

How to use the 3Rs to plan for better Science

Adrian Smith

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norecopa.no/SAAE-I

"better science?"

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

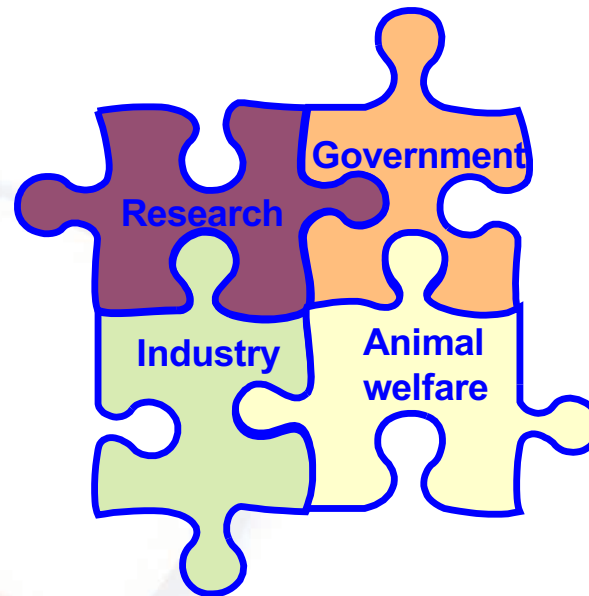


colourbox.com



*Norecopa is a National Consensus Platform for the 3Rs:
Replacement, Reduction and Refinement of animal experiments*

*A member of **ecopa**:
European Consensus-Platform for Alternatives
which recognises National Consensus Platforms with
4 stakeholders equally represented:*



Norecopa: PREPARE for better Science

40-slide powerpoint presentation about the 3Rs



ccac.ca

All three Rs of Russell and Burch:

Replacement, Reduction & Refinement

English, French and Spanish versions (soon German)

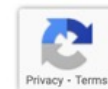
Free download from norecopa.no/3Rs

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

The screenshot shows the top section of the norecopa.no website. It features a blue header with the norecopa logo (a stylized star) and the text 'norecopa'. To the right, there are language options for 'NORSK' and 'ENGLISH', and a search bar with a magnifying glass icon. Below the header is a navigation menu with links for 'About Norecopa', 'Alternatives', 'Databases & Guidelines', 'Education & training', 'Legislation', 'Meetings', 'More resources', 'News', 'PREPARE', 'Species', and 'Wiki'. A secondary menu lists various topics such as 'Anaesthesia and analgesia', 'Animal facilities', 'Animal welfare organisations', 'Blood sampling', 'Culture of care', 'Email discussion lists', 'Environmental enrichment', 'Ethics', 'Experimental design and reporting', 'Harm-Benefit Assessment', 'Health and safety', 'Health monitoring', 'Humane', 'Literature searches and systematic reviews', 'Organisations', and 'Suppliers'. A breadcrumb trail at the bottom of the screenshot reads 'norecopa.no / More resources / Experimental design and reporting'. An orange callout box is overlaid on the page, containing the text: 'approx. 10,000 webpages', 'approx. 1,000 hits per day', and '7-8 detailed newsletters per year'.

Design and reporting of animal experiments

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



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November 2023

- ▶ [Puzzles for mice - investigating intelligence and improving well-being](#), webinar (Katharina Hohlbaum), [registration](#), 2 November 2023
- ▶ [Different strategies on the way to in-vitro bone modelling](#), webinar (Moritz Pfeiffenberger), [registration](#), 2 November 2023
- ▶ [Danish 3R-Center's Annual Symposium](#), Copenhagen, 6-7 November 2023
- ▶ [Fin3R Annual Symposium: Improving the quality and translatability of biomedical research through the 3R principle](#), Helsinki/online, 6-7 November 2023
- ▶ [GA Rodent Colony Management](#), London, 6-7 November 2023
- ▶ [CBMAIt 2023](#), Rio de Janeiro, 6-9 November 2023
- ▶ [International Forum on Cell Manufacturing & Engineering](#), Berlin, 7-8 November 2023
- ▶ [Launch of the Norwegian Forum for Animal Law](#), Oslo, 8 November 2023
- ▶ [Improving Openness in Animal Research in Denmark](#), Copenhagen, 8 November 2023
- ▶ [The COLAAB: The Author Guide for Addressing Animal Methods Bias in Publishing](#), webinar, 8 November 2023
- ▶ [The new OECD \(Q\)SAR Assessment Framework: guidance for assessing \(Q\)SAR models and predictions](#), webinar, 9 November 2023
- ▶ [Veterinary Skills Net - simulation-based education in Berlin](#), webinar (Samira Schlesinger), [registration](#), 9 November 2023
- ▶ [Assessment and refinement of the wellbeing of mice during metabolic cage housing](#), webinar (Philipp Villiger), [registration](#), 9 November 2023
- ▶ [Altertox and EPITHELIX: Lung in vitro models](#), Geneva, 9-10 November 2023
- ▶ [Systematic review and meta-analysis of animal studies](#), workshop, 10 November 2023
- ▶ [Designing a good score sheet for animal welfare assessment](#), webinar (Philipp Villiger), 10 November 2023
- ▶ [18th Transgenic Technology Meeting](#), Houston, 12-15 November 2023
- ▶ [Practical course in zebrafish husbandry and procedures](#), Stockholm, 13-15 November 2023
- ▶ [EPAA annual conference](#), Brussels, 15 November 2023
- ▶ [Biomimetic robots - a new way to fulfil the 3Rs requirements](#), webinar (David Bierbach), [registration](#), 16 November 2023
- ▶ [Brain organoids to model human brain diseases](#), webinar (Agnieszka Rybak-Wolf), [registration](#), 16 November 2023
- ▶ [RSPCA Focus on Severe Suffering: Humane Endpoints in Regulatory Toxicology](#), Surrey, 16 November 2023
- ▶ [Importance of systematic assessment of scientific validity in in vivo study design](#), webinar, 16 November 2023
- ▶ [Networking meeting for Nordic zebrafish managers](#), Stockholm/online, 16-17 November 2023
- ▶ [Practical approaches and challenges for microbiological monitoring of rodents and zebrafish](#), Milan, 16-17 November 2023
- ▶ [Mice learning in social interaction and consequences for welfare and data quality](#), webinar (Benjamin Lang), 17 November 2023
- ▶ [Online media training for veterinarians](#), EARA webinar, 20 November 2023
- ▶ [6th Annual SAAE-India Conference: Alternatives to Higher Animals in Biological Research](#), Aligarh (India), 20-22 November 2023
- ▶ [Oxford / Berlin Autumn School on Open and Responsible Research](#), Oxford, 20-24 November 2023
- ▶ [LASA Annual Meeting](#), 21-23 November 2023
- ▶ [QASH2 \(Quantitative Atlantic Salmon Health\) - 1st meeting](#), program to be announced, Bergen, 22 November 2023
- ▶ [EALAS-2023](#), online, 22-24 November 2023
- ▶ [Wetlabs](#), Rome, 22-24 November 2023
- ▶ [EASA 2023](#), Copenhagen, 23 November 2023
- ▶ [Animal Care and Use Committee \(ACUC\) Training](#), Copenhagen, 23 November 2023
- ▶ [Genetics to tackle inflammatory and genetic diseases of human epithelia](#), webinar (Sarah Hedtrich), [registration](#), 23 November 2023
- ▶ [Pain Recognition and Analgesia in Zebrafish](#), webinar (Lynne Sneddon), 27 November 2023
- ▶ [Rodent Surgery Course \(3 or 5 days\)](#), Almere, 27 November - 1 December 2023
- ▶ [Assessment, Prevention and Alleviation of Pain in Laboratory Animals workshop](#), online, 27-30 November 2023
- ▶ [SGV Annual Meeting](#), Zurich, 28-29 November 2023
- ▶ [Lab Animal Publication School](#), online course, 28-30 November 2023
- ▶ [CLAST course on Researching data and using information](#), start 30 November 2023
- ▶ [Brain organoids for the discovery of novel mechanisms and targets in stroke and neurodegeneration](#), webinar (Philipp Mergenthaler), [registration](#), 30 November 2023
- ▶ [6R: Robustness, Registration and Reporting aspects in 3R in vitro research](#), webinar (Maren Hülsemann), [registration](#), 30 November 2023



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norecopa.no/meetings/meetings-calendar

+ webpages for recorded meetings, sorted by PREPARE topics

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3RS & ETHICS BY DESIGN

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Our Training:



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challenge your understanding of ethics
in research.



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and exploring opportunities to use New
Approach Methodologies (NAMs).



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and networking with other researchers.

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<https://frame.beaconforms.com/form/5dea91b6>

Programme:

<https://frame.org.uk/app/uploads/2023/10/3Rs-and-Ethics-by-Design-Training-Programme-DRAFT-Online-V2.pdf>

Norecopa: PREPARE for better Science

Databases & Guidelines

- > [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 five 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 papers, published in 2020
 - ▶ [Non-animal models for cardiovascular diseases](#), citing over 400 models, identified in a literature review of over 14,000 papers, published in 2022

The EU Commission has now published [30 datasets of this type](#).

Here is [an alphabetical global list of all the databases](#) cited on the Norecopa website.

norecopa.no/databases-guidelines

links to over 70 other databases



3R-Guide (over 400 guidelines for implementation of the 3Rs)

norecopa.no/3r-guide



Working Party Report

Guidance on the severity classification of scientific procedures involving fish: report of a Working Group appointed by the Norwegian Consensus-Platform for the Replacement, Reduction and Refinement of animal experiments (Norecopa)

P Hawkins (Convenor), N Demisson, G Goodman, S Hetherington, S Llywelyn-Jones, K Ryder and A J Smith*

Abstract
The severity classification of procedures using animals is an important tool to help focus the implementation of refinement and to assist in reporting the application of the 3Rs (replacement, reduction and refinement). The recently revised Directive that regulates animal research and breeding within the European Union requires Member States to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe', using assignment criteria set out by the European Commission (EC). However, these are focused upon terrestrial species, so are of limited relevance to fish users. A Working Group set up by the Norwegian Consensus Platform for the 3Rs (Norecopa) has produced guidance on the classification of severity in scientific procedures involving fish, including examples of 'sub-lethal', 'mild', 'moderate', 'severe' and 'upper threshold' procedures. The aims are to complement the EC guidelines and help to ensure that suffering which is effectively predicted and minimized. Norecopa has established a website (www.norecopa.no) collated where more information on severity classification for procedures using fish, including field research, will be made available.

Keywords: Fish, harm-benefit assessment, humane endpoints, refinement, severity

Laboratory Animals 2011; 1-6. DOI: 10.1056/la.2011.010181

Background
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because physiological and behavioural responses to suffering can significantly affect data quality. Severity classification is thus an important tool to help focus the implementation of refinement, including monitoring its progress, and to assist in reporting the application of the 3Rs (replacement, reduction and refinement) of Russell and Burch, which is now an integral part of the legislation on animal research and testing in many countries. Predictors of severity are also fundamental to the harm-benefit

assessments undertaken by bodies such as regulatory authorities and ethical committees when deciding whether or not a project should be licensed or funded.

There may also be a legal requirement to predict and classify severity. For example, the new Directive regulating animal use within the European Union, which must be implemented within all Member States by January 2013, requires the severity of each procedure to be classified on the basis of the 'degree of pain, suffering, distress or lasting harm expected to be experienced by an individual animal during the course of the procedure', with the aim of enhancing transparency, facilitating the project authorization process and providing tools for monitoring compliance. Member States will have to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe' on a case-by-case basis, using the assignment

assessments undertaken by bodies such as regulatory authorities and ethical committees when deciding whether or not a project should be licensed or funded.

Laboratory Animals 2011; 1-6

AVMA Guidelines for the Euthanasia of Animals: 2020 Edition*

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*The AVMA Panel on Euthanasia developed the content of the guidelines, with support from its working groups. The panel is required to do a comprehensive review and update of the report at least every 10 years, although more frequent major revisions are possible based on substantive information gained from new research and experience with practical implementation. To ensure the guidelines remain as up-to-date as possible, interim revisions (including substantial updates) that do not affect acceptance criteria that a major revision is also acknowledged.

A Gold Standard Publication Checklist to Improve the Quality of Animal Studies, to Fully Integrate the Three Rs, and to Make Systematic Reviews More Feasible

Carlijn R. Hooijmans, Marlies Leenaars and Merel Ritsema-Hoitinga
Radboud University Nijmegen Medical Centre, Central Animal Laboratory and 3R Research Centre, Nijmegen, The Netherlands

Summary—Systematic reviews are generally regarded by professionals in the field of evidence-based medicine as the highest level of medical evidence, and they are already standard practice for clinical studies. However, they are not yet widely used nor undertaken in the field of animal experimentation, even though there is a lot to be gained from the process. Therefore, a gold standard publication checklist (GSPC) for animal studies is presented in this paper. The items on the checklist have been selected on the basis of a literature analysis and the resulting scientific evidence that these factors are decisive in determining the outcome of animal studies. In order to make future systematic reviews and meta-analyses of animal studies possible, to allow others to replicate and build on work previously published, decrease the number of animals needed in animal experimentation (reduction), improve animal welfare (refinement) and, above all, improve the quality of scientific papers on animal experimentation, this publication checklist needs to be used and followed. We have discussed and optimized this GSPC through feedback from interviewees with expertise in the field of animal experimentation. From these interviews, it became clear that scientists will submit the GSPC when journals demand it. The GSPC was compared with the current instructions for authors from nine different journals, selected on the basis that they featured a high number of publications on animal studies. In general, the journals' demands for the description of the animal studies are so varied that it is not possible to repeat the studies, let alone carry out a systematic review. By using the GSPC for animal studies, in general, the journals' demands for the description of the animal studies are so varied that it is not possible to repeat the studies, let alone carry out a systematic review. By using the GSPC for animal studies, it is of major importance that journal editors become convinced of and adopt these recommendations, because only then will scientists follow these guidelines to the full extent.

Key words: animal experimentation, meta-analysis, publication checklist, scientific quality, systematic review

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Introduction
A systematic review (SR) is a literature review focused on a single question which aims to identify, appraise, select and synthesize all available high-quality research evidence relevant to that question (1). SRs are generally regarded by evidence-based medicine professionals as the highest level of medical evidence, and they are already standard practice in clinical studies. However, SRs are not yet widely used nor undertaken in the animal experimentation field, although there would be a lot to be gained from the process. A systematic approach to incorporate all available relevant literature into the design of an animal experiment is a prerequisite for research which is of high scientific quality. Good science, from a scientific as well as an animal welfare point of view, is the basis of the book, *The Principles of Humane Experimental Technique*, by Russell and Burch (2). In this book, they recommended that the Three Rs principles (Replacement, Reduction and Refinement) should be applied wherever possible in animal studies. Besides producing high-quality research, SRs of animal experiments will result in direct implementation of the Three Rs. SRs may provide the proper argumentation to decide which animal model will give the best answer to the clinical research question (3, 4) and to detect whether there are gaps in scientific knowledge that require new animal experiments (replacement and refinement). This will also aid in preventing unnecessary duplication of animal experiments (reduction), and thus decrease unnecessary animal use and time loss. A SR of animal studies will also lead to a better interpretation of the already existing scientific results from animal experiments, through which a better



Tim Allen, USDA

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TextBase:

1,500 books related to
Lab Animal Science, welfare
and alternatives:

norecopa.no/textbase

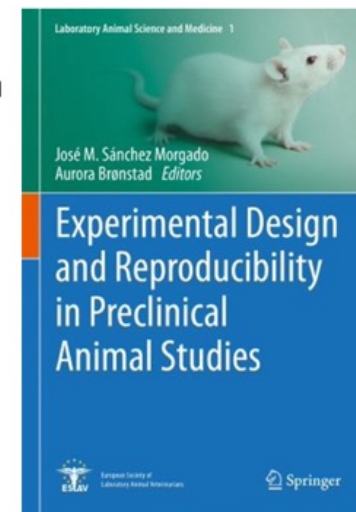
Experimental Design and Reproducibility in Preclinical Animal Studies

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.

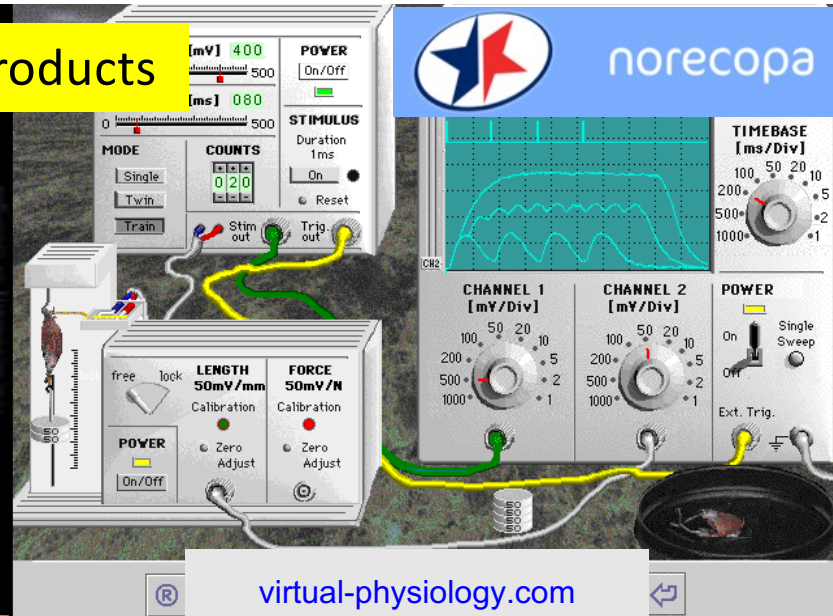


norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies

NORINA database: approx. 3,000 products



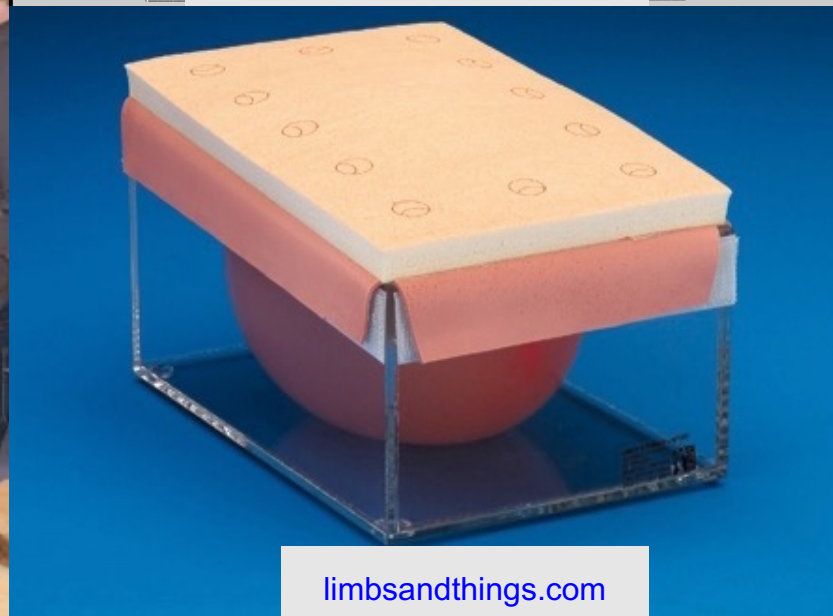
3dglasshorse.com



virtual-physiology.com



rescuecritters.com



limbsandthings.com


The pathway to better science



Norecopa: PREPARE for better Science

norecopa.no/PREPARE and ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1

We cannot improve our research by
better reporting alone...



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*Precision and replicability in the aviation industry:
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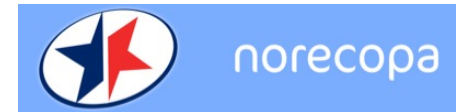
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Checklists

- 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
- Make sure that everyone is "**on the same page**"



Original Article

Laboratory Animals
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PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Litley³, 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 Norecoba website, with links to guidelines for animal research and testing, at <https://norecoba.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

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Norecoba: PREPARE for better Science

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



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

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PREPARE¹ består av retningslinjer for planlegging av dyreforsøk. Disse som f.eks. ARRIVE². PREPARE dekker de tre store områdene som beste
 1. **Designet av studiet**
 2. **Dialogen mellom forskerne og dyreavdelingen**
 3. **Kvalitetskontroll av de ulike komponentene i studiet**
 I praksis vil ikke temaene alltid behandles i den rekkefølgen som er på PREPARE-sjekklisten kan endres for å ivareta spesielle behov, f.eks. ved dyreavdelinger, fordi laboratorieforsøk er helt avhengige av deres kvalité Norecopia's nettsider, med lenker til globale ressurser, på <https://morecopia.no>. PREPARE-retningslinjene er et dynamisk sett som vil videreutvikles etterhvert som "best praksis" innenfor forskedyrmyndighet forbedres.

+ 2 online versions
35 languages

Tema	Anbefaling
(A) Designet av studiet	
1. Litteratursøk	<input type="checkbox"/> Formulere en klar hypotese, med primære og sekundære mål. <input type="checkbox"/> Vurdere å foreta en systematisk undersøkelse av litteraturen (Systematic Review). <input type="checkbox"/> Bestemme hvilke databaser og informasjonsspesialister som skal brukes, og konstruere søkebegrep. <input type="checkbox"/> Vurdere relevansen av dyrearten som skal brukes, dens biologi og egnethet til å svare på de eksperimentelle spørsmålene med minst mulig lidelse, og artens velferdsbehov. <input type="checkbox"/> Evaluere prosjektets reproduserbarhet og overførbarhet.
2. Juridiske spørsmål	<input type="checkbox"/> Vurdere hvordan forsøket er påvirket av relevant lovgivning for dyreforsøk og andre aktuelle områder som f.eks. dyretransport og helse, miljø og sikkerhet. <input type="checkbox"/> Finne relevante veiledningsdokumenter (f.eks. EUs retningslinjer for prosjektevaluering).
3. Etske spørsmål, kostnad-nytteanalyse og humane endepunkter	<input type="checkbox"/> Skrive et sammendrag av prosjektet på legmannsspråk. <input type="checkbox"/> I dialog med etske komitéer, vurdere om uttalelser om denne typen forsøk er allerede blitt produsert. <input type="checkbox"/> Adressere "de 3 R-ene" (Replacement, Reduction, Refinement) og "de 3 S-ene" (Good Science, Good Sense, Good Sensibilities). <input type="checkbox"/> Vurdere forhåndsregistrering av forsøket og publisering av negative resultater. <input type="checkbox"/> Foreta en kostnad-nytteanalyse ("Harm-Benefit Assessment") og diskutere eventuelle lidelser som kan oppstå under forsøket. <input type="checkbox"/> Diskutere læringsmålene dersom dyrene skal brukes i undervisnings- eller treningsøyemed. <input type="checkbox"/> Klassifisere prosjektet etter belastningsgraden. <input type="checkbox"/> Definiere objektive, lett målbare og utvetydige humane endepunkter. <input type="checkbox"/> Diskutere behovet (hvis det er noe) for å bruke død som endepunkt for forsøket.
4. Eksperimentelt design og statistisk analyse	<input type="checkbox"/> Vurdere pilotforsøk og diskutere statistisk styrke og signifikansnivåer. <input type="checkbox"/> Definiere den eksperimentelle enheten og bestemme antallet forsøksdyr. <input type="checkbox"/> Bestemme metodene for randomisering, fortløpende observasjonsskjemaer, og bestemme inklusjons- og eksklusjonskriterier.

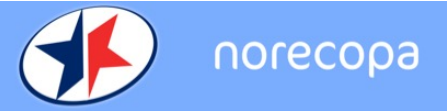
Tema	Anbefaling
(B) Dialogen mellom forskerne og dyreavdelingen	
5. Mål og tidshorisont, finansiering og arbeidsfordeling	<input type="checkbox"/> Arrangere møter med alle relevante personell når tidlige planer for prosjektet foreligger. <input type="checkbox"/> Lag en omtrentlig tidsramme for prosjektet, som viser behovene for assistanse med forberedelser, dyrestell, prosedyrer og avfallshåndtering/dekontaminasjon. <input type="checkbox"/> Diskutere og legge frem alle forventede og potensielle kostnader. <input type="checkbox"/> Lage en detaljert plan for fordelingen av både arbeidsgjøvning og utgiftene, på alle stadiene i forsøket.

fasilitetene, for å evaluere bygningsmassen, standarden på utstyret og ved perioder med ekstra risiko.
 fansen hos personalet og evaluere behovet for videreutdanning og en, foreta en risikoevaluering som omfatter alle personene og dyrene direkte, av studiet.
 dusere, spesifikke retningslinjer for alle stadiene av prosjektet.
 , dekontaminere og avhende alt utstyret som skal brukes i studiet.

Tema	Anbefaling
(C) Kvalitetskontroll av de ulike komponentene i studiet	
9. Testsubstanser og -prosedyrer	<input type="checkbox"/> Oppgi så mye informasjon som mulig om testsubstansene. <input type="checkbox"/> Evaluere gjennomførbareheten og validiteten av testprosedyrene, og de praktiske ferdighetene som er nødvendige for å gjennomføre dem.
10. Forsøksdyr	<input type="checkbox"/> Bestemme egenskapene til dyrene som er essensielle for studiet og som må rapporteres. <input type="checkbox"/> Unngå produksjon av overskuddsdyr.
11. Karantene og helsemonitorering	<input type="checkbox"/> Diskutere dyrenes sannsynlige helsestatus, og eventuelle behov for transport, karantene og isolasjon, samt helsemonitorering og konsekvensene for personalet.
12. Oppstalling og stell	<input type="checkbox"/> Ta hensyn til dyrenes spesifikke instruksjoner og behov, i samråd med eksperter. <input type="checkbox"/> Diskutere akklimatisering, optimale oppstallingsforhold og prosedyrer, miljøfaktorer og eventuelle begrensninger på disse (f.eks. fasting eller oppstalling i enebur).
13. Eksperimentelle prosedyrer	<input type="checkbox"/> Utvikle optimale metoder for fangst, immobilisering, merking og frisetting eller omplassering. <input type="checkbox"/> Utvikle optimale metoder for å gi dyrene behandling, samt for prøvetaking, sedasjon og anestesi, kirurgi og andre inngrep.
14. Human avlivning, frisetelse eller omplassering	<input type="checkbox"/> Konsultere relevant lovgivning og retningslinjer i god tid før studiet. <input type="checkbox"/> Definiere de primære metodene for avlivning, samt metoder som kan brukes i en nødsituasjon. <input type="checkbox"/> Evaluere kompetansen til personene som må foreta disse handlingene.
15. Obduksjon	<input type="checkbox"/> Lage en systematisk plan for alle stadiene i obduksjonen, inkl. hvor den skal foregå, og identifikasjon av alle dyrene og prøvene som tas.

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

Mer informasjon
<https://morecopia.no/PREPARE> | post@norecopia.no | [@norecopia](https://twitter.com/norecopia)



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

norecoba.no/PREPARE

A screenshot of the norecoba.no website. The header is blue with the Norecoba logo and the word "norecoba" in white. In the top right corner, there are language options "NORSK" and "ENGLISH" (underlined), and a search bar with the text "Search: Q". The navigation menu below the header includes links for "About Norecoba", "Alternatives", "Databases & Guidelines", "Education & training", "Legislation", "Meetings", "More resources", "New", "PREPARE" (circled in red), and "Species". Below the navigation menu, a list of links for the PREPARE Checklist is displayed, including "1-Literature searches", "2-Legal issues", "3-Ethical issues, Harm-Benefit Assessment and humane endpoints", "4-Experimental design and statistical analysis", "5-Objectives and timescale, funding and division of labour", "6-Facility evaluation", "7-Education and training", "8-Health risks, waste disposal and decontamination", "9-Test substances and procedures", "10-Experimental animals", "11-Quarantine and health monitoring", "12-Housing and husbandry", "13-Experimental procedures", "14-Humane killing, release, re-use or re-homing", "15-Necropsy", and "Comparison with ARRIVE". At the bottom left of the page, the breadcrumb "norecoba.no / PREPARE" is visible, and at the bottom right, there are social media icons for Facebook, Twitter, Email, and a plus sign for more options.

Norecoba: PREPARE for better Science

norecopa.no/PREPARE

- 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).
 - 3f 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.

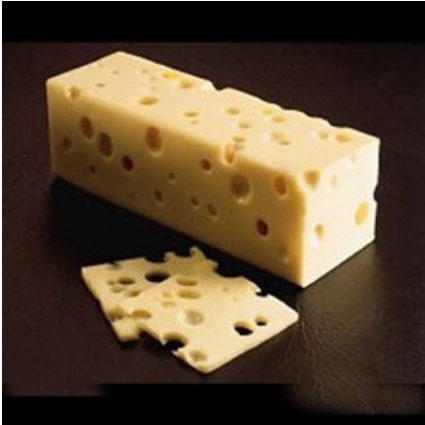
Links to quality guidelines and scientific papers worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design

2. Will any advances in this research be published, and if so, will the publication only index the title and abstract, or will the full text be made available? Will the project be rejected?
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?

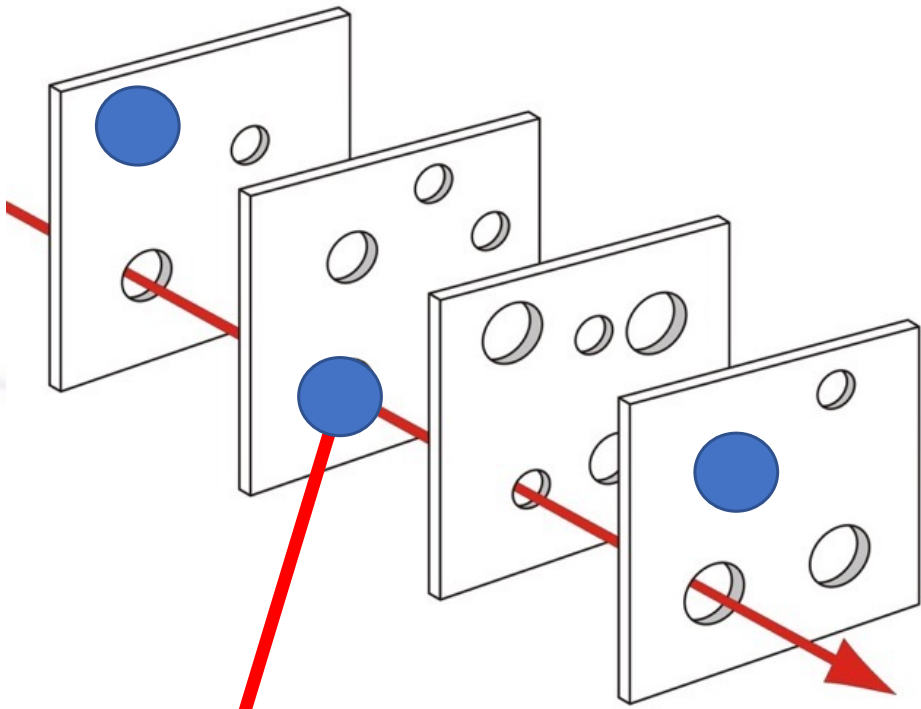
Many more [links to resources on ethics are available here](#). Details about pre-registration of animal studies and reporting of critical incidents are to be found in the section on [Experimental Design and Statistical Analysis](#).

Harm-Benefit Assessment

“Threat and Error Management”



eaugallecheese.com/Swiss-Cheese



Weaknesses / dangers

Serious incidents

wikipedia.org/wiki/Swiss_cheese_model



CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

Refine - Reduce - Replace

Homepage

Project

Team

FAQ



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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

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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- 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
- Clicker training
- Contingency plans
- Decapitation
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- EMLA cream
- Embryo transfer
- Experimental Autoimmune Encephalomyelitis (EAE)
- Facial expression analysis
- Food crunchers
- General discussion on use of analgesics
- Genotyping mice
- Habituation training
- High-fat diets
- Hot Bead Sterilisers
- Housing nude mice
- Housing research fish
- Humane endpoints
- Hydrodynamic gene delivery
- Intra-ocular injections
- Intranasal administration
- Intraperitoneal injection
- Intraperitoneal pentobarbitone
- Ketamine and alpha-2 agonist combinations
- Long-term anaesthesia in rodents
- Lumpfish
- Main Page
- Marble Burying Test
- Metabolic cages
- Minipumps
- Montanide adjuvant
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Oestrus suppression in ferrets
- Pneumocystis murina
- Recapping needles
- Rotarod Test
- Screening cell lines
- Sedation of cattle
- Splenectomy
- Sterilisation of instruments
- TTEAM and TTouch
- Tail vein injection
- Tramadol
- Transport stress
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing



Culture of Care

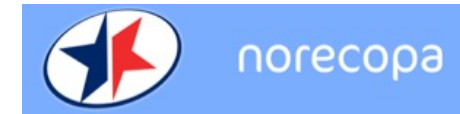
The International Culture of Care Network

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

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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/update meetings for all organised by NTCO



Special events

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



ELH organises an informal meeting for all, in which anyone can raise welfare issues



Building 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

Culture of Care facilitates honest discussion along the path



"because we've always done it that way"

"as often as necessary"

"there are no alternatives"

Closely related to a culture of care is

a **Culture of Challenge** (Louhimies, 2015).

Look for the acceptable, rather than choosing the accepted.



Culture of Care Network

norecopa.no/coc



norecopa.no/global3r

Centres

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

Associations

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

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norecopa.no/PREPARE and ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1

arriveguidelines.org

The ARRIVE guidelines 2.0

This section of the website provides detailed explanations about each item of the guidelines. Use the left-hand side menu to navigate to each item.

To facilitate a step-wise approach to improving reporting, the guidelines are organised into two prioritised sets:

ARRIVE Essential 10

These ten items are the basic minimum that must be included in any manuscript describing animal research. Without this information readers and reviewers cannot assess the reliability of the findings.

Recommended Set

These items complement the Essential 10 set and add important context to the study described. Reporting the items in both sets represents best practice.

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The screenshot shows the ARRIVE guidelines website. The top navigation bar includes 'Home', 'About', 'ARRIVE guidelines', 'Supporters', 'Resources', 'Publications', and 'News'. The left sidebar contains a list of guidelines, with 'Recommended Set' and '11. Abstract' 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 items: 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](#)



norecopa

"We ARRIVED, because we were PREPARED"

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



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More than 3Rs

The 3 Rs to minimise the harm:

- *Replace the unnecessary experiments*
- *Reduce the number of animals used*
- *Refine the conditions for the animals*

The 3 Ss - your commonsense and your heart

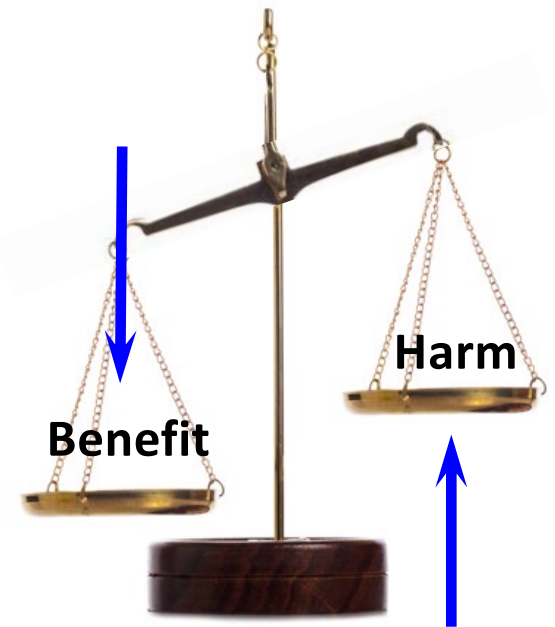
- *Good Science*
- *Good Sense*
- *Good Sensibilities*



The 3 Vs to increase the validity of the experiment:

- *Construct Validity (can the model answer the question?)*
- *Internal Validity (has the experiment been correctly designed?)*
- *External Validity (are the results translatable to the target group?)*

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norecopa.no/3R

norecopa.no/3S

norecopa.no/3V

NAMs og NATs

NAMs: New Approach Methodologies (not *Non-Animal Methods!*)
Avoidance (methods which don't directly replace animal experiments)

e.g. "Read-Across"
 studies on the human placenta



colourbox.com

NATs: Non-Animal Technologies
Alternatives to animal experiments

e.g. organoids (mini-organs)
 organs-on-chips
 experiments on fruit flies

	Chemical 1	Chemical 2	Chemical 3	Chemical 4
Structure	xxxxxxxx	xxxxxxxx	xxxxxxxx	xxxxxxxx
Property 1	● → ○	○	● → ○	○
Property 2	● → ○	○	○ ← ●	●
Property 3	○ ← ●	●	● → ○	○
Activity 1	● → ○	○	● → ○	○
Activity 2	● → ○	○	○ ← ●	●
Activity 3	○ ← ●	●	● → ○	○

● Existing data point ○ Missing data point

NB. Those who work with NAMs may not even be aware that they use a method that can reduce animal use. It is therefore important to build bridges between the lab animal community and the NAMs/NATs-communities !

<https://www.oecd.org/chemicalsafety/risk-assessment/groupingofchemicalschemicalcategoriesandread-across.htm>

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https://nc3rs.org.uk/sites/default/files/documents/NonAnimalTechCO082_RYE_4_nrfinal2.pdf

We need more dialogue between the experts in their different fields



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English-language newsletters



norecopa.no/news/newsletters

1,300 international subscribers

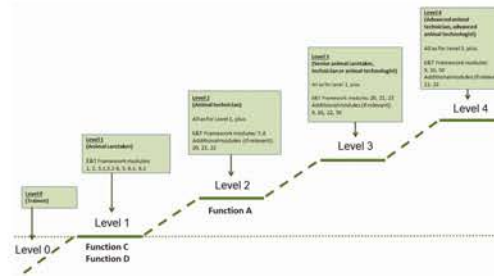
7-8 times a year

- Norecopa's Annual Meeting and 3R Prize
- Updates about Norecopa
- Nordic Zebrafish Network and course
- News of PREPARE
- News of other 3R Centres and activities
- Harmonisation of education and training
- New forum for behavioural research
- New textbook on anaesthesia
- Fish research
- Glimpses from research
- Food for thought
- For Norwegian readers
- From the media
- Webinars and Meetings Calendar
- Have your colleagues subscribed?



Hands-on zebrafish husbandry course 2023
13 - 15 November, Stockholm, Sweden

Nordic zebrafish meeting 2023
16 - 17 November, Stockholm



www.thebehaviourforum.org

Q&A forum for the discussion of scientific matters relating to the use of behavioural research in laboratory animals with special relevance for home-cage monitoring.

TheBehaviourForum.org

Do you have questions on:

- Experimental design
- Software & hardware
- Data handling
- Animal welfare

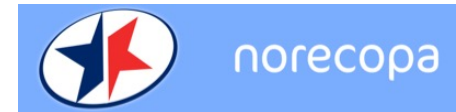
Share protocols and useful experiences about, how you test behaviour, analyse data, use methods and devices.

Post and find out:

- What's new in the world of animal behaviour, methods, software/hardware, publications...
- Information on events, meetings & training in the world of animal behaviour
- Academic job opportunities

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