



Norecopa: PREPARE for better Science

Norecopa

Norway's National Consensus Platform for the
Three Rs: Replacement, Reduction and Refinement
and a source of global 3R resources



<https://norecopa.no>

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Centres

- [Replacement](#) ⓘ
- [Reduction](#) ⓘ
- [Refinement](#) ⓘ
- [ecopa](#) ⓘ

Associations

- [AFLAS \(includes South Korea\)](#) ⓘ
- [Culture of Care Network](#) ⓘ
- [EU-NETVAL](#) ⓘ
- [EU3Rnet](#) ⓘ
- [FELASA](#) ⓘ
- [FESSACAL](#) ⓘ
- [Norecopa](#) ⓘ
- [Scand-LAS](#) ⓘ
- [ecopa](#) ⓘ

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

Inclusive
Emphasis on quality resources

approx. 8,500 webpages
>300,000 hits annually
7-8 detailed newsletters per year

The screenshot shows the norecopa.no website. At the top is a blue header with the norecopa logo (a stylized star) and the text 'norecopa'. Below the header is a navigation menu with items like 'Alternatives', 'Databases & Guidelines', 'Education & training', 'Legislation', 'Meetings', 'More resources', 'News', and 'PREPARE'. The main content area features a large article titled 'Design and reporting of animal experiments'. Below the title, there is a sub-header 'Experimental design' and a paragraph of text: 'This page supplements advice given in Section 4 of the PREPARE guidelines. PREPARE covers all aspects of design (including animal and facility related issues)'. The page also includes a breadcrumb trail: 'norecopa.no / More resources / Experimental design'.

The search filters sidebar is located on the right side of the page. It has a blue header 'Search filters'. Below the header, there are two dropdown menus: 'Order by:' set to 'Relevance' and 'Typo tolerance:' set to 'Default'. The main section is titled 'Database' and contains a list of databases with checkboxes and counts: '3R Guide database (403)', 'Classic AVs database (118)', 'European Commission Inventory of 3Rs Education & Training Resources (567)', 'European Commission Inventory of 3Rs Knowledge Sources (807)', 'European Commission Inventory of NAMs for Respiratory tract diseases (280)', 'NAL records (1688)', 'NORINA database (3141)', 'TextBase database (1501)', and 'Website (761)'. Below this is a section 'Browse the databases' with a list of categories: 'eBooks (286)', 'Free (199)', 'Held at NMBU Oslo (contact Kristine Hansen, 67 23 21 89) (431)', 'Key products (68)', 'On loan (6)', and 'Reviewed (85)'. The final section is 'Search in the databases' with a list of search criteria: 'All Text', 'Title', 'Author', 'Publisher', 'Supplier', and 'Record Number'.

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 might 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 testing.](#)
- > **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. [Please give us feedback](#) 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 Library
- > 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](#) cited on the Norecopa website.

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norecopa.no/databases-guidelines

links to over 70 other databases

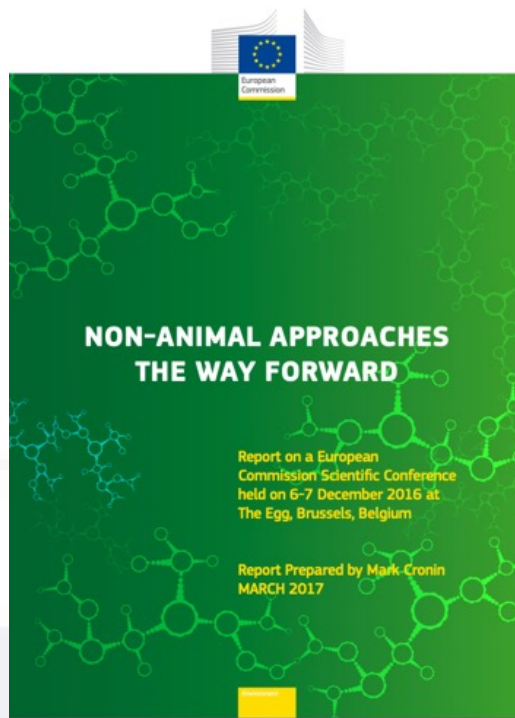
Webinar and Meetings calendar

November 2021

- > [In Vitro Lung Models](#), Hamburg, 8-9 November 2021
- > [Environmental monitoring for rodent health surveillance](#), webinar (Megan LaFollette & Megan LaFollette), 9 November 2021
- > [Assessing and Alleviating the Burden of Animal Research](#), distance learning
- > [Pre-clinical animal research: Navigating the guidelines and principles](#), online meeting, 10 November 2021
- > [Cognition, Welfare, and the Problem of Interspecies Comparisons](#), panel discussion, 10 November 2021
- > [Guide to developing a culture of integrity](#), webinar (Nikki Osborne), 10 November 2021
- > [Annual RepRefRed 3R Days](#), 10-12 November 2021
- > [36th Annual Meeting of the BSTP: Pathology of mice with human immune systems \(HIS\)](#)

+ webpages for past meetings and recorded meetings

The evolution of the PREPARE planning guidelines:



- Discussions and learning material on courses in Laboratory Animal Science from 1986 onwards
- Development of planning guidelines – too obvious to publish!
- European Commission

25 minutes to present 30 years of work...

- The realisation that the community was asking for planning guidelines, not just reporting guidelines
- Published ahead of print in August 2017

norecopa.no/legislation/eu-directive-201063

Reporting guidelines are not new...

e.g.

- Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments, 1985 (GV-SOLAS)
- Reporting animal use in scientific papers, 1997 (Smith *et al.*)
- Animal definition: a necessity for the validity of animal experiments? 2000 (Öbrink & Rehbinder)
- Guidelines for reporting the results of experiments on fish, 2000 (Smith & Brattelid)
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*)
- Gold Standard Publication Checklist (GSPC), 2010 (SYRCLE)
- Institute for Laboratory Animal Research, 2011 (NRC)
- Instructions to authors, in many journals
- ARRIVE 2.0 Guidelines, 2019 (Percie du Sert *et al.*)

1994:

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 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 representative 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 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 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).



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

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Frequently highlighted causes of 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

The burnt cake fallacy:

We can improve research by

- "better reporting"
- "courses in "Experimental Design" that leave out the animal & facility-related issues"



reddit.com

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Perspective | Open Access | Published: 10 January 2017

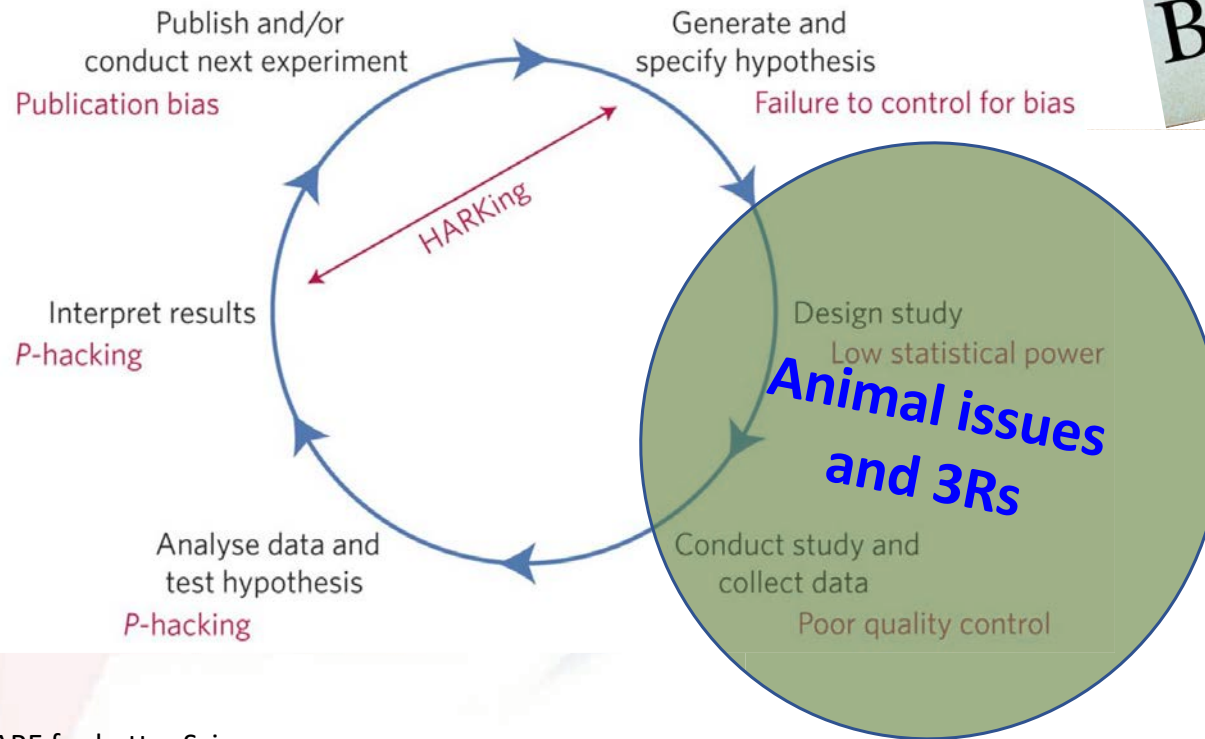
A manifesto for reproducible science

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

Nature Human Behaviour 1, Artic

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

Figure 1: Threats to reproducible science.





'achieving reproducible and reliable preclinical research results is a joint responsibility that requires a partnership between the investigative team and the animal care and use program staff.'

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Improving Replicability, Reproducibility, And Reliability In Preclinical Research: A Shared Responsibility ^{FREE}

Christopher Cheleuitte-Nieves, Neil S Lipman ✉

ILAR Journal, Volume 60, Issue 2, 2019, Pages 113–119, <https://doi.org/10.1093/ilar/ilaa009>

Published: 23 June 2020 Article history ▼

A correction has been published: *ILAR Journal*, ilaa022, <https://doi.org/10.1093/ilar/ilaa022>

How do others achieve reproducibility?



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



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...and precision in a variable environment?



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10-15 checklists even on short routine flights with experienced crew



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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, ground staff and air traffic control
- Make sure that everyone is "**on the same page**"

Most of the checklists must be followed before they ARRIVE ...

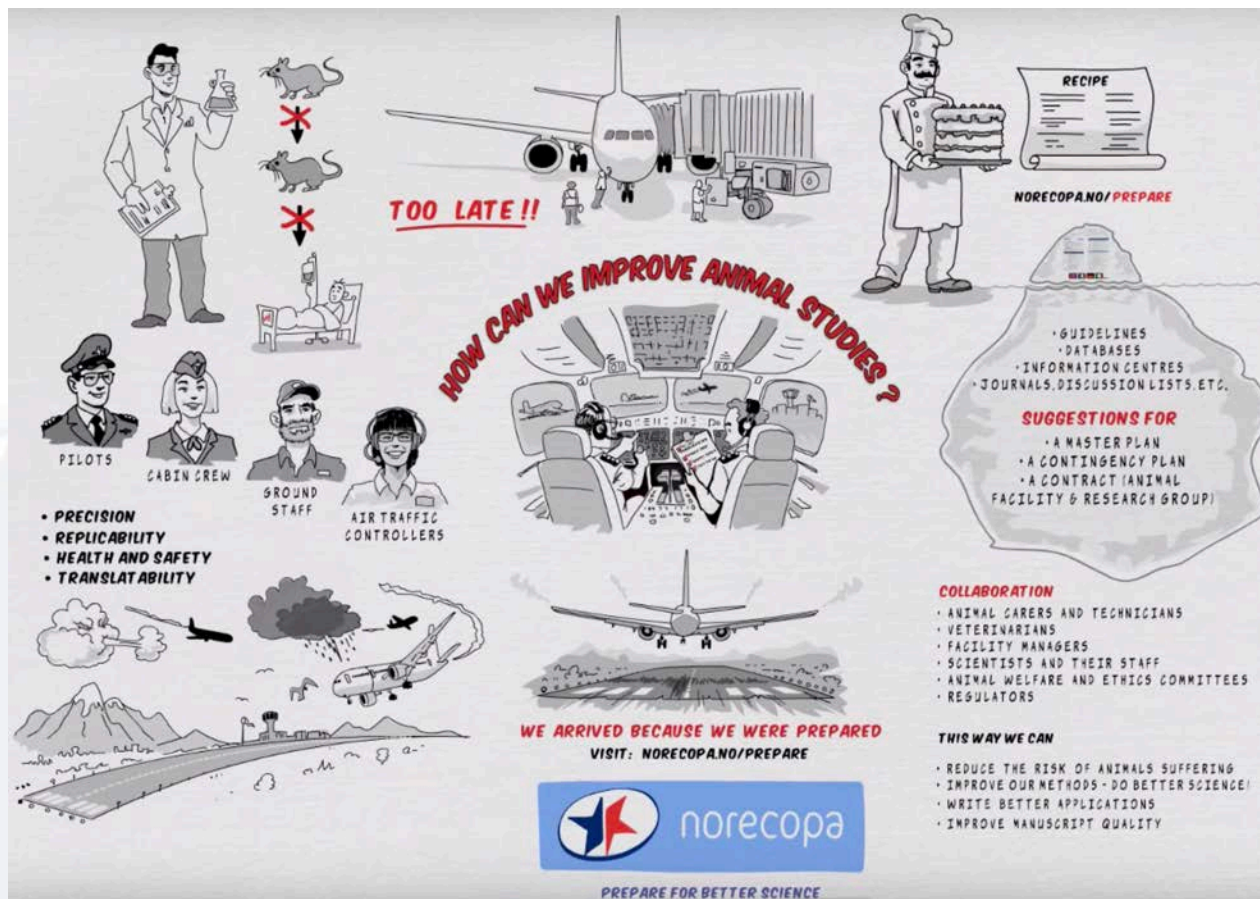


colourbox.com

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norecopa.no/PREPARE/film

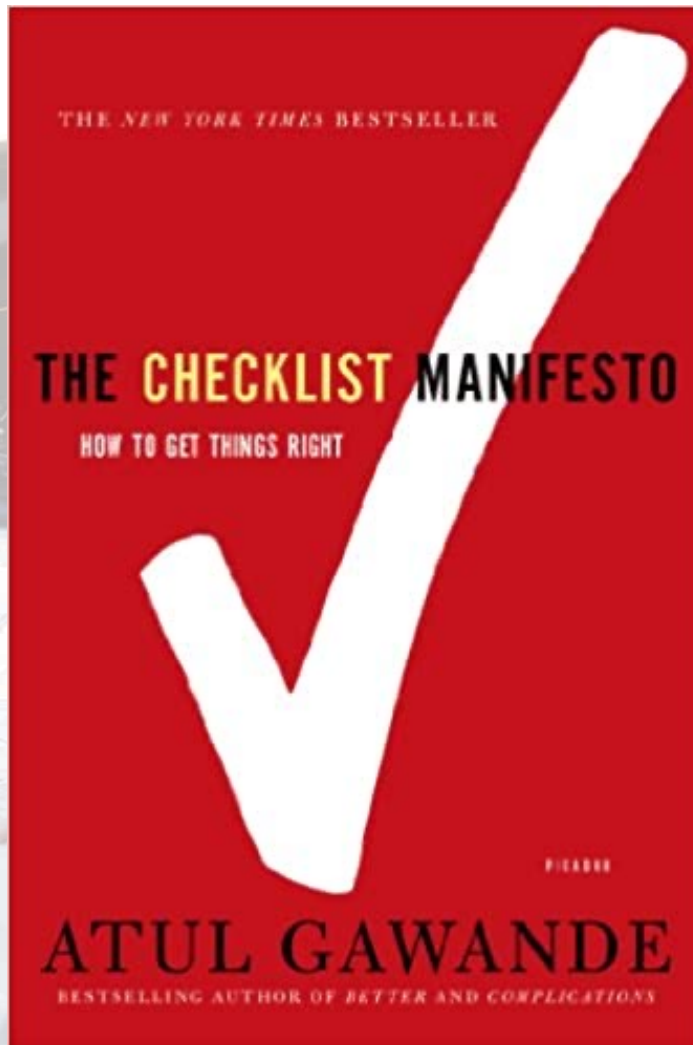
3-minute film



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Surgical Safety Checklist



Patient Safety
A World Alliance for Safer Health Care

Before induction of anaesthesia

(with at least nurse and anaesthetist)

Has the patient confirmed his/her identity, site, procedure, and consent?

Yes

Is the site marked?

Yes
 Not applicable

Is the anaesthesia machine and medication check complete?

Yes

Is the pulse oximeter on the patient and functioning?

Yes

Does the patient have a:

Known allergy?

No
 Yes

Difficult airway or aspiration risk?

No
 Yes, and equipment/assistance available

Risk of >500ml blood loss (7ml/kg in children)?

No
 Yes, and two IVs/central access and fluids planned

Before skin incision

(with nurse, anaesthetist and surgeon)

Confirm all team members have introduced themselves by name and role.

Confirm the patient's name, procedure, and where the incision will be made.

Has antibiotic prophylaxis been given within the last 60 minutes?

Yes
 Not applicable

Anticipated Critical Events

To Surgeon:

What are the critical or non-routine steps?
 How long will the case take?
 What is the anticipated blood loss?

To Anaesthetist:

Are there any patient-specific concerns?

To Nursing Team:

Has sterility (including indicator results) been confirmed?
 Are there equipment issues or any concerns?

Is essential imaging displayed?

Yes
 Not applicable

Before patient leaves operating room

(with nurse, anaesthetist and surgeon)

Nurse Verbally Confirms:

The name of the procedure
 Completion of instrument, sponge and needle counts
 Specimen labelling (read specimen labels aloud, including patient name)
 Whether there are any equipment problems to be addressed

To Surgeon, Anaesthetist and Nurse:

What are the key concerns for recovery and management of this patient?

This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged.

Revised 1 / 2009

© WHO, 2009

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

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amazon.com/gp/product/0312430000



Original Article

PREPARE: guidelines for planning animal research and testing

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

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 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 checklist is available on the Norecopa website, with links to guidelines for animal research and testing, at <https://norecopa.no/PREPARE>.

Keywords
guidelines, planning, design, animal experiments, animal research

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

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,^{1,2} even after the production and journal endorsement of reporting guidelines.³ There is also widespread concern 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 positive results and can lead to the acceptance of claims as fact.⁹ This has understandably sparked a demand for reduced waste when planning experiments involving animals.¹⁰⁻¹² 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).¹³ The importance of attention to detail at all stages is, 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

Laboratory Animals
0311-7
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DOI: 10.1177/0023677217724823
journals.sagepub.com/home/lan
SAGE

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Eddie Clutton, Elliot Lilley, Kristine Hansen & Trond Brattelid

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<https://doi.org/10.1177/0023677217724823>



Over 21,000 views/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

Maybe the study
should not go ahead

Systematic review of
published research?

PREPARE:

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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 Lilley³, Kristine E. Aa. Hansen⁴ & Trond Bratteild⁵
¹Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; ²Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; ³Research Animals Department, Science Group, RSPCA, Wiberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; ⁴Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box #140 Dep., 0033 Oslo, Norway; ⁵Division 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 ARRIVE[®]. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies:

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 they are presented here, and some topic checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on facilities, since in-house experiments are dependent upon their quality. The full version of the guideline website, with links to global resources, at <https://norecopa.no/PREPARE>.

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.

Three Rs!

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	<input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes. <input type="checkbox"/> Consider the use of systematic reviews. <input type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms. <input type="checkbox"/> Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and to welfare needs. <input type="checkbox"/> Assess the reproducibility and translatability of the project.
2. Legal issues	<input type="checkbox"/> Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. <input type="checkbox"/> Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	<input type="checkbox"/> Construct a lay summary. <input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced. <input type="checkbox"/> Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities). <input type="checkbox"/> Consider pre-registration and the publication of negative results. <input type="checkbox"/> Perform a harm-benefit assessment and justify any likely animal harm. <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> Avoid a merely descriptive aim to test project. <input type="checkbox"/> Define objective, easily measurable and unequivocal humane endpoints. <input type="checkbox"/> Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	<input type="checkbox"/> Consider pilot studies, statistical power and significance levels. <input type="checkbox"/> Define the experimental unit and decide upon animal numbers. <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.

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.
6. Facility inspection and staffing	<input type="checkbox"/> Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. <input type="checkbox"/> Discuss staffing levels at times of extra risk. <input type="checkbox"/> Assess the current competence of staff members and the need for further education or training prior to the study.
7. Risk assessment, waste disposal and decontamination	<input type="checkbox"/> Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. <input type="checkbox"/> Assess, and if necessary produce, specific guidance for all stages of the project. <input type="checkbox"/> 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	<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 & Bratteild 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)



In addition to the checklist, much more information is available on:

norecopa.no/PREPARE



- PREPARE
- PREPARE checklist
- Comparison with ARRIVE
- Endorsements
- Film
- 1-Literature searches
- 2-Legal issues
- 3-Ethical issues,

PREPARE

The PREPARE Guidelines, and this section of the Norecopa website, have been developed with the involvement and support of the [RSPCA](#).



As part of ongoing efforts to reduce waste, promote animal alternatives (all [the three Rs](#)), and increase the reproducibility of research and testing, a group of experts from the UK and Norway, led by Norecopa, has produced a set of guidelines for planning experiments:

PREPARE (*Planning Research and Experimental Procedures on Animals: Recommendations for Excellence*)

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- 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).
 - 3d 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

- 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

- 2. Will any advances in this research be published, to avoid publication bias? Will the project undergo pre-registration and will negative results be published, to avoid publication bias? Will the project undergo pre-registration and will negative results be published, to avoid publication bias? Will the project undergo pre-registration and will negative results be published, to avoid publication bias?

- 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

The screenshot shows the ARRIVE guidelines website. The top navigation bar includes 'Home', 'About', 'ARRIVE guidelines', 'Supporters', 'Resources', 'Publications', and 'News'. A left-hand navigation menu lists 14 items, with 'Recommended Set' circled in red. The main content area is titled 'RECOMMENDED SET' and '11. Abstract'. A purple box contains the text: '11 Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.' Below this are tabs for 'Explanation' and 'Examples'. The 'Explanation' tab is active, showing a paragraph: 'A transparent and accurate abstract increases the utility and impact of the manuscript, and allows readers to assess the reliability of the study [1]. The abstract is often used as a screening tool by readers to decide whether to read the full article or whether to select an article for inclusion in a systematic review. However, abstracts often either do not contain enough information for this purpose [2], or contain information that is inconsistent with the results in the rest of the manuscript [3,4]. In systematic reviews, initial screens to identify papers are based on titles, abstracts and keywords [5]. Leaving out of the abstract information such as the species of animal used or the drugs being tested, limits the value of preclinical systematic reviews as relevant studies cannot be identified and included. For example, in a systematic review of the effect of the MVA85A vaccine on tuberculosis challenge in animals, the largest preclinical trial did not include the vaccine name in the abstract or keywords of the publication, the paper was only included in the systematic review following discussions with experts in the field [6]. To maximise utility, include details of the species, sex and strain of animals used, and accurately report the methods, results and conclusions of the study. Also describe the objectives of the study, including whether it was designed to either test a specific hypothesis or to generate a new hypothesis (see item 13 – Objectives). Incorporating this information will enable readers to interpret the strength of evidence, and judge how the study fits within the wider knowledge base.' Below this is a 'References' section with two entries: 1. Haynes RB, Mulrow CD, Huth EJ, Altman DG and Gardner MJ (1990). More informative abstracts revisited. *Ann Intern Med.* doi: 10.7326/0003-4819-113-1-69 2. Hair K, Macleod MR, Sena ES, Sena ES, Hair K, Macleod MR, Howells D, Bath P, Irvine C, MacCallum C, Morrison G,

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](#).
3. 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, SPF)
 - > Re-use of animals, which should be justified by legislation
 - > Any plans for release or re-homing, which must be justified

More resources

- > [Examples and references](#) from the NC3Rs
- > [Information on inbred strains of mice and rats](#)
- > [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](#)

Resource hubs

3Rs resources

We provide an extensive library of 3Rs resources. This includes guidelines, practical information and themed hubs. Links to publications, other online resources, and video and training materials are also provided.


Search 3Rs resources

Hubs and microsites

<p>The NC3Rs and the 3Rs during COVID-19</p>  <p>Advice and resources for researchers and animal care staff.</p>	<p>Webinars</p>  <p>Upcoming webinars and recordings of past webinars on different 3Rs topics.</p>	<p>3Rs self-assessment tools</p>  <p>Free-to-use interactive tools for research groups and institutions to benchmark their activities and identify new 3Rs opportunities.</p>	<p>Embedding the 3Rs in COVID-19 return to research plans</p>  <p>Guidance on key considerations and resources for researchers returning to working with laboratory animals.</p>
<p>3Rs advice for project licence applicants</p>  <p>Guidance and resources to help applicants address the 3Rs aspects of a Home Office project licence application.</p>	<p>3Rs for the public</p>  <p>Resources and information on the 3Rs aimed at a non-specialist audience.</p>	<p>3Rs video presentation</p>  <p>Demonstrating the 3Rs in principle and practice.</p>	<p>3Rs in toxicology and regulatory sciences</p>  <p>NC3Rs programmes in drug and chemical safety testing.</p>

nc3rs.org.uk/3rs-resources









Resource hubs



Science Home | Companion animals | Farm animals | **Animals in science** | Wildlife | Animal Sentience

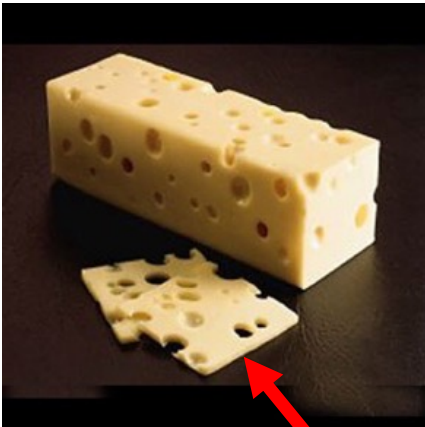
Implementing the 3Rs | Ethical review | Focus on severe suffering | Our international work | **Reports and resources**

[Print](#)

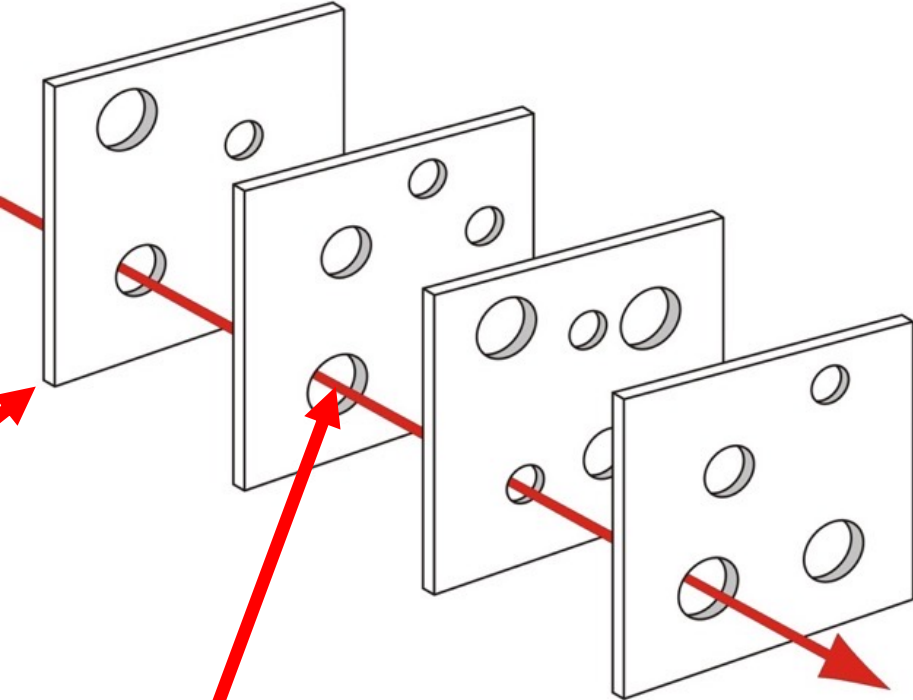
 <p>Ethical review</p>	 <p>Culture of care</p>	 <p>Severe suffering</p>	 <p>Welfare and severity assessment</p>
 <p>Housing and care</p>	 <p>Refining procedures</p>	 <p>Genetically altered animals and biotechnology</p>	 <p>Non-human primates</p>

science.rspca.org.uk/sciencegroup/researchanimals/reportsandresources

Threat and Error Management



eaugallecheese.com/Swiss-cheese



"Layer of defence"
or redundancy

Weakness / hazard

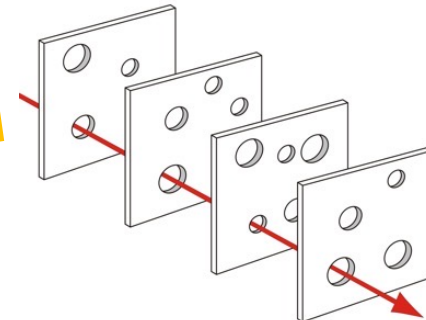
Loss

wikipedia.org/wiki/Swiss_cheese_model

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
 - serious haemorrhages
 - fainting
 - allergic and anaphylactic reactions
 - bites
 - 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

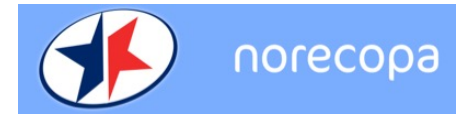
These need to be revised or supplemented in the light of Covid-19



Temporary staff at weekends and holidays

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

Increased focus on contingency plans



Suggested considerations for establishment working under ASPA during the COVID19 lock-down

CATEGORY		CONSIDERATIONS/SUGGESTIONS
PERSONNEL Provide 'essential worker' letter to show authorities, include home address. Consider whether company/photo i.d. would be helpful All personnel must prioritise their health and the health of others by wearing suitable PPE and by observing social distancing as advised by the government Support mental health Consider mindfulness apps, Convert empty animal room into a relaxation/yoga room (online yoga classes).	ANIMAL TECHNICIANS	Run 2 or more teams if possible to lower the risk of transmission (each team is treated as 'household') to the wider team. Examples of how onsite teams might be run include alternate days, 2days on 2days off and utilising an early shift / a late shift to reduce contact and total staff in an area at any one time. If people are in isolation or have caring responsibilities they may (if well enough) be able to work offsite as part of a "virtual office" team Where teams can't be separated use full PPE/ RPE and have staggered entry/break/exit times or other means of avoiding people not in PPE. Physically segregate in unit if possible Review teams regularly – this may need to be daily in some situations Introduce regular and frequent routines for surface decontamination, paying particular attention to door handle/ door plates, taps and work surfaces. Clean with detergent / 70% isopropyl alcohol or similar Limit reliance on public transport methods. Accommodate parking where possible to allow individuals to travel by car
	RESEARCHERS	Ensure all alarm systems are checked regularly and are functional. Monitor, record and act on all alarms Review contingencies for critical system failure (e.g. HVAC) and have an action plan. Make sure all backup systems are fully functional and that sufficient spare parts are available and accessible
	ESTABLISHMENT LICENCE HOLDER	DELIVERIES VETS
	ENGINEERS	ANIMALS BREEDING REDUCE STOCK
	ACCESS	Do not start new work unless absolutely essential/ internal review has been performed that confirms that the work can be properly serviced Essential research work may continue if staffing levels allow it. A local decision making process which records decision making as to which projects may remain ongoing should be in place. Examples of what may be reasonable are COVID-19 work, aged animal work and work to complete studies There may be reasons for prioritising ongoing work with some species (e.g. NHPs) If the facilities allow, consolidate animals to one area, check light cycle, room temps & designation first Spread work evenly / reduce cleaning of cages – but not to extent that welfare could be compromised Re-assess stock levels / staff levels at least once per week Cull animals that are not going to be needed for colony management and cannot otherwise be used Avoid unnecessary movement of animals Prioritise the movement of animals to other facilities or establishments for contingency of valuable lines. Check your facility/ies will be open – Provide a list of names requiring access. Check with security how and when essential staff will access Confirm how essential supplies and waste contractors will service the facility/ies
	SUPPLIES	Stock up on diet, bedding, nesting materials, PPE, disinfectants and other essentials, aim for a minimum of 3 months Ensure there will there be Liquid nitrogen / dry ice for cryopreserved stocks Have stocks of CO ₂ and sodium pentobarbitone and any other drugs as directed by the NVS
	ESTATES / ENGINEERS	Check your contractors are working and get emergency contacts. Maintain a list of mobile numbers, available to everyone Consider if essential equipment will require servicing or repair. Ensure that you have a plan to enable this Will waste be being removed from site? – prepare an area for on-site storage if necessary Record all difficult decisions taken. What/ when /why and any related evidence
	RECORDS	

norecopa.no/be-prepared

Contingency and redundancy

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

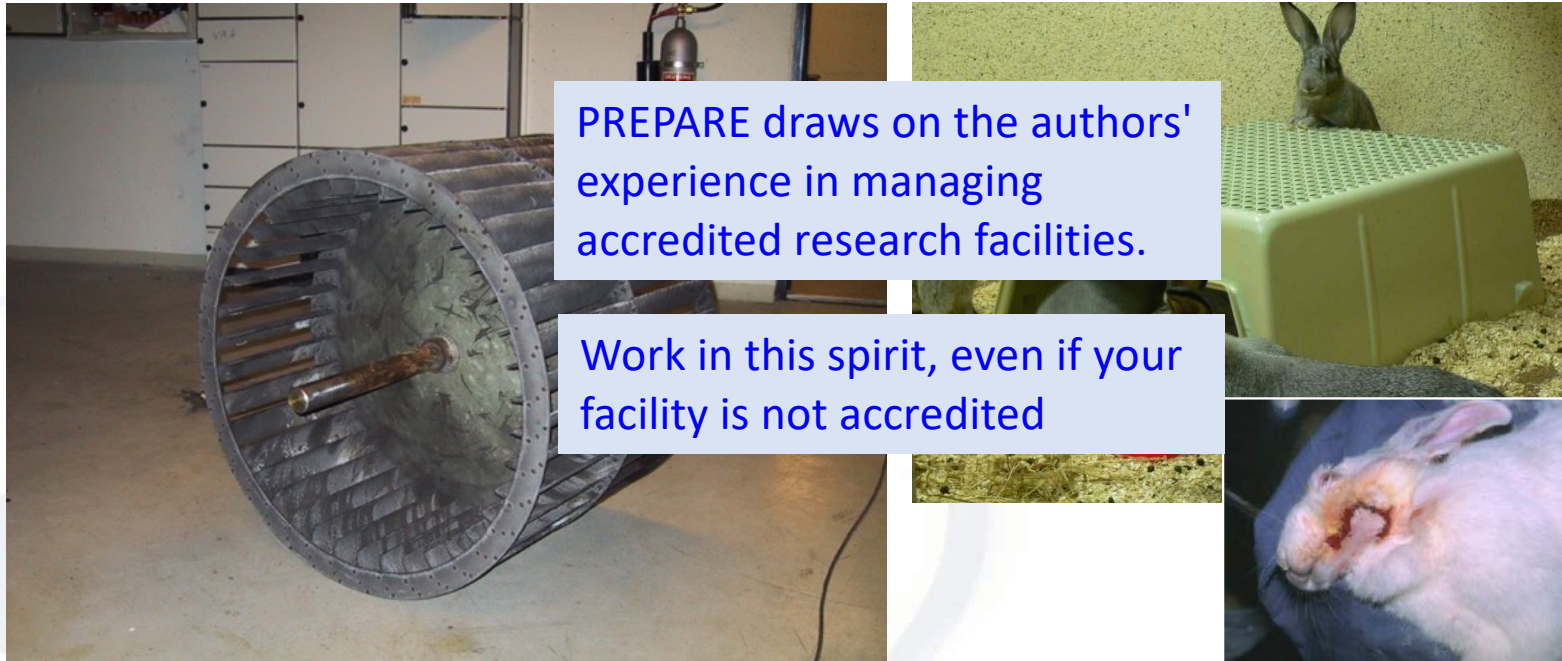


Photo: NMBU

A checklist for the entire facility



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

aaalac.org/program-description

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63 pages

A simple but effective Master Plan



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A contract between the animal facility and the research group

The division of labour and responsibilities

Clarifying all stages of the experiment

Ensuring that all necessary data are recorded

	Animal facility	Researcher	Not 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 \pm variation)			
Light schedule			
Relative humidity (mean \pm 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			

norecopa.no/more-resources/division-of-labour-costs-and-responsibility



CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

Refine - Reduce - Replace

What if things go wrong?

Detect
a critical
incident

Anonymous
report

CIRS-LAS.de



Get involved!

We all
learn
from it!

Expert
analysis

MUTUAL LEARNING from errors, near misses, critical or even adverse events occurring in the context of animal experimentation prevents unnecessary repetition of unsuccessful experiments

CRITICAL DISCUSSIONS on causes and approaches to solutions lead to an increase in animal welfare

OPEN DIALOGUE ensures transparency in laboratory animal science



NASA



cbsnews.com



no.wikipedia.org

- Complex machines/animals create *known or unknown unknown interactions*
- **Design weaknesses** (*which the engineers knew about!*)
- **External pressure to launch** (political, media) - "Publish or perish"
- **Management decisions** (pushing the safety envelope):
"We've got away with it before" / "We've managed to publish this before"
- A combination of many factors, each of which may be appear insignificant until they occur simultaneously

We need a Culture of Care!



Culture of Care

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, including the public

It goes beyond simply complying with the law!

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Communication and the Culture of Care

Penny Hawkins, RSPCA Research Animals Department
on behalf of the International Culture of Care Network*

Effective two-way communication between scientists and animal technologists is essential for a good Culture of Care
The European Commission suggests the 'development of formal and informal communication channels, for mutual benefit with respect to science and animal welfare'
Here are some examples from International Culture of Care network members

Regular meetings

Scheduled meetings for scientists, animal technologists, vets, unit managers and AWERB members



Regular refresher/updates

Special events

Duo-talks: researcher talks about their science, and animal technologists talk about techniques and animal care within the project



+ Quick Start Guide

Communication into existing processes

Each study has a pre-start and wash-up meeting involving everybody



Three Rs improvements reported to AWERB & shared at external user meetings



Other ideas

A 'boxless' event: anyone can submit 'out of the box' ideas to improve practice



A staff survey for all e.g. how much do you agree with statements such as 'in our group we listen to each others' ideas about animal welfare'



*norecopa.no/culture-of-care

The Refinement Wiki

wiki.norecopa.no

A lot of good ideas on refinement circulate among care staff and on discussion forums, but never get published.

Designed to be

- a portal for rapid publication and dissemination of these ideas





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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)^[1]. 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.

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 training 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. ↑ ^{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.
3. ↑ Leidinger, Charlotte; Herrmann, Felix; Thöne-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

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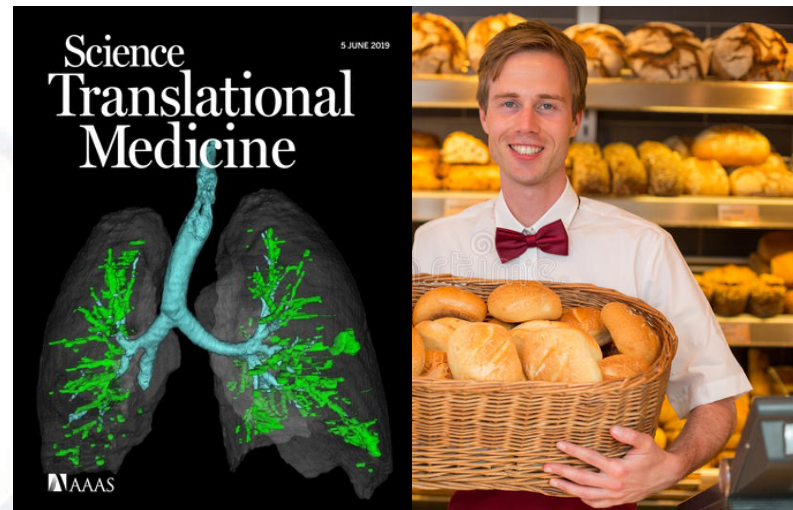


<https://www.bls.gov/ooh/images/3077.jpg>



PREPARE *from day 1*

ARRIVE



<https://www.dreamstime.com>

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norecopa

"We ARRIVED, because we were PREPARED"

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

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'Navigating the guidelines and principles...'



Utrecht University



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Feedback

English-language newsletters

Contact oss
+47 41 22 09 49
post@norecopa.no

Street address
Ullevålsveien 68
0454 Oslo


Postal address
% Norwegian Veterinary
Institute
P.O. Box 750 Sentrum
N-0106 Oslo, Norway


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