00			
15.27.12	+00.01	Kaptein	Cockpit	Oh ---
15.27.13	+00.02	Styrmann	Cockpit	Oh yeah
15.27.14	+00.03	Styrmann	Cockpit	Uh oh
15.27.15	+00.04	Kaptein	Cockpit	We got one rol... both of 'em rolling back
15.27.18	+00.07	Kaptein	Cockpit	Ignition, start
15.27.21	+00.10	Kaptein	Cockpit	I'm starting the APU
15.27.23	+00.12	Kaptein	Cockpit	My aircraft
15.27.24	+00.13	Styrmann	Cockpit	Your aircraft
15.27.28	+00.17	Kaptein	Cockpit	Get the QRH... loss of thrust on both engines
15.27.32	+00.21	Kaptein	Radio	Mayday mayday mayday. Uh this is Cactus fifteen thirty [sic] nine, hit birds. We've lost thrust on both engines. We're turning back towards LaGuardia.



- A. Animal Care and Use Program**
- B. Animal environment, Housing and Management**
- C. Veterinary Care**
- D. Physical plant**

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63 pages!

www.aalac.org/program-description

Good Laboratory Practice (GLP)

- Planning
- The actual experiment
- Notetaking
- Reporting
- Monitoring
- Archiving

A guarantee for animal welfare?

Depends upon the SOPs (Standard Operating Procedures)

Make sure that everyone understands and uses the SOP ...





[wikipedia](#)

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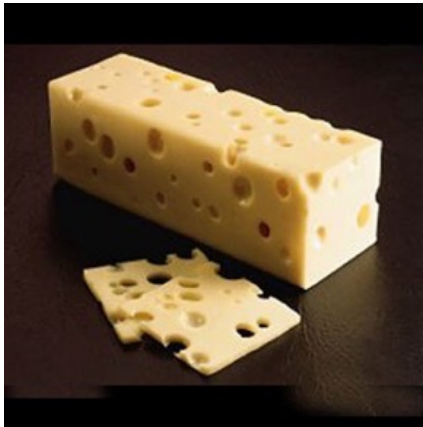
Boeing's 737 factory in Renton will halt its production line on January 25 so employees can focus on "quality." [Courtesy: Boeing]

The sessions allow all teammates who touch the airplane to pause, evaluate what we're doing, how we're doing it, and make recommendations for improvement.

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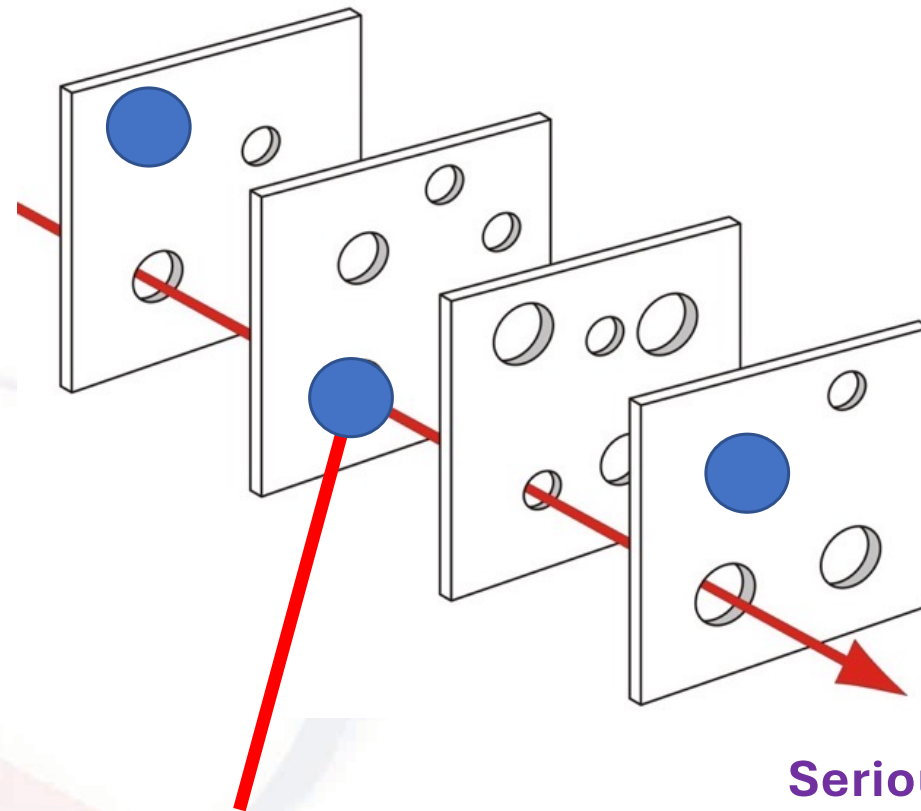
<https://www.flyingmag.com/boeing-to-shut-down-facility-for-day>

“Threat and Error Management”



eaugallecheese.com/Swiss-Cheese

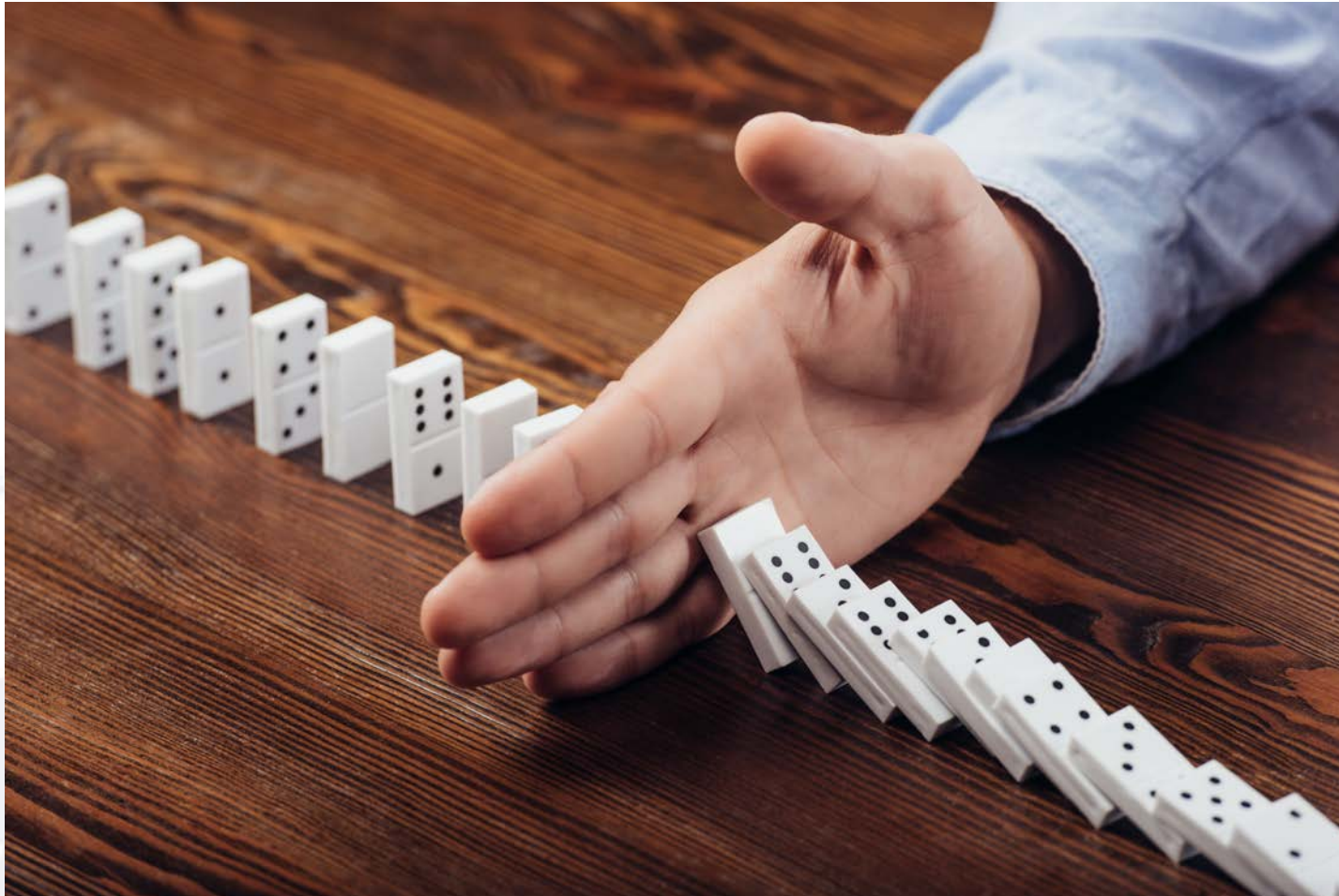
Embrace the opportunity to learn something from an incident, reducing the risk for future incidents



Weaknesses / dangers

Serious incidents

wikipedia.org/wiki/Swiss_cheese_model



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An analogy from NASA:

Animals are complex, **tightly-coupled** organisms

Identify the **critical points**
in your experiment

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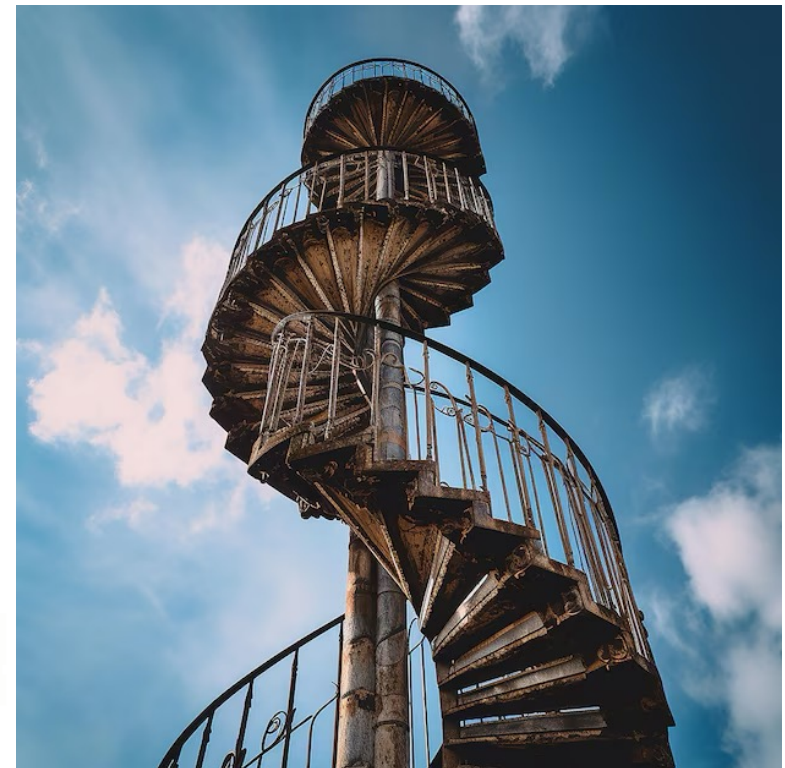
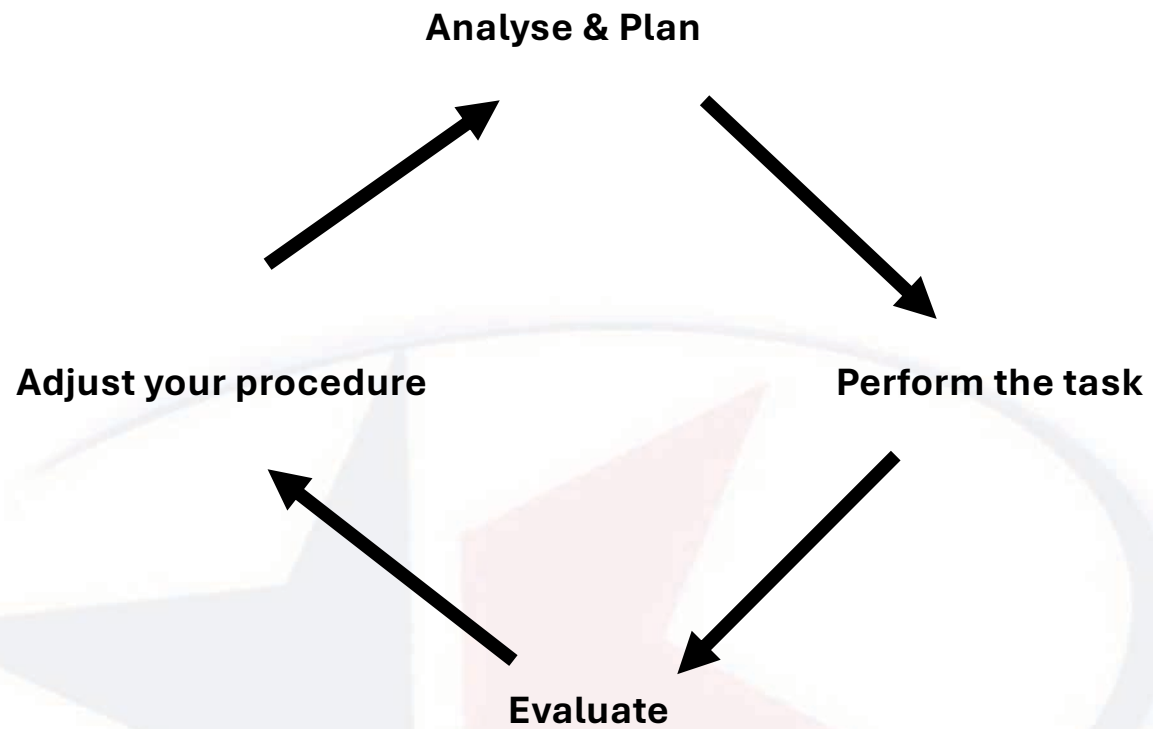
cbsnews.com
colourbox.com no-wikipedia.org

Contingency and redundancy

Anything that can go wrong, will go wrong (Murphy's Law)
when it's least convenient (Sod's Law)



Photo: NMBU



freepik.com

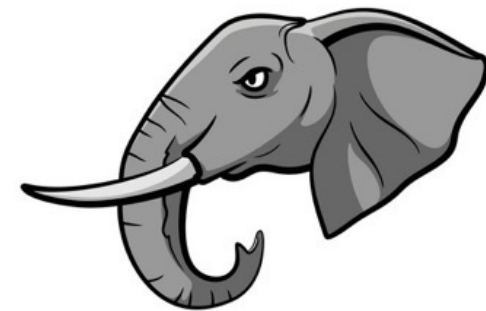
The pathway to open (better) science



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<https://riojournal.com/article/105198>

The elephants in the room...



...the largest of them all is inadequate attention to detail during planning of animal studies, including collaboration with the animal facility from day one

<https://www.forbes.com/sites/rodgerdeanduncan/2014/10/14/is-there-an-elephant-in-the-room-name-it-and-tame-it>

Some of the elephants...

- poor literature searches
- lack of humane endpoints
- poor study design, including choice of procedures
- vague distribution of work and costs between the scientists and the animal facility
- insufficient evaluation of the facility's competence and infrastructure
- too little attention to transport and acclimation
- ignoring health risks for all involved
- lack of standard procedures for necropsy
- poor planning of waste disposal
- little discussion about the fate of the animals





ARRIVE

PREPARE

Reporting guidelines like ARRIVE describe the experiment. Guidelines like PREPARE are used to plan the experiment (choose the «ingredients» and «baking time»)

"We ARRIVED, because we were PREPARED"

- ✓ *Better Science*
- ✓ *Improved animal welfare*
- ✓ *Advancement of the 3Rs*
- ✓ *Safer working environment*



PREPARE:

Planning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence

PREPARE covers 15 topics:

Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

Methods

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Items in pink are not typically highlighted in reporting guidelines



PREPARE

The PREPARE Guidelines Checklist
Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith¹, R. Eddie Clutton², Elliot Lilley¹, Kristine E. Aa. Hansen¹ & Trond Bratteli¹

¹Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; ²Animal Welfare and Ethical Review Centre, School of Veterinary Medicine, University of Bristol, Langford House, Langford House, Langford, Wiltshire, BA15 2LJ, UK; ³Research Animals Department, Science Group, Middlesbrough, EH25 9RG, U.K.; ⁴Research Animals Department, Science Group, Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; ⁵Division for Research in Sciences, 5020 Bergen, Norway.

PREPARE¹ consists of planning guidelines which are complementary to the ARRIVE² guidelines. PREPARE covers the three broad areas which determine the quality of the study:

1. Formulation of the study
2. Dialogue between scientists and the animal facility
3. Quality control of the components in the study

The topics will not always be addressed in the order in which the checklist can be adapted to meet special needs, such as field studies, since in-house experiments are dependent upon their own facilities, with links to global resources, at <https://norecopa.no/>. The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

+ 2 online versions
35 languages

Topic	Recommendation
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding and division of labour	<input type="checkbox"/> Arrange meetings with all relevant staff when early plans for the project exist. <input type="checkbox"/> Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. <input type="checkbox"/> Discuss and disclose all expected and potential costs. <input type="checkbox"/> Construct a detailed plan for division of labour and expenses at all stages of the study.
of the facilities, to evaluate building and equipment standards and needs. nes of extra risk.	
ence of staff members and the need for further education or training prior	
in collaboration with the animal facility, for all persons and animals affected study.	
duce, specific guidance for all stages of the project.	
nent, decontamination, and disposal of all items in the study.	
(C) Quality control of the components in the study	
9. Test substances and procedures	<input type="checkbox"/> Provide as much information as possible about test substances. <input type="checkbox"/> Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	<input type="checkbox"/> Decide upon the characteristics of the animals that are essential for the study and for reporting. <input type="checkbox"/> Avoid generation of surplus animals.
11. Quarantine and health monitoring	<input type="checkbox"/> Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	<input type="checkbox"/> Attend to the animals' specific instincts and needs, in collaboration with expert staff. <input type="checkbox"/> Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).
13. Experimental procedures	<input type="checkbox"/> Develop refined procedures for capture, immobilisation, marking, and release or rehoming. <input type="checkbox"/> Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	<input type="checkbox"/> Consult relevant legislation and guidelines well in advance of the study. <input type="checkbox"/> Define primary and emergency methods for humane killing. <input type="checkbox"/> Assess the competence of those who may have to perform these tasks.
15. Necropsy	<input type="checkbox"/> Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

References
 1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Bratteli T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
 2. Kilkenny C, Browne WJ, Cuthill IC et al. Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLoS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

Further information
<https://norecopa.no/PREPARE> | post@norecopa.no | [@norecopa](https://twitter.com/norecopa)

- 3-Ethical issues, harm-benefit assessment and humane endpoints ^
- 3a Construct a lay summary.
- 3b In dialogue with ethics committees, consider whether statements about this type of research have already been produced.
- 3c Address the 3Rs (Replacement, Reduction, Refinement) and the 3Ss (Good Science, Good Sense, Good Sensibilities).
- Assessment and justify any likely animal harm.
- 3f Discuss the learning objectives, if the animal use is for educational or training purposes.
- 3g Allocate a severity classification to the project.
- 3h Define objective, easily measurable and unequivocal humane endpoints.
- 3i Discuss the justification, if any, for death as an end-point.
- 4-Experimental design and statistical analysis v

- 5. Have the experiments been carried out before, and is any repetition justifiable?
- 6. What [approaches to reduce distress](#) have been considered?

3a Construct a lay summary.

General principles For fish researchers

- 1. Have national or local research ethics committees already produced statements relevant to the research being planned? Consideration should also be paid to the broader context of the research. For example, research directed at increasing the productivity of farming at the expense of (or without improving) individual animal welfare, or wildlife research whose primary aim is population management.

Links to quality guidelines and scientific papers worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design

- 3. Have the Three S's ([Good Science, Good Sense and Good Sensibilities](#)) been addressed? Sufficient time should be allocated to this point, since two of the three S's are highly subjective, but equally important. The use of commonsense and critical anthropomorphism are justifiably part of the work to assess the impact of research on animals, not least when a scientific evidence base does not exist.
- 4. Does the proposed study have a clear rationale and scientific relevance, and what will be the next step if the hypothesis is supported or rejected?
- 5. Have the experiments been carried out before and is any repetition justifiable?
- 6. What [approaches to reduce distress](#) have been considered?
- 7. Will the project undergo [pre-registration](#) and will negative results be published, to avoid publication bias?

Many more [links to resources on ethics are available here](#).

Details about pre-registration of animal studies and reporting of critical incidents are to be found in the section on [Experimental Design and Statistical Analysis](#).

Harm-Benefit Assessment

norecopa.no/PREPARE/film
3-minute whiteboard film



TOO LATE!!

HOW CAN WE IMPROVE ANIMAL STUDIES?

WE ARRIVED BECAUSE WE WERE PREPARED
VISIT: NORECOPA.NO/PREPARE

PRECISION
REPLICABILITY
HEALTH AND SAFETY
TRANSLATABILITY

PILOTS
CABIN CREW
GROUND STAFF
AIR TRAFFIC CONTROLLERS

RECIPE
NORECOPA.NO/PREPARE

SUGGESTIONS FOR
• GUIDELINES
• DATABASES
• INFORMATION CENTRES
• JOURNALS, DISCUSSION LISTS, ETC.

COLLABORATION
• ANIMAL CARERS AND TECHNICIANS
• VETERINARIANS
• FACILITY MANAGERS
• SCIENTISTS AND THEIR STAFF
• ANIMAL WELFARE AND ETHICS COMMITTEES
• REGULATORS

THIS WAY WE CAN
• REDUCE THE RISK OF ANIMALS SUFFERING
• IMPROVE OUR METHODS - DO BETTER SCIENCE!
• WRITE BETTER APPLICATIONS
• IMPROVE MANUSCRIPT QUALITY

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PREPARE FOR BETTER SCIENCE

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PILOTS



CABIN CREW



GROUND
STAFF



AIR TRAFFIC
CONTROLLERS



EU / National



Facility



Project



Procedure

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Quick, cheap and dirty?



- because it's the number of publications in high-status journals that counts
- because the funders approved the research, so it must be good
- because our PI insisted that we used his method
- because the method has been approved and published previously
- because we used poorly trained assistants
- because we forgot about the costs of decontamination, waste disposal and compassion fatigue



*Don't give up!
Ask for help!*

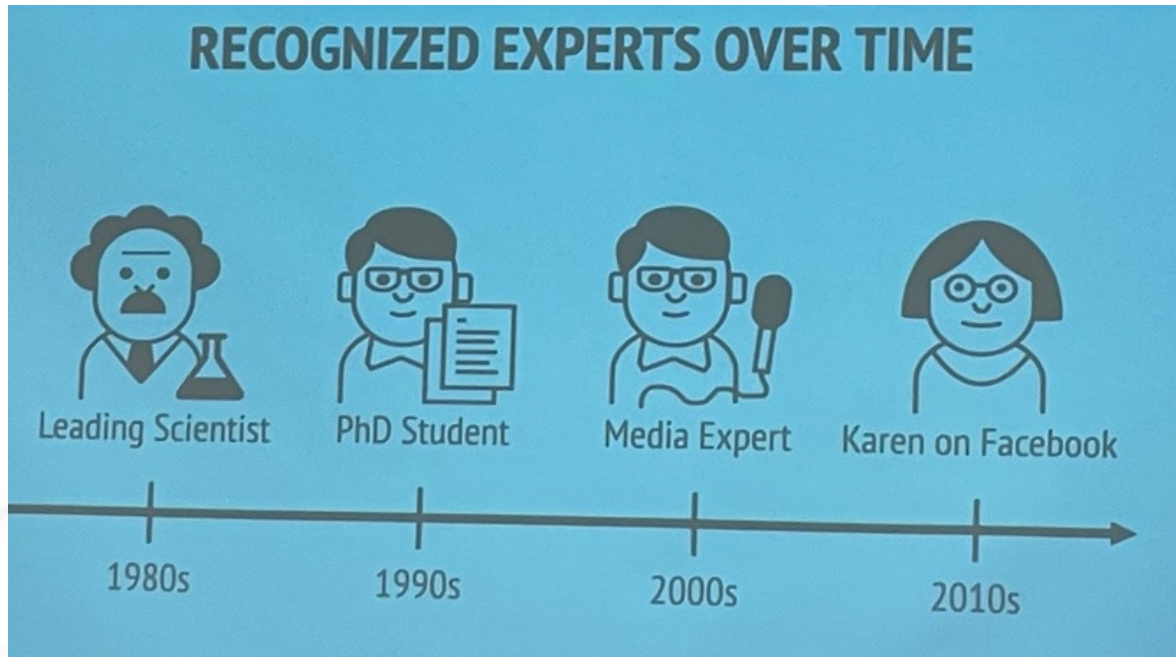
The difficulty is, that changing a university is like moving a graveyard, you get no help from the people inside!

Geoffrey Boulton, University of Edinburgh

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<https://eher.org/changing-a-university-is-like-moving-a-graveyard>

<https://www.weedonbucks.org.uk/index.php/parish-council/weedon-chapel-graveyard>







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Dyrevernalliansen



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Thank you for listening!