

Experiences with planning animal studies: how to improve scientific output and animal welfare

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norecopa.no/ASAB

Disclosures: Secretary of Norecopa & lead author of the PREPARE guidelines

"better scientific output and animal welfare?"

- valid data (a true treatment effect)
- reproducible and translatable experiments
- best possible animal welfare (happy animals give better science)
- health & safety (of animals and people)
- a culture of care in the research group
- communication of best practice to others
- more ethically defensible studies





How do other professionals achieve

- precision
- reproducibility
- translatability
- safety

norecopa

A case study



Birdstrike Both engines failed

travelandleisure.com/airlines-airports/what-happens-when-planes-hit-birds

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 to	day
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 rolli	ng 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 t	ooth engines
15.27.32	+00.21	Kaptein	Radio	Mayday mayday mayday. Uh this [sic] nine, hit birds. We've lost thru	ust on both engines.

Norecopa: PREPARE for better Science

no.wikipedia.org/wiki/US_Airways_Flight_1549





16 seconds after the birdstrike...



flightsafety.org

less than 3 minutes in the air before crash-landing



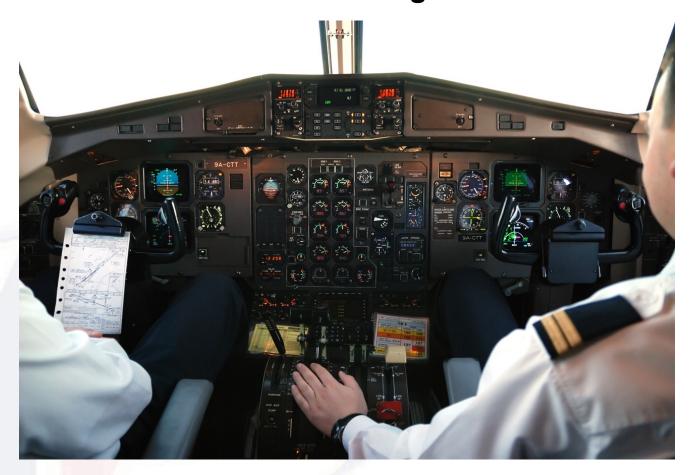


All 155 passengers and crew saved

en.wikipedia.org



10-15 checklists even on short routine flights





Checklists

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



Pilots achieve reproducibility...



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



...and precision in a complex and variable environment.



norecopa.no/PREPARE/film

3-minute whiteboard film



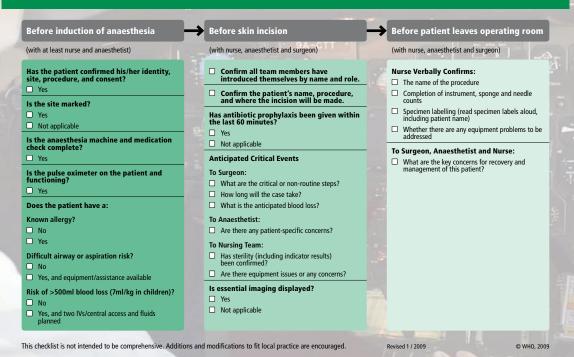


Surgical Safety Checklist



Patient Safety

A World Alliance for Safer Health Care



THE CHECKLIST MANIFESTO
HOW TO GET THINGS RIGHT

amazon.com/gp/product/0312430000

who.int/patientsafety/topics/safe-surgery/checklist/en





My opinion

- Based on planning, conducting and supervising animal research, and holding courses in Laboratory Animal Science since the early 1980's
- Based on managing accredited lab animal facilities
- One of the greatest challenges to validity and reproducibility lies in the animals that scientists use and the way they use them
- I suspect that many scientists are unaware of the size of this challenge, or they assume that the animal facility is dealing with it



Issues that are frequently raised about the "reproducibility crisis"...

- 1. Publication bias (reporting only positive results)
- 2. Low statistical power
- 3. P-value hacking (manipulating data to obtain significance)
- 4. HARKing (Hypothesizing after the results are known)
- 5. Lack of randomisation and blinding

norecopa.no/concerns

nature human behaviour



Perspective | Open Access | Published: 10 January 2017

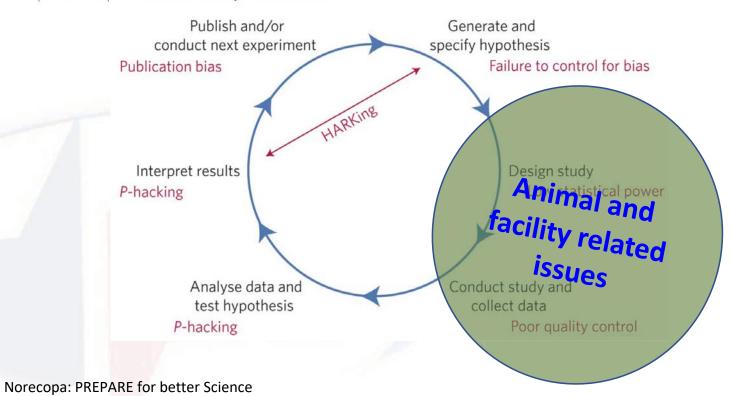
A manifesto for reproducible science

Marcus R. Munafò ☑, Brian A. Nosek, Dorothy V. M. Bishop, Katherine S. Button, Christopher D. Chambers, Nathalie Percie du Sert, Uri Simonsohn, Eric-Jan Wagenmakers, Jennifer J. Wa

Figure 1: Threats to reproducible science.

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations | From: A manifesto for reproducible science



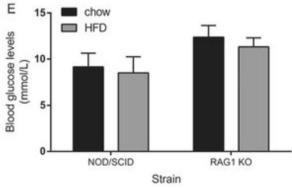






The scientist





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The mouse

Breeding
New social groups
Transportation
Acclimation to research facility
Allocation to experimental group
Adaptation to new diet
Handling and immobilisation

Blood sampling

often also: injections, gavaging, surgery pain and distress developing illness and death

Neglected Factors in Pharmacology and Neuroscience Research: Biopharmaceutics, Animal Characteristics, Maintenance, Testing Conditions

By Claassen, Volkert

Record number: 13335 (legacy id: 6153)

The objective of this book (2) is to indicate those variables which in general may need a better control. Examples, gathered from the literature, are presented to illustrate the impact that those neglected variables may have on various characteristics. The book presents a series of representatives studies from a broad field of interest so that insight can be obtained about the potential effects of these parameters in experimental outcomes. In this way, an impetus should be given to the critical consideration of test design and limitations of conclusions from experimental results. In part, the book is written as a reaction to frustrations endured during pharmacological research of many years' standing, and therefore the choice of examples from the literature is largely related to this discipline. As pharmacological research is to a large extent based on the other life sciences, this volume may be of interest to a much broader audience. This may certainly



be or interest to a much product addition. This may certainly be the case for pharmacokineticists and toxicologists for whom drugs are the main object of study. This book may also help to improve test designs for biochemists and physiologists, not only when using drugs as tools in their experiments, but also to improve generally the control of animal using drugs as tools in their experiments, but also to improve generally the control of animal characteristics and test conditions. This book is Volume 12 in a series entitled *Techniques in the Behavioral and Neural Sciences*.

Comments & References: First Edition. 496 pages. Paperback. A review is available in Laboratory Animals . April 1996, Volume 30 (2).

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Volkert Claassen, 1994

Review:

'This book is essential reading for anybody that wishes to take the problem of experimental variability seriously.

There are no magic cures offered for experimental problems, but there are many explanations offered within this book. A worthwhile addition to any library.'

norecopa.no/textbase/neglected-factors-in-pharmacology-and-neuroscience-research-biopharmaceutics-animal-characteristics-maintenance-testing-conditions

A contract between the animal facility and the research group

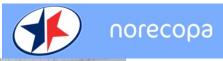
Division of labour, responsibilities and cost

Clarifying all stages of the experiment

Ensuring that all necessary data are recorded



	Animal	Researcher	Not
	facility		applicable
Animal:			
Arrival date			
Species			
Strain/stock and substrain			
Supplier (full name and address) or bred on the premises			
Number and sex			
Age, weight, stage of life cycle on arrival			
Pre-treatment (surgical or medical) from supplier			
Quality (e.g. SPF, germ-free, gnotobiotic, conventional)			
Acclimation time before the start of the experiment			
Time and duration of fasting (with/without water and bedding)			
Environment:			
Type of housing: barrier/conventional			
Temperature (mean ± variation)			
Light schedule			
Relative humidity (mean ± variation)			
Number of air changes in the animal room/cabinet per hour			
Environmental enrichment			
Housing:	*		
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			





https://norecopa.no/prepare/6-facility-evaluation/master-plan-and-sops/contingency-plan



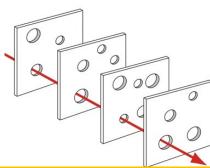
A Contingency Plan, based upon risk assessment

- Access to emergency services (police, fire, medical and veterinary help, security guards, personnel transport in cases of acute illness)
- Means of communication with staff members at all levels
- SOPs for acute illness, including
- Many needed to be revised in the light of COVID-19

norecopa.no/be-prepared

- corrosive injuries
- and forms for reporting such injuries
- Firefighting, evacuation of personnel and animals
- Access to specialist services (e.g. ventilation system, plumbing, electrical installations, suppliers of equipment)
- Routines in cases of power failure, water leaks and (if applicable) natural disasters such as flooding
- Routines for emergency killing of animals
- Routines in cases of threats to the facility or personnel

https://norecopa.no/prepare/6-facility-evaluation/master-plan-and-sops/contingency-plan



Temporary staff at weekends and holidays





Program Description

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

Work in the spirit of accreditation, even if not accredited!

III. Veterinary Care	
III. Veterinary Care A. Animal Procurement and Transportation	
A. Animal Procurement and Transportation Animal Procurement Transportation of Assistance	2
2. Transportation of Asian	
Animal Procurement Transportation of Animals B. Preventive Medicine Animal Biosecurity Quarantine and Stokits	29
1. Animal Biosecurit	29
2. Quarantine and Status	29
Separation by Health Status and a	29
3. Separation by Health Status and Species C. Clinical Care and Management 1. Surveillance, Diagnosis 7.	30
C. Clinical Care and Management 1. Surveillance, Diagnosis, Treatment and Control of Disease 2. Emergency Care	30
2. Emergency Care 3. Clinical Record Keeping 4. Diagnostic Resources 5. Drug Storage and Control	30
4. Diagnostic Resources 5. Drug Storage and Control D. Surgery	31
Drug Storage and Control Surgery Pre-Surgical Planning	31
1 Pro S.	32
D. Surgery	32
3. Surgical Procedure	32
4. Aseptic Technique	
3. Surgical Procedures 4. Aseptic Technique 5. Intraoperative Monitoring	
and ing	33



The ethics of animal research in a nutshell:

Better Design

Better Reporting



reddit.com



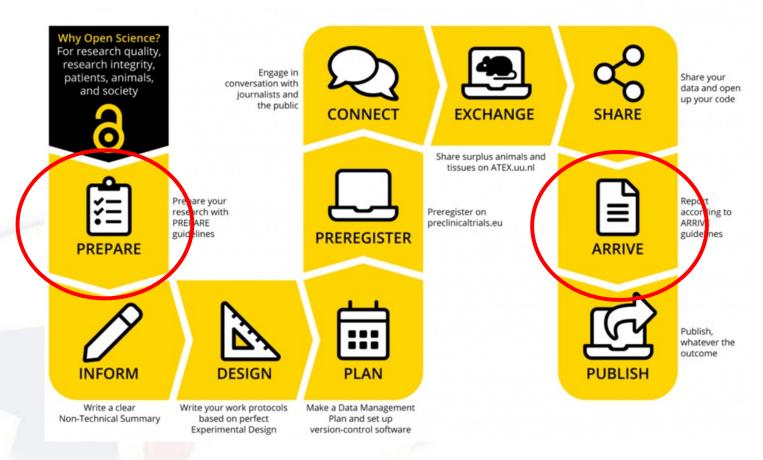
Reporting guidelines are not new...and they have not solved the reproducibility crisis alone

- Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments (GV-SOLAS, 1985)
- Reporting animal use in scientific papers (Jane Smith et al.), 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals*, 2000
- Guidelines for reporting the results of experiments on fish (2000)
- ARRIVE Guidelines, 2010 & 2020 (Kilkenny et al.; Percie du Sert et al.)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals

The pathway to better research: from planning guidelines to reporting guidelines







Norecopa: PREPARE for better Science

norecopa.no/PREPARE







PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Lilley³, Kristine E Aa Hansen⁴ and Trond Brattelid⁵

SSAGE

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 guid-ance 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 scientists 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 check-list is available on the Norecopa website, with links to guidelines for animal research and testing, at https://

guidelines, planning, design, animal experiments, animal research

Date received: 5 April 2017: accepted: 27 June 2017

Introduction

scrutiny, for good scientific and ethical reasons. Studies respects have been well-designed, and generate health of papers reporting animal experiments have revealed alarming deficiencies in the information provided, 1,2 even after the production and journal endorsement of reporting guidelines. There is also widespread concern which are safe and scientifically sound, address animal about the lack of reproducibility and translatability of laboratory animal research.⁴⁻⁷ This can, for example, contribute towards the failure of drugs when they enter human trials.8 These issues come in addition to other concerns, not unique to animal research, about publication bias, which tends to favour the reporting of posi-tive results and can lead to the acceptance of claims as tive results and can lead to the acceptance of claims as fact.? This has understandably sparked a demand for reduced waste when planning experiments involving animals, horse, peopring guidelines lance 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 of the 3Rs of the implementation of the data at all stages is, 1870 Seatrum, 010b Date, Norway. Breat address-memblearceapano.

in our experience, often underestimated by scientists. Introduction

Even small practical details can cause omissions or artefacts that can ruin experiments which in all other risks for all involved. There is therefore, in our opinion, an urgent need for detailed but overarching guide-

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Southwater, Horsham, West Sussex, UK

Pre-published under Open Access on 3 August 2017, sponsored by the Universities Federation for Animal Welfare (UFAW), UK

https://doi.org/10.1177/0023677217724823



Over 24,000 downloads from the journal website so far



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 typically highlighted in reporting guidelines



PREPARE encourages scientists to collaborate with animal carers and technicians from Day 1

- they have a right to know and will be more motivated
- they know the possibilities (and limitations) in the animal facility
- they often possess a large range of practical skills and are good at lateral thinking
- they know the animals best
- the animals know them best
- lack of involvement creates anxiety, depression and opposition to animal research, as well as limiting creativity which might improve the experiments

norecopa.no/PREPARE/prepare-checklist







The PREPARE Guidelines Checklist

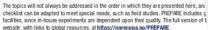
Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith^a, R. Eddie Clutton^a, Elliot Lilley^a, Kristine E. Aa. Hansen^a & Trond Brattelid^a

*Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; *Royal (Dick) School of Veterinary Studies, Easter Bush, Mildothian, EH25 9RG, U.K.; Rasearch Animais Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.;
"Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; 'Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE' consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE2. PREPARE covers the three broad areas which determine the quality of the preparation for animal shudion

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





and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
	(A) Formulation of the study
1. Literature searches	Form a clear hypothesis, with primary and secondary outcomes. Consider the use of systematic reviews. Consider the use of systematic reviews. Assess the relevance of the species to be used, its biology and suitability to answer the experimental systematic with the least sufficiency and its walfase needs. Assess the reproducibility and translatability of the project.
2. Legal issues	Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. Locate relevant guidance documents (e.g., EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	Construct a lay summary. In dialogue with ethics committees, consider whether statements about this type of research have already been produced. Address the 38s #pelacement, reduction, refinement) and the 3Ss (good science, good sense, good sense), good sense).
	Decision sensitives: 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. Allocuss the learning objectives, if the animal use is for educational or training purposes. Allocuss the learning objective, if the animal use is for educational or training purposes. Define objective, easily measurable and unequivocal humane endpoints. Discuss the justification, if any, for death as an end-point.
Experimental design and statistical analysis	Consider processures, statistical power and significance levels. Define the experimental unit and decide upon animal numbers. Choose methods of anatomisation, prevent observer bas, and decide upon inclusion and substation criteria.

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Торіс	Recommen dation
	(B) Dialogue between scientists and the animal facility
5. Objective's and timescale, funding and division of labour	Arrange meetings with all relevant staff when early plans for the project exist. Construct an approximate timescale for the project, indicating the need for assistance with preparation animal care, procedures and waste disposal/decontamination. Discuss and disclose all expected and potential costs. Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility evaluation	Conduct a physical inspection of the facilities, b evaluate building and equipment standards and needs Discuss staffing levels at times of extra risk.
7. Education and training	Assess the current competence of staff members and the need for further education or training pric to the study.
8. Health risks, waste disposal and decontamination	Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affecte directly or indirectly or indirectly or indirectly or indirectly of the study. Assess, and if necessary produce, specific guidance for all stages of the project. Discuss means for containment, decontamination, and disposal of all items in the study.
	(C) Quality control of the components in the study
9. Test substances and procedures	Provide as much information as possible about test substances. Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	Decide upon the characteristics of the animals that are essential for the study and for reporting. Avoid generation of surplus animals.
11. Quarantine and health monitoring	☐ Discuss the arimals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	Attend to the animals' specific instincts and needs, in collaboration with expert staff, Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on base (e.g. food deprivation, solitary bousing)
13. Experimental procedures	Develop refined procedures for capture, immobilisation, marking, and release or rehoming. Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	Consult relevant legislation and guidelines well in advance of the study. Define primary and emergency methods for humane killing. Assess the competence of those who may have to perform these tasks.
15. Necropsy	Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

- Smith AJ, Clutton RE, Lilley E, Hansen KEA & Brattelid T. PREPARE: Guidelines for Planning Animal Research and Testing.
- Labora bry Animals, 2017, D.DI: 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; D0I: 10.1371/journal.pbio.1000412.

Further information https://norecopa.no/PREPARE | post@norecopa.no | Onorecopa



norecopa.no/PREPARE/prepare-checklist

Three versions of the checklist:

- 1. plain pdf file
- 2. fillable pdf file
- 3. shared online version





The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith*, R. Eddie Clutton*, Elliot Lilley*, Kristine E. Aa. Hansen* & Trond Brattelid*

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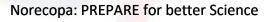
- 3. Quality control of the components in the study

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE to regions are not always an exactivation are court in winch may are presented met, and some topics overtap. The PREMATE

And some topics overtap.

And some topics

(A) Formulation of the study	
1. Literature searches	Form a clear hypothesis, with primary and secondary outcomes. Consider the use of systematic reviews. Dedde topo database 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 responducibility and translatibility of the project.
2. Legal issues	Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. Locate relevant guidance documents (e.g., EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	Construct a lay summary. In dialogue with ethics committees, consider whether statements about this type of research have already been produced. Address the 38s replacement, reduction, refinement) and the 38s (good science, good sense, good sensibilities). Consider per-registration and the publication of negative results. Perform a harm-benefit assessment and justity any likely serimal harm. Discuss the learning objectives, if the animal use is for educational or training purposes. Allocate a severity classification to the project. Discuss the learning objectives, if the nimited use is for educational or training purposes.
Experimental design and statistical analysis	Consider pilot studies, statistical power and significance levels. Define the experimental unit and decide upon animal numbers. Independent of the control





Topic	Recommendation
	(B) Dialogue between scientists and the animal facility
5. Objectives and timescale, funding and division of labour	Arrange meetings with all relevant staff when early plans for the project exist. Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontainatation. Discuss and decise all expected and perioritial costs. Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility evaluation	Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. Discuss staffing levels at times of extra risk.
7. Education and training	Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health risks, waste disposal and decontamination	Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. Assess, and if excessary produce, specific guidance for all stages of the project. Discuss means for confairment, decontamination, and disposal of all items in the study.
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15. Necropsy	☐ Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

- Reference of the Research Associated TREFARE Quidelines for Planning Animal Research and Testing, Laboratory Animals, 2017, 200, 310, 317(20)2287(21)2794232.

 Laboratory Animals, 2017, 200, 310, 317(20)2287(21)2794232.

 Z. Killemry G. Bennay M. Camill C. et al. proving Beconcern Research Reporting. The ARRIVE Quidelines for Reporting Animal Research, Artist Biology, 2010, 500, 18, 1127 (journal plan. 1)200112.

In addition to the checklist:





- 5. Have the experiments been carried out before, and is any repetition justifiable?
- 6. What approaches to reduce distress rehave been considered?



 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

nd will any advances in this ses only index the title and rejected?



- 3. Have the Three S's (Good Science, Good Sense and Good Sensibilities (g)) 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 rehave been considered?
- 7. Will the project undergo pre-registration and mill regative results be published, to avoid publication bias?

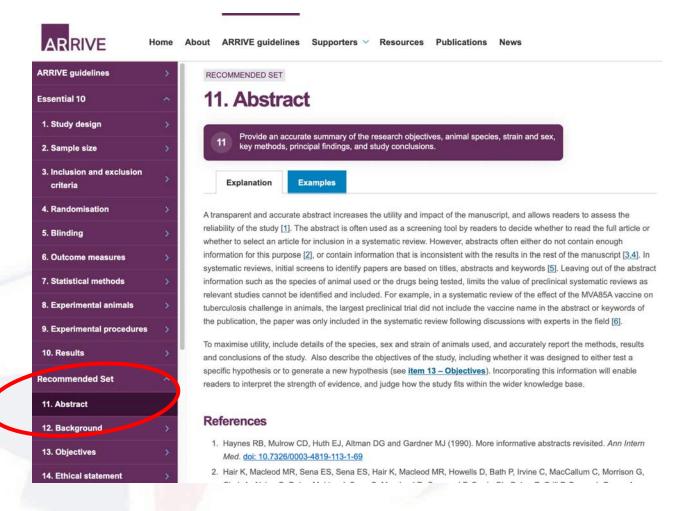
Many more links to resources on ethics are available here ...

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

arriveguidelines.org





There are three broad areas which need to be considered when planning animal studies:

- 1. The suitability of the species or strain as a model of the target organism
- 2. The ethical issues surrounding their use: 'choosing the right animal for the right reason' . The large increase in use of genetically altered lines has created increasing concern about the suitability of these animals as models of human conditions .
- Characterisation of the animals. Items to be considered, in collaboration with the supplier, include:
 - > Species, strain, line and phenotype (with an explanation of any genetic modifications)
 - > Age, developmental stage, sex and weight
 - > Stage of oestrous cycle and any previous breeding history
 - Any necessary pre-treatment (e.g. castration for this
 - Name and address of the supplier/breeder, method of capture and transport
 - > Health status (e.g. germ-free, gnotobiotic, SI
 - Re-use of animals, which should be justified legislation
 - > Any plans for release or re-homing, which m

More resources

- > Examples and references r from the NC3Rs
- > information on inbred strains of mice and rats (2)
- > Strategies to minimise genetic drift and maximise experimental reproducibility in mouse research 🗗
- > Mouse Locator, UK
- > The Collaborative Cross panel of inbred mouse strains @
- > Nude mice more than what meets the eye 🗗
- > The Rat Guide 🗗
- > Rat Behavior and Biology 🗷



While we are waiting for the scientific evidence for best practice in animal research...

Carol M. Newton (1925-2014)



National Library of Medicine

The three S's

- Good Science
- Good Sense
- Good Sensibilities

https://norecopa.no/3S

Our contribution to more ethically acceptable research:

Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of *global* 3R resources



https://norecopa.no

we welcome more from you!

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





Norecopa: PREPARE for better Science

Centres

- ✓ Replacement
- ✓ Reduction < 1</p>
- ☑ Refinement ①
- ✓ ecopa

Associations

- ✓ ACURET ①
- ✓ AFLAS (includes South Korea)
- ✓ Culture of Care Network < 1</p>
- ✓ ecopa ①
- ☑ EU-NETVAL

 ①
- FELASA 1
- FESSACAL 1
- Scand-LAS 1
- Concordat on Openness



norecopa.no/meetings/meetings-calendar

- > ESLAV/ECLAM Summer School on Anesthesia, Analgesia and Euthanasia &, online (part A: 21-23 June 2022) & Bologna (part B: 8-9 September 2022)
- > ONE Health, Environment & Society Conference 2022 @, Brussels and virtual event, 21-24

> 2022 Animal Research Tomorrow (ART) Award Ceremony and Conference 7, 21 June 2022

- > Ethics of Animal Behaviour and Welfare Research , virtual ASAB workshop, 21-22 June 2022
- > Practical guide to developing a 3R strategy @, webinar (Nikki Osborne), 22 June 2022
- > Stress-reduced handling of rats and mice , virtual workshop, 22 June 2022
- > Innovative Approaches in Cosmetic Testing, in Compliance with European Regulations & Genova, 22-23 June 2022
- > 9th Annual 3Rs Symposium (online) and Workshop (Baltimore) 7, 22-24 June 2022
- > Factors to consider in the art and science of anesthesia and analgesia for experimental reproducibility , webinar (Gabrielle Musk), 24 June 2022
- > Annual CALAS Symposium , Toronto, 25-28 June 2022
- > 27th ESACT Meeting 2022 (European Society for Animal Cell Technology) &, Lisbon, 26-29 June 2022
- > Training to enhance the reproducibility and rigour of research involving the use of animals and animal derived material 7, online course, 27-30 June 2022
- > Developments and future directions in regulatory fish acute toxicity testing &, webinar, 28 June
- > Advancing Animal Welfare Science 7, UFAW International conference, Edinburgh, 28-29 June 2022
- > IV Summer Shoal of Fish Ethology and Welfare 7, 28 June 1 July 2022
- > Humane Slaughter Association (HSA) International Conference &, Edinburgh, 30 June 1 July 2022
- > Information about the Aachen M.Sc. in Laboratory Animal Science &, webinar, 30 June 2022

Pdf files of approx. 80 presentations held at Norecopa's meetings









Norecopa: PREPARE for better Science



norecopa.no/meetings/presentations



Most of the presentations on this page are from events arranged by Norecopa. A few of them are from external events where Norecopa's staff have lectured.

They are grouped into

- > General presentations
- > Care and use of animals in field research
- > Care and use of farm animals in research
- > Care and use of fish in research

Title	Speaker	Affiliation	Year
General presentations			
Design of animal studies: Increasing	Adrian Smith	Norecopa	2020
reproducibility and animal welfare			
PREPARE before you ARRIVE: Good	Adrian Smith	Norecopa	2019
reporting relies on good planning			
Animal-free testing and humans-on-a-chip:	Leopold Koenig	TissUse GMBH,	2017
How far have we come? 🗗		Berlin, Germany	
Nordic 3R-Centres: What can we offer?	Tom Bengtsen	Denmark's 3R- Center	2017
Prize-winning 3R activity in Norway 🗷	Gøril Eide	University of Tromsø, Norway	2017
Have the 3Rs made any difference? 🗷	Elliot Lilley	RSPCA, UK	2017



Databases & Guidelines

Published lists of resources are difficult to search and quickly become outdated. Lists on a website are easier to search, but do not enable the use of filters or intelligent search engines.

Norecopa has therefore constructed four databases, which together with all the text on this website can be searched simultaneously using the search field at the top of every page.

- 3R Guide: a global overview of databases, guidelines, information centres, journals, email lists, regulations and policies which may be of use when planning experiments which hight include animals. A quick overview of all the guidelines can be accessed here. Norecopa has written several of these, including the PREPARE guidelines for planning animal research and teating.
- NORINA: a global overview of audiovisual aids and other items which may be used as alternatives or supplements to animals in education and training at all levels from junior school to University, including dissection alternatives and surgical simulators.
- > TextBase: a global overview of textbooks and other literature within laboratory animal science and related topics.
- Classic AVs: a subset of NORINA covering audiovisual aids that are based on older technology.

These databases are updated regularly. <u>Please give us feedback</u> if you discover errors or omissions.

The Norecopa website also includes four other collections:

- > NAL: a collection of literature references relating to the 3Rs from the US National Agricultural
- > European Commission datasets:
 - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
 3Rs Education and Training Resources, over 560 items collected in 2018
 - Non-animal models for respiratory tract diseases, over 280 models identified in a literature review of over 21,000 publications

Here is an alphabetical global list of all the databases cites on the Norecopa website.

Norecopa: PREPARE for better Science

norecopa.no/databases-guidelines

links to over 70 other databases





researchanimaltraining.com

Articles v eModules v Log in

Training resources for animal research



National Legislation (EU1)

Understand the national and international legal and regulatory framework within which projects involving animals are constructed and managed and of the legal responsibilities of the people involved.



Ethics, Animal Welfare and the 3Rs (EU2)

Identify the ethical and welfare issues raised by the use of animals in scientific procedures and understand the basic principles of the 3Rs.



Basic and Appropriate Biology (EU3)

Discover the basic principles of animal behaviour, care, biology and husbandry.



Animal Care, Health and Management (EU4)

Examine information on various aspects of animal health, care and management including, environmental controls, husbandry practices, diet, health status and disease.



Recognition of Pain, Suffering and Distress (EU5)

Identify the normal condition and behaviour of experimental animals and differentiate between a normal animal and one which is showing signs of pain, suffering or distress.



Minor Procedures without Anaesthesia (EU7)

An introduction to the theory relating to minor procedures and information about appropriate methods of handling, restraint, appropriate techniques for injection, dosing and sampling relevant to the species.



Humane Methods of Killing (EU6.1) Learn the principles of humane killing

including descriptions of the different methods available and information to help you compare the methods permitted to determine the most appropriate method.



Anaesthesia for Minor Procedures (EU20)

Guidance and information for individuals. who, during their work with animals, will need to apply sedation or short-term anaesthesia for a brief period and mild pain level procedure.

eModules



eModule - Recognition and Prevention of Pain, Suffering and Distress (EU5)



eModule – Humane Methods of Killing (EU6)



eModule - Design of procedures and projects (level 1) (EU10)



eModule - Design of procedures and projects (level 2) (EU11)



eModule - The Severity Assessment Framework (EU12)



eModule - Anaesthesia for Minor Procedures (EU20)



eModule - Pre-Anaesthetic Preparations (EU21-1)



eModule - Choosing an Anaesthetic (EU21-2)



eModule - Anaesthetic Monitoring and Intraoperative Care (EU21-



eModule - Anaesthetic Breathing Systems, Airway Management and Neuromuscular Blocking Agents (EU21-4)



eModule - Anaesthetic Management and Preventing Problems (EU21-



eModule - Post Anaesthetic Care (EU21-6)



eModule - Project Evaluation (EU25)



TextBase:

1,500 books related to LAS:

norecopa.no/textbase

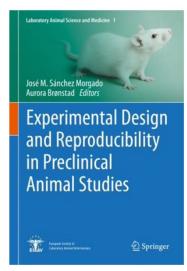
Experimental Design and Reproducibility in Preclinical Animal Studies

By José M. Sánchez Morgado & Aurora Brønstad (Eds.)

Record number: 8619d

This book provides grounds on how to plan and conduct animal experiments that can be reproduced by others. It touches on factors that may impact the reproducibility of animal studies including: the animal genetic background, the animal microbial flora, environmental and physiological variables affecting the animal, animal welfare, statistics and experimental design, systematic reviews of animal studies, and the publishing process.

The book addresses advanced undergraduates, graduate students and all scientists working with animals.



norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies

From **3R-Guide** (400 guidelines for animal research and testing)



norecopa.no/3r-guide



Guidance on the severity classification of procedures involving fish

Report from a Working Group convened by Norecopa



http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf

P Hawkins, N Dennison, G Goodman, S Hetherington, S Llywelyn-Jones, K Ryder and AJ Smith

Laboratory Animals, 45: 219-224, 2011

Norecopa: PREPARE for better Science norecopa.no/categories





The International Culture of Care Network norecopa.no/coc

A demonstrable commitment, throughout the establishment, to improving:

- animal welfare
- scientific quality
- care of staff
- transparency for all stakeholders

It goes beyond simply complying with the law!



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Clicker training

Clicker training is an operant conditioning based on positive reinforcement. When the animal offers the desired behavior, a *click* or another distinctive sound (secondary reinforcer) is delivered and within the following few seconds the reward is presented (primary reinforcer). The *click* bridges the time between the desired behavior and the presentation of the reward^[1]. A target stick providing a visual guide for the animal can be used for the training.

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Animals are usually trained individually, though it is also possible to perform clicker training in a groups, e.g. in mice, rats, and rabbits. For rats, it was demonstrated that they learned tasks by observing the clicker transining of their cage mates^[2].

Clicker training can be used to train animals in a stress-free way. The following behaviours are examples for what this technique can be used for:

Mice: entering a tunnel, following a target stick, climbing on the palm of the hand [3]

Rats: following a target stick, voluntarily change to a cage, observational learning [2]

Rabbits: following a target stick, rearing/standing up to inspect the abdomen, approaching a human, being touched and lifted by a human, trimming nails, coming on command

Pigs: Pigs can be easily trained to cooperate if they are treated empathetically and desired behavior is reinforced by providing food stuff in form of treats and apple juice^[4].





Clicker training with mice using a target stick. Left: The mouse is following the target stick and is climbing on the experimenter's hand. If the hand is lifted, the mouse will remain on the palm of the hand. Right: The mice are trained in a group. Two mice are following the target stick on the palm of the experimenter's hand.

- 1. † 1.0 1.1 Feng, Lynna C.; Howell, Tiffani J.; Bennett, Pauleen C. (1 August 2016). "How clicker training works: Comparing Reinforcing, Marking, and Bridging Hypotheses" & Applied Animal Behaviour Science. 181: 34–40. doi:10.1016/j.applanim.2016.05.012 & ISSN 0168-1591 &
- † 2.0 2.1 Leidinger, Charlotte Sophie; Kaiser, Nadine; Baumgart, Nadine; Baumgart, Jan (25 October 2018). "Using Clicker Training and Social Observation to Teach Rats to Voluntarily Change Cages" & JoVE (Journal of Visualized Experiments) (140): e58511. doi:10.3791/58511 & ISSN 1940-087X & PMC 6235608 PMID 30417890 &.
- 1 Leidinger, Charlotte; Herrmann, Felix; Th\u00f6ne-Reineke, Christa; Baumgart, Nadine; Baumgart, Jan (6 March 2017). "Introducing Clicker Training as a Cognitive Enrichment for Laboratory Mice" & JoVE (Journal of Visualized Experiments) (121): e55415. doi:10.3791/55415 & ISSN 1940-087X & PMC 5408971 & PMID 28287586 &.
- 4. † "Positive Reinforcement Training in Large Experimental Animals" @ (PDF).

Experts for clicker training in mice and rats: TARC , Mainz, Germany

This page was created and edited by KH191219 (talk).

This page was last edited on 27 May 2020, at 11:23.

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Refinement Wiki

- Acclimatisation
- Adrian Smith
- Alphaxalone
- · Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
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- EMLA cream
- Embryo transfer
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- Food crunchers

- General discusson on use of analgesics
- Genotyping mice
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- Marble Burying Test
- Metabolic cages
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Newsletter no. 2-2022 from Norecopa

Welcome to Norecopa's second newsletter in 2022!

Please share this newsletter with your colleagues and friends!

Norecopa maintains an international Webinars and Meetings Calendar [7], which is updated several times a week, with links to recorded webinars and events here .

You will find shortcuts to several other key resources on our front page 📝

We continue to maintain a list of resources related to the Covid-19 pandemic and about preparedness in general: Be PREPAREd . Let us know if you have additions.

You can tip a friend, subscribe or unsubscribe, and share the newsletter on social media using the links above. We are on Facebook [and Twitter [].

All Norecopa's newsletters can be read here 🔀 and their content is indexed by the search engine on Norecopa's website [?.

This newsletter contains the following items (if some links do not work, check that your mail program has opened the whole of the newsletter):

- Norecopa's Annual Report
- eneral update on Norecopa's activities

English-language newsletters

norecopa.no/news/newsletters

7-8 times a year

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norecopa.no/ASAB