PREPARE before you ARRIVE:

How to plan animal experiments

norecopa.no/Barcelona

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7,600 webpages
80,000 references
22,000 unique links
160,000 pageviews/year

70,000 euros
International consensus meetings

Harmonisation of the Care and Use of:
  Fish (2005)
  Wildlife (2008)
  Fish (2009)
  Agricultural animals (2012)
  Wildlife (2017)

https://norecopa.no/meetings

All presentations and consensus statements are on the internet: a lasting resource
Laura-Kim Schüller, Veterinary School, Berlin

Rikke Langebæk, University of Copenhagen

Workshop 11. april i Oslo

norecopa.no/education-training/homemade-educational-materials
This has the undesirable effect of creating pressure on the throat, which is likely to be unpleasant for the animal.

http://bitly.com/scruff-technique
TRES DEDOS MEJOR QUE DOS
Refinamiento de la técnica de scruffing (piel de la nuca)

http://bitly.com/scruff-technique
An useful additional (but largely unknown) tool...
Carol M. Newton (1925-2014)

The three S’s

• Good Science
• Good Sense
• Good Sensibilities

norecopia.no/3S

Meetings calendar

(Links to a selection of past meetings can be accessed here)

› ESLAV-ECLAM-AAALAC-SECAL Conference [link], Barcelona, 15-16 October 2018
› Modeling the Mammalian Microbiota Host Superorganism, Current Tools and Challenges [link], Paris, 15-16 October 2018
› 20th International Congress on In Vitro Toxicology (ESTIV2018) [link], Berlin, 15-18 October 2018
› Construction Noise and Vibration: Best Practice for Minimizing Impacts on Animals, Ongoing Research Studies, and Relationships with Scientists [link], AALAS webinar, 17 October 2018
› International Veterinary Simulation in Teaching (InVeST) conference [link], Knoxville, 17-19 October 2018
› New Prospects in Interdisciplinary Research: 1st International Symposium of ICAR3R [link], Giessen, 18-19 October 2018
› Care, Use and Welfare of Marmosets as Animal Models for Gene-Based Biomedical Research [link], Washington, 22-23 October 2018
› Literature searches for alternatives to animal experiments [link], webinar, 25 October 2018
Norecopa’s English-language newsletters
Swiss survey highlights potential flaws in animal studies

Poor experimental design and statistical analysis could contribute to widespread problems in reproducing preclinical animal experiments.

Ramin Skibba
20 December 2016

Pain management in pigs undergoing experimental surgery; a literature review (2012–4)

A. G. Bradbury, M. Eddleston, R. E. Clutton


Published: 03 October 2015

with analgesic properties, but only 87/233 (37%) described postoperative analgesia. No article provided justification for the analgesic chosen, despite the lack of guidelines for analgesia in porcine surgical models and the lack of formal studies on this subject. Postoperative pain assessment was reported in only 23/233 (10%) articles. It was found that the reporting of postoperative pain management in the studies was remarkably low, reflecting either under-reporting or under-use. Analgesic description, when given, was frequently too limited to enable reproducibility. Development of a

More than 70% of researchers have tried and failed to reproduce another scientist’s experiments, and more than half have failed to reproduce their own experiments. Those are some of the telling figures from Nature’s survey of 1,576 researchers who took a brief online questionnaire on reproducibility in research.
Why is it taking so long to improve reproducibility?

Berti & Cima 1955, quoted in Öbrink and Rehbinder
Hurni 1969, quoted in Öbrink and Rehbinder

Fig 6 The generation of experimental animals from genotype over phenotype to dramatype
There are many guidelines for reporting animal studies, e.g.

- GV-Solas, 1985
- Öbrink & Waller, 1996
- Jane Smith et al., 1997
- ARRIVE Guidelines, 2010 (Kilkenny et al., NC3Rs)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals
  e.g. Nature’s Reporting Checklist
Are we wasting time discussing the quality of the lock on the door of the stable from which the horse has already bolted?
PREPARE

ARRIVE
Why do we need PREPARE when we have ARRIVE?

The ARRIVE guidelines claim that they ‘provide a logical checklist with all the things that need to be considered when designing an experiment’.*

In our experience when planning animal research, a number of additional points need to be addressed at the planning stage.

These items improve

✔ study quality and scientific validity
✔ animal welfare
✔ health and safety for both the animals and the humans affected directly or indirectly by the work

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.
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
PREPARE: guidelines for planning animal research and testing

Adrian J Smith1, R Eddie Clutton2, Eilidh Lilley3, Kristine E Aa Hansen4 and Trond Bratteid5

Abstract
There is widespread concern about the quality, reproducibility and translatability of studies involving research animals. Although there are a number of reporting guidelines available, there is very little overarching guidance on how to plan animal experiments, despite the fact that this is the logical place to start ensuring quality. In this paper we present the PREPARE guidelines: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies: formulation, dialogue between scientifics and the animal facility, and quality control of the various components in the study. Some topics overlap and the PREPARE checklist should be adapted to suit specific needs, for example in field research. Advice on use of the checklist is available on the Norcopa website, with links to guidelines for animal research and testing, at https://norcopa.no/prepare.

Keywords
Guidelines, planning, design, animal experiments, animal research

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Introduction
The quality of animal-based studies is under increasing scrutiny, for good scientific and ethical reasons. Studies of papers reporting animal experiments have revealed alarming deficiencies in the information provided, even after the production and journal endorsement of reporting guidelines. There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research. This can, for example, contribute towards the failure of drugs when they come into human trials. These issues come in addition to other concerns, not unique to animal research, about publication bias, which tends to favour the reporting of positive results and can lead to the acceptance of claims as fact. This has understandably sparked a demand for robust ways when planning experiments involving animals. Reporting guidelines alone cannot solve the problem of wasteful experimentation, but thorough planning will increase the likelihood of success and is an important step in the implementation of the 3Rs of Russell & Burch (replacement, reduction, refinement).

The importance of attention to detail at all stages in our experience, often underestimated by scientists. Even small practical details can cause omissions or artefacts that can ruin experiments which in all other respects have been well-designed, and generate health risks for all involved. There is, therefore, in our opinion, an urgent need for detailed but overarching guidelines for researchers on how to plan animal experiments which are safe and scientifically sound, address animal

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### The PREPARE Guidelines Checklist

**Formulation of the study**

- Prepare a clear hypothesis, with primary and secondary outcomes.
- Consider the use of systematic reviews.
- Decide upon databases and information specialists to be consulted, and construct search terms.
- Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs.
- Assess the reproducibility and translatability of the project.

**Legal issues**

- Ensure the research is performed in accordance with relevant legislation, including the research conducted at the institution.

**Ethical issues**

- Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety.
- Ensure that all relevant ethical guidance documents are followed on project evaluation.

**Harm-Benefit Assessment and humane endpoints**

- Construct a key summary.
- In dialogue with ethics committees, consider whether statements about this type of research have already been produced.
- Address the 3Rs (Replacement, Reduction, Refinement) and the 5Is (Good Science, Good Senior, Good Supervisor).
- Consider pre-registration and the publication of negative results.
- Perform a Harm-Benefit Assessment and justify any likely animal harm.
- Discuss the learning objectives, if the animal use is for educational or training purposes.
- Evaluate a severity classification to the project.
- Define objectives, easily measurable and unequivocal, humane endpoints.
- Discuss the justification, if any, for the death of an animal.

### The ARRIVE Guidelines Checklist

#### Animal Research: Reporting In Vivo Experiments

**Objectives**

1. Provide as accurate and concise a description of the content of the article as possible.

2. Formulate the study and animal facility.

3. Quality control of the components in the study.

4. Consideration of the ethical issues.

5. Discussion of the ethical issues.


7. Experimental design and statistical analysis.

8. Experimental animals.

9. Experimental procedures.

10. Background.

11. Aim of the study.


13. Results.

14. Discussion.

15. Conclusion.
PREPARE: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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 highlighted in ARRIVE
In addition to the checklist, much more information is available on norecopa.no/PREPARE

Links to quality guidelines worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design
Contract between the animal facility and the research group

The division of labour and responsibilities between the two parties, with the aim of clarifying all stages of the experiment and ensuring that all necessary parameters are recorded.

https://norecopa.no/prepare/prepare-checklist
An example: i.v. injection of a radioactive isotope:

norecopa.no/PREPARE

PREPARE Checklist
1-Literature searches  2-Legal issues
3-Ethical issues, Harm-Benefit Assessment and humane endpoints  4-Experimental design and statistical analysis
5-Objectives and timescale, funding and division of labour  6-Facility evaluation
7-Education and training  8-Health risks, waste disposal and decontamination
9-Test substances and procedures  10-Experimental animals
11-Quarantine and health monitoring  12-Housing and husbandry
13-Experimental procedures  14-Humane killing, release, re-use or re-homing
15-Necropsy

Comparison with ARRIVE
Crisis management in anaesthesia - what can we learn from airline pilots?

Colin Dunlop  BVSc DACVA
Nathan Koch  BVSc BSc

Pilots use checklists, even on routine flights ...
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