

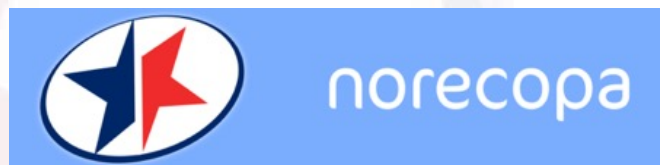
PREPARE for Better Science: The PREPARE and ARRIVE guidelines

Adrian Smith

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[@adrian_3r](#)

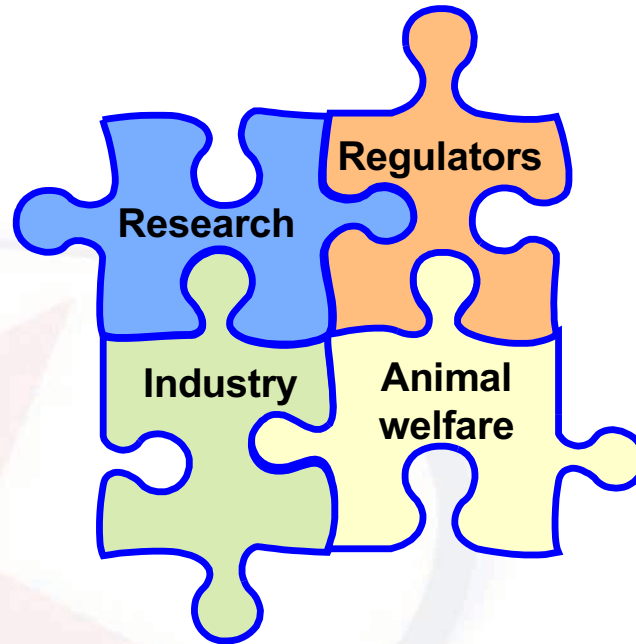
norecopa.no/161123



<https://norecopa.no>

Norecopa is Norway's National **Consensus**-platform,
working to advance *all the three R's*:
Replacement, Reduction and Refinement

Its Board represents:



Established in 2007

40-slide powerpoint presentation about the 3Rs



ccac.ca

The 3Rs of Russell and Burch:

Replacement, Reduction & Refinement

Available at norecopa.no/3Rs

With some material from:

Smith AJ & Richmond J (Forthcoming). The Three-Rs.
In: *The UFAW Handbook on the Care and Management of Laboratory and Other Research Animals*. 9th edition.
Richardson CA and Golledge HDR (eds).
Oxford: Wiley-Blackwell.

English, French and Spanish



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Norecopa: PREPARE for better Science

Disclosures about resources which will be mentioned

- *Webmaster for the Norecopa site - information about global guidelines*
- *Lead author of several databases on the Norecopa site*
- *Lead author of the PREPARE guidelines*
- *Manager of the Refinement Wiki*

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



norecopa.no / More resources / [Experimental design and reporting](#)

Design and reporting of animal experiments

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

approx. 9,700 webpages
approx. 1,000 hits daily

7-8 detailed newsletters per year

Norecopa: PREPARE for better Science



"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



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3RS & ETHICS BY DESIGN

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Our Training:

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-  **Engagement with 3Rs** and exploring opportunities to use New Approach Methodologies (NAMs).
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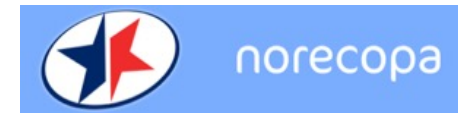
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Programme:

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

Norecopa: PREPARE for better Science

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

we need reporting **and** planning guidelines



[reddit.com](https://www.reddit.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

How do others achieve success and reproducibility?



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



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...and precision in a variable environment?



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



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



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Hudson River, 2009

en.wikipedia.org

All 155 passengers and crew saved

10-15 checklists even on short routine flights



Norecopa: PREPARE for better Science

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**"



Rapid evacuation by trained cabin crew saved many lives

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



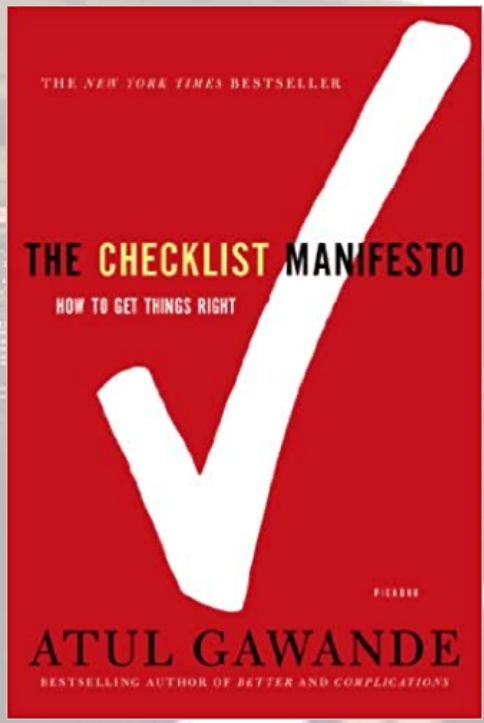
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Surgical Safety Checklist



World Health Organization | Patient Safety
A World Alliance for Safer Health Care

Before induction of anaesthesia <small>(with at least nurse and anaesthetist)</small>	Before skin incision <small>(with nurse, anaesthetist and surgeon)</small>	Before patient leaves operating room <small>(with nurse, anaesthetist and surgeon)</small>
Has the patient confirmed his/her identity, site, procedure, and consent? <input type="checkbox"/> Yes	<input type="checkbox"/> Confirm all team members have introduced themselves by name and role. <input type="checkbox"/> Confirm the patient's name, procedure, and where the incision will be made. Has antibiotic prophylaxis been given within the last 60 minutes? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable	Nurse Verbally Confirms: <input type="checkbox"/> The name of the procedure <input type="checkbox"/> Completion of instrument, sponge and needle counts <input type="checkbox"/> Specimen labelling (read specimen labels aloud, including patient name) <input type="checkbox"/> Whether there are any equipment problems to be addressed
Is the site marked? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable	Anticipated Critical Events To Surgeon: <input type="checkbox"/> What are the critical or non-routine steps? <input type="checkbox"/> How long will the case take? <input type="checkbox"/> What is the anticipated blood loss? To Anaesthetist: <input type="checkbox"/> Are there any patient-specific concerns? To Nursing Team: <input type="checkbox"/> Has sterility (including indicator results) been confirmed? <input type="checkbox"/> Are there equipment issues or any concerns?	To Surgeon, Anaesthetist and Nurse: <input type="checkbox"/> What are the key concerns for recovery and management of this patient?
Is the anaesthesia machine and medication check complete? <input type="checkbox"/> Yes	Is essential imaging displayed? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable	
Is the pulse oximeter on the patient and functioning? <input type="checkbox"/> Yes		
Does the patient have a: Known allergy? <input type="checkbox"/> No <input type="checkbox"/> Yes Difficult airway or aspiration risk? <input type="checkbox"/> No <input type="checkbox"/> Yes, and equipment/assistance available Risk of >500ml blood loss (7ml/kg in children)? <input type="checkbox"/> No <input type="checkbox"/> Yes, and two IVs/central access and fluids planned		



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

amazon.com/gp/product/0312430000

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

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





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 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

Laboratory Animals
0301 1-7
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Norecoba: PREPARE for better Science

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Welfare (UFAW), UK

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



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journal website so far

Also downloadable from
norecoba.no/PREPARE

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

Adrian J. Smith*, R. Eddie Clutton†, Elliot Lilley*, Kristine E. Aa. Hanssen* & Trond Bratteli‡
 *Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; †Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; ‡Research Animals Department, Science Group, RSPCA, Millthorpe Stn, Doncaster, Yorkshire, West Sussex, DN11 0DD, U.K.;
 †Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, P.O. Box 8148 Dep., 0033 Oslo, Norway; ‡Division for Research Management, Sciences, 5020 Bergen, Norway.

PREPARE består av retningslinjer for planlegging av dyreforsøk. Disse som f.eks. ARRIVE. PREPARE dekker de tre store områdene som beste
 1. **Designet av studiet**
 2. **Dialogen mellom forskerne og dyrevæddingen**
 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 dyrevæddinger, fordi laboratorieforsøk er helt avhengige av deres kvalité Norecopas nettsider, med lenker til globale ressurser, på <https://norecopa.no>. PREPARE-retningslinjene er et dynamisk sett som vil videreutvikles etter produseres, og etter hvert som "best praksis" innenfor forskedyrmyllet 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 Sensibillities). <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, forhindre observasjonsskjøvheter, og bestemme inklusjons- og eksklusjonskriterier.

Tema	Anbefaling
(B) Dialogen mellom forskerne og dyrevæddingen	
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 arbeidsgjøvne og utgiftene, på alle stadiene i forsøket.
	fasilitetene, for å evaluere bygningsmassen, standarden på utstyret og ved perioder med ekstra risiko. tansen 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.
(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 gjennomførbarheten 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 Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLoS Biology*, 2010. DOI: 10.1371/journal.pbio.1000412.

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



Three versions of the checklist:

PREPARE

The PREPARE Guidelines Checklist
Planning Research and Experimental Procedures on Animals: Recommendations for Excellence
 Adrian J. Smith¹, R. Eddie Clutton², Elliot Lilley¹, Kristine E. Aa. Hanssen¹ & Trond Brattheld¹
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, Wilberforce 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 8148 Dep., 0033 Oslo, Norway; ⁵Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE¹ consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE². PREPARE covers the three broad areas which determine the quality of the preparation for animal 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 topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa 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.

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 its 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"/> Allocate a severity classification to the 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.

1. plain pdf file

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 evaluation	<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.
7. Education and training	<input type="checkbox"/> Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health risks, waste disposal and decontamination	<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 & Brattheld T. PREPARE Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/002367721724823.
 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
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norecopa.no/PREPARE/prepare-checklist

Three versions of the checklist:

2. fillable pdf file

norecopa.no/PREPARE-Word

Norecopa: PREPARE for better S

PREPARE



The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

^aNorecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; ^bRoyal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; ^cResearch Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.;

^dSection of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; ^eDivision for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE¹ consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE². PREPARE covers the three broad areas which determine the quality of the preparation for animal 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 topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa 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.

Formulation of the study

1. Literature searches

✓ Form a clear hypothesis, with primary and secondary outcomes.

Text stored in the file

Consider the use of systematic reviews.

Decide upon databases and information specialists to be consulted, and construct search terms.

norecopa.no/PREPARE/prepare-checklist

PREPARE



Three versions of the checklist:

3. online version

norecopa.no/PREPARE/Mychecklist

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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

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Create new PREPARE checklist

Open existing checklist

Your auth code for this checklist is **deeb7d** Please save this code so you are able to open your checklist at a later time. You can also bookmark this page.

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 checked="" 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 its welfare needs.
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.

Decide upon databases and information specialists to be consulted, and construct search terms.

Decide upon databases and information specialists to be consulted, and construct search terms.

Decide upon databases and information specialists to be consulted, and construct search terms.

Decide upon databases and information specialists to be consulted, and construct search terms.

text only stored on author's computer

norecopa.no/prepare/mychecklist?id=deeb7d

Nore

- 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, 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

**PREPARE is closely linked to
norecopa.no : an updated overview of global 3R resources**

The screenshot shows the norecopa.no website interface. At the top, there is a blue header with the norecopa logo and a search bar. A yellow arrow points to the search bar. Below the header is a navigation menu with various categories. The main content area displays the title "Design and reporting of animal experiments" and a paragraph of text. On the right side, there is a "Search filters" sidebar with several sections: "Search filters", "Database", "Browse the databases", and "Search in the databases".

Search filters

Order by: Relevance
Typo tolerance: Default

Database

- 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)
- Website (761)

Browse the databases

- eBooks (286)
- Free (199)
- Held at NMBU Oslo (contact Kristine Hansen, 67 23 21 89) (431)
- Key products (68)
- On loan (6)
- Reviewed (85)

Search in the databases

- All Text
- Title
- Author
- Publisher
- Supplier
- Record Number

norecopa.no / More resources / Experimental design and reporting

Design and reporting of animal experiments

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

Norecopa: PREPARE for better Science

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.

norecopa.no/databases-guidelines

links to over 70 other databases

Norecopa: PREPARE for better Science

norecopa.no/3RGuide

Links to over 400 guidelines

A good practice guide to the administration of substances and removal of blood, including routes and volumes

3R Guide database/c6721 (legacy id: 15079)

This paper provides the researcher in the safety evaluation laboratory with an up-to-date, easy-to-use set of data sheets to aid in the study design process whilst at the same time affording maximum welfare considerations to the experimental animals.

A guide to defining and implementing protocols for the welfare assessment of laboratory animals

3R Guide database/68ba4 (legacy id: 15065)

Eleventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement

A guide to the care and use of native Australian mammals in research and teaching

3R Guide database/502ff (legacy id: 15377)

The Guide supports implementation of the Australian Code for the care and use of animals for scientific purposes (8th edition, 2013) and ensures that the specific and unique needs of Australian native mammals are met when these animals are used for scientific purposes.

AAALAC Position Statements

3R Guide database/ef566 (legacy id: 15155)

In connection with its work of accreditation of animal care and use programmes, AAALAC International has issued position statements on a number of key elements in such a programme.



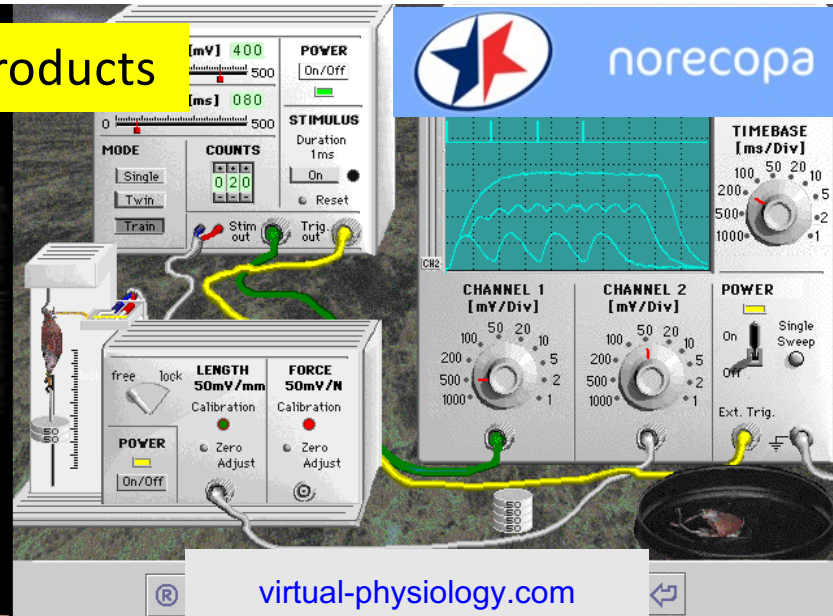
colourbox.com

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NORINA database: approx. 3,000 products



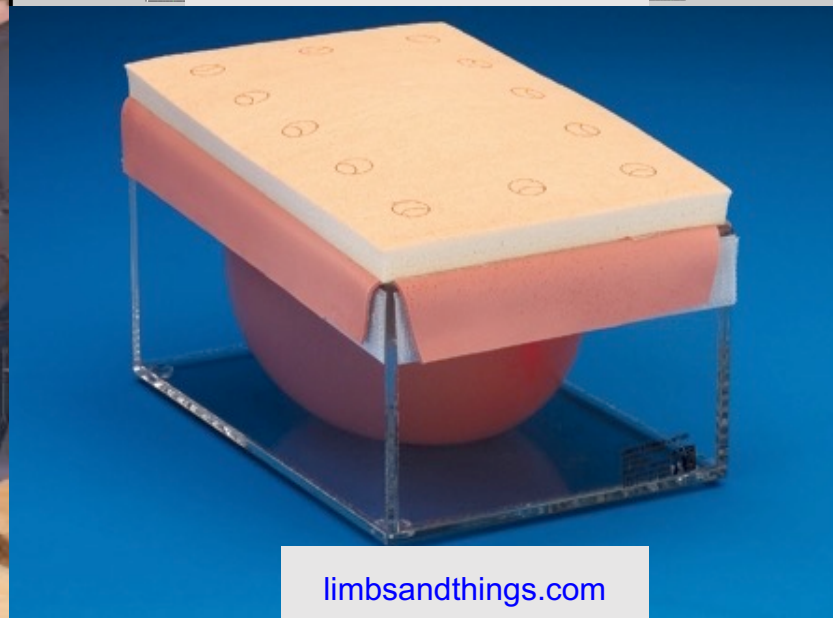
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virtual-physiology.com



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limbsandthings.com

norecopa.no/education-training/films-and-slide-shows



Rat s.c. injection
Norecopa | 1,380 views



Testing anaesthetic depth in the chicken
Norecopa | 598 views



Blood sampling from the pig
Norecopa | 3,914 views



Subcutaneous injection in the rabbit
Norecopa | 1,479 views



Rat i.p. injection (method 2)
Norecopa | 1,280 views



Blood collection from the saphenous vein in the mouse
Norecopa | 6,777 views



Intravenous injection in a rabbit
Norecopa | 2,025 views



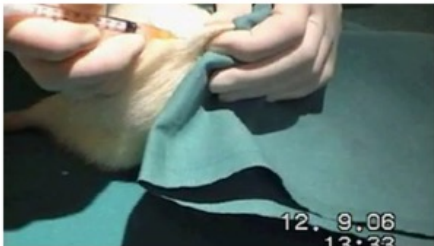
Subcutaneous injection in the chicken
Norecopa | 1,806 views

ANATOMÍA DE LA RATA

Dra. Dolores Vallejo Ruiz
Departamento de Biología de Sistemas, Universidad de Alcalá (Madrid)

Asesoría Científica: Dr. José María Orellana Muriana
Centro de Experimentación Animal, CAI Medicina-Biología, Universidad de Alcalá

Anatomía de la rata
Norecopa | 977 views



Subcutaneous injection in the rat - Technique 1
Norecopa | 2,249 views











Lifting a rabbit
Norecopa | 2,420 views









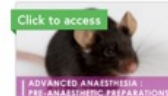

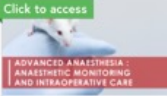




Immobilisation of the rabbit
Norecopa | 2,072 views

Norecopa: PREPARE for better Science

Training resources for animal research

 <p>National Legislation (EU1) Understand the national and international legal and regulatory framework within which projects involving animals are constructed and managed and of the legal responsibilities of the people involved.</p>	 <p>Ethics, Animal Welfare and the 3Rs (EU2) Identify the ethical and welfare issues raised by the use of animals in scientific procedures and understand the basic principles of the 3Rs.</p>
 <p>Basic and Appropriate Biology (EU3) Discover the basic principles of animal behaviour, care, biology and husbandry.</p>	 <p>Animal Care, Health and Management (EU4) Examine information on various aspects of animal health, care and management including: environmental controls, husbandry practices, diet, health status and disease.</p>
 <p>Recognition of Pain, Suffering and Distress (EU5) Identify the normal condition and behaviour of experimental animals and differentiate between a normal animal and one which is showing signs of pain, suffering or distress.</p>	 <p>Humane Methods of Killing (EU6.1) Learn the principles of humane killing including descriptions of the different methods available and information to help you compare the methods permitted to determine the most appropriate method.</p>
 <p>Minor Procedures without Anaesthesia (EU7) An introduction to the theory relating to minor procedures and information about appropriate methods of handling, restraint, appropriate techniques for injection, dosing and sampling relevant to the species.</p>	 <p>Anaesthesia for Minor Procedures (EU20) Guidance and information for individuals who, during their work with animals, will need to apply sedation or short-term anaesthesia for a brief period and mild pain level procedure.</p>

eModules

 <p>eModule – Recognition and Prevention of Pain, Suffering and Distress (EU5) ACCESS</p>	 <p>eModule – Humane Methods of Killing (EU6) ACCESS</p>	 <p>eModule – Design of procedures and projects (level 1) (EU10) ACCESS</p>	 <p>eModule – Design of procedures and projects (level 2) (EU11) ACCESS</p>
 <p>eModule – The Severity Assessment Framework (EU12) ACCESS</p>	 <p>eModule – Anaesthesia for Minor Procedures (EU20) ACCESS</p>	 <p>eModule – Pre-Anaesthetic Preparations (EU21-1) ACCESS</p>	 <p>eModule – Choosing an Anaesthetic (EU21-2) ACCESS</p>
 <p>eModule – Anaesthetic Monitoring and Intraoperative Care (EU21-3) ACCESS</p>	 <p>eModule – Anaesthetic Breathing Systems, Airway Management and Neuromuscular Blocking Agents (EU21-4) ACCESS</p>	 <p>eModule – Anaesthetic Management and Preventing Problems (EU21-5) ACCESS</p>	 <p>eModule – Post Anaesthetic Care (EU21-6) ACCESS</p>
 <p>eModule – Project Evaluation (EU25)</p>			

TextBase:

1,500 books related to
Laboratory Animal Science:

norecopa.no/textbase

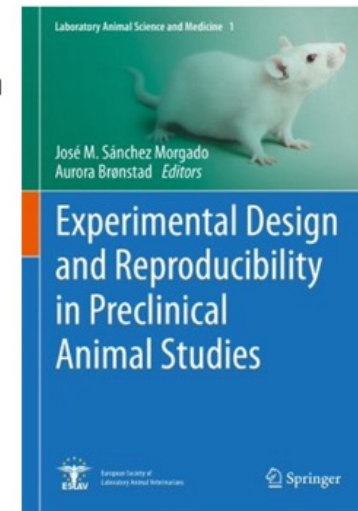
Experimental Design and Reproducibility in Preclinical Animal Studies

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

The Refinement Wiki



wiki.norecopa.no

Born from the knowledge that a lot of good ideas on refinement circulate on discussion forums, but never get published.

Designed to be

- a portal for rapid publication and dissemination of these ideas
- a place to identify experts on specific refinement techniques



Susanna Louihimies

Return to homepage



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- Tools**
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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).



- 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



PILOTS



CABIN CREW



GROUND
STAFF



AIR TRAFFIC
CONTROLLERS



EU / National



Facility



Project



Procedure

https://environment.ec.europa.eu/topics/chemicals/animals-science_en



Animals in science

EU actions for the protection of animals used for scientific purposes

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[EU networks](#)

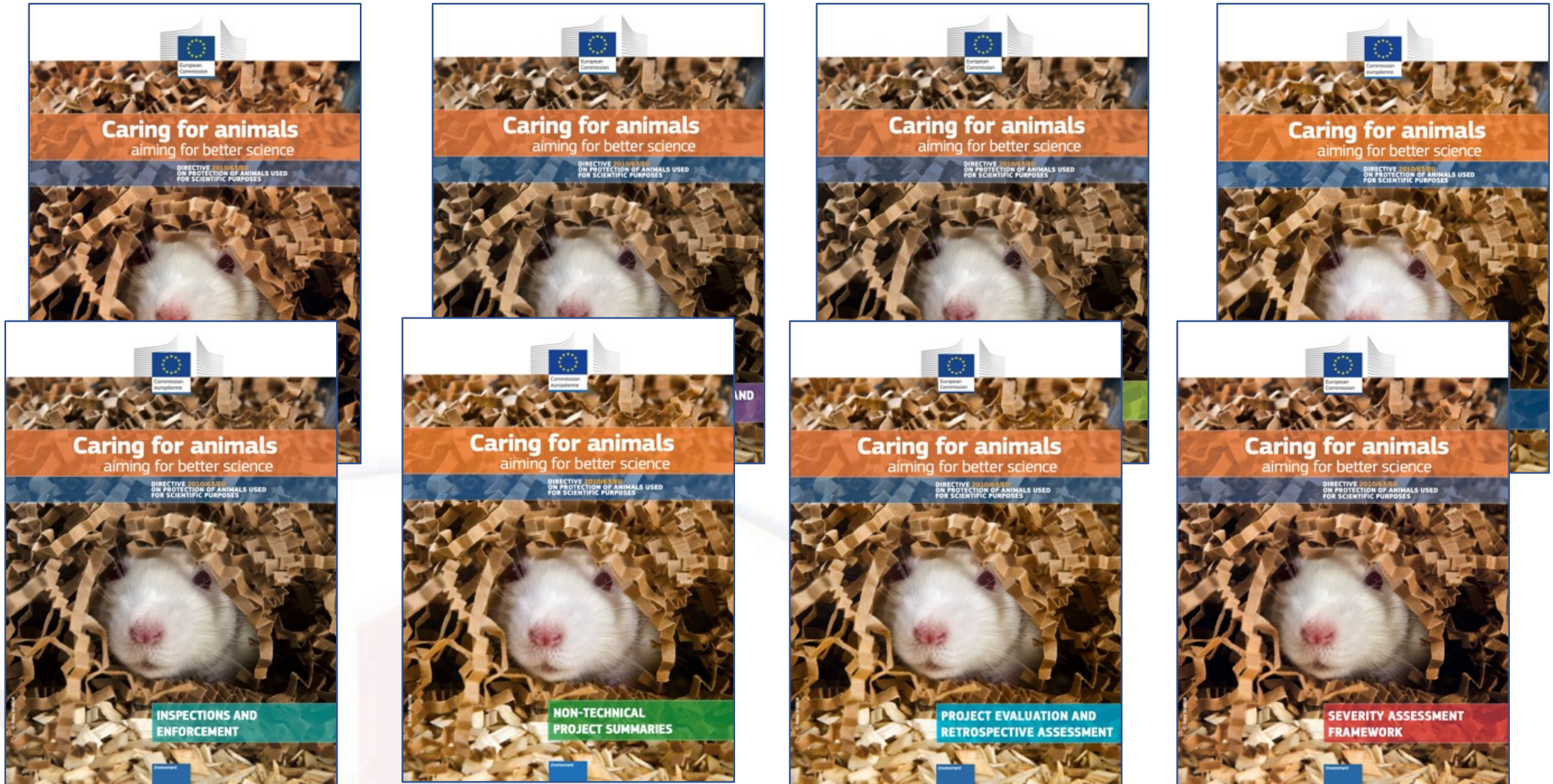
[Implementation](#)

[Tools](#)

[Related links](#)

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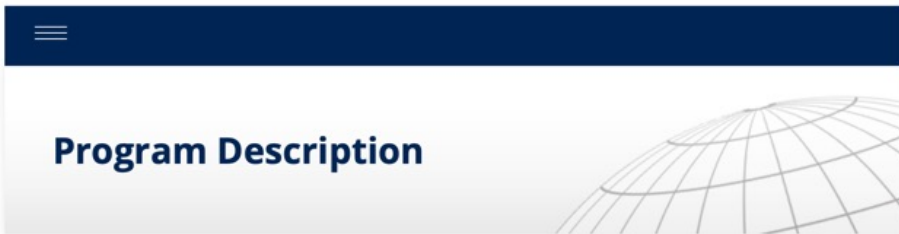


https://environment.ec.europa.eu/topics/chemicals/animals-science_en#implementation

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Facility



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

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www.aaalac.org/program-description

A simple but effective Master Plan



norecopa.no/more-resources/master-plan-and-sops

Norecopa: PREPARE for better Science

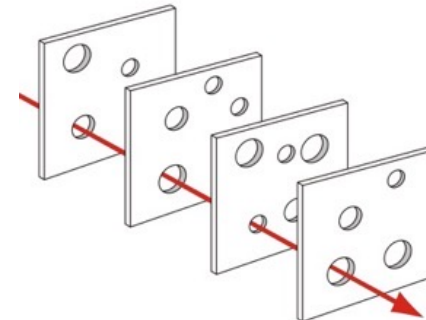
A Contingency Plan, based upon risk assessment

- 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 reactions

Many of these needed revision in the light of Covid-19
norecopa.no/be-prepared

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

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



Temporary staff at weekends and holidays

Contingency and redundancy

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

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



Photo: NMBU



[wikipedia](#)

Norecopia: PREPARE for better Science



CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

Refine - Reduce - Replace

Homepage

Project

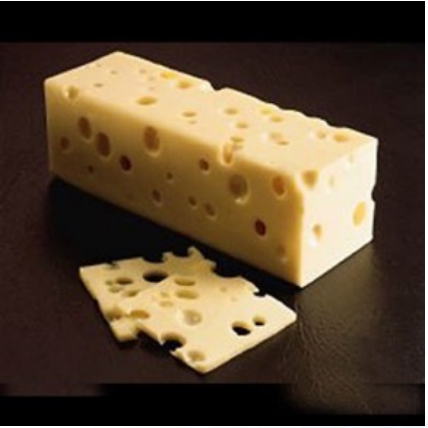
Team

FAQ

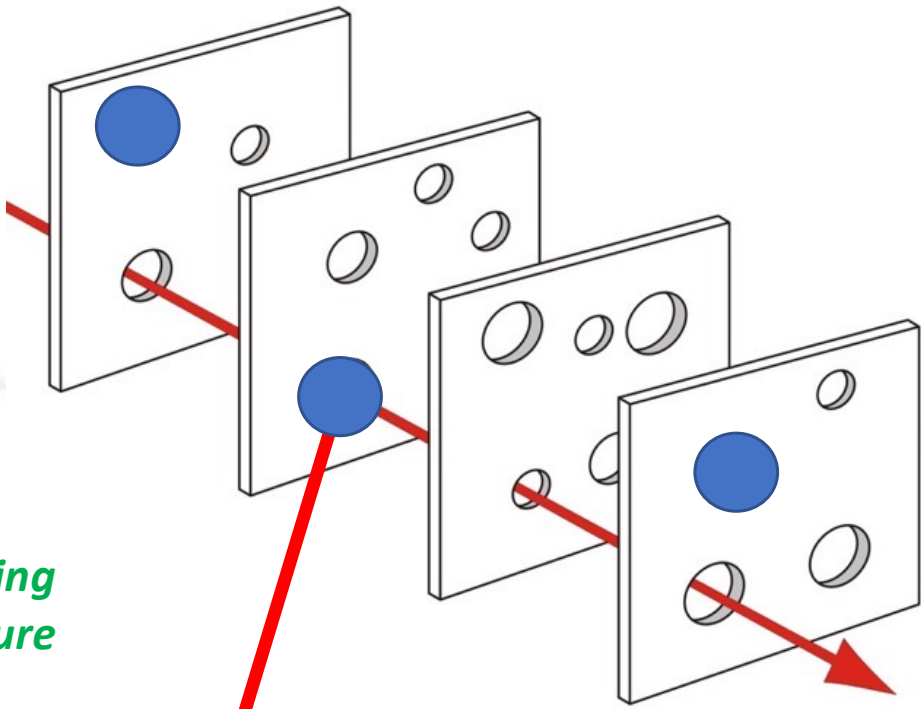


Norecopa: PREPARE for better Science

“Threat and Error Management”



eaugallecheese.com/Swiss-Cheese

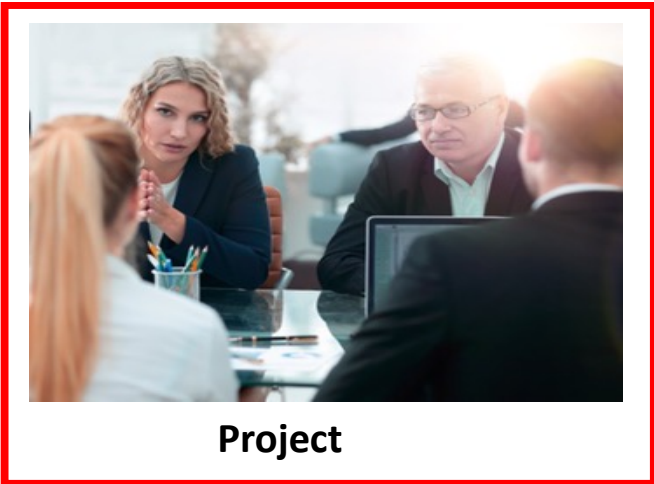


Serious incidents

Weaknesses / dangers

wikipedia.org/wiki/Swiss_cheese_model

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



A contract between the animal facility and the research group

- Division of labour, responsibilities and cost
- Clarifying all stages of the experiment
- Ensuring that all necessary data are recorded

	Animal 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 ± variation)			
Light schedule			
Relative humidity (mean ± variation)			
Number of air changes in the animal room/cabinet per hour			
Environmental enrichment			
Housing:			
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			



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!

Norecopa: PREPARE for better Science

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



"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.



norecopa.no/global3r

Centres

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

Associations

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

Norecopa: PREPARE for better Science

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

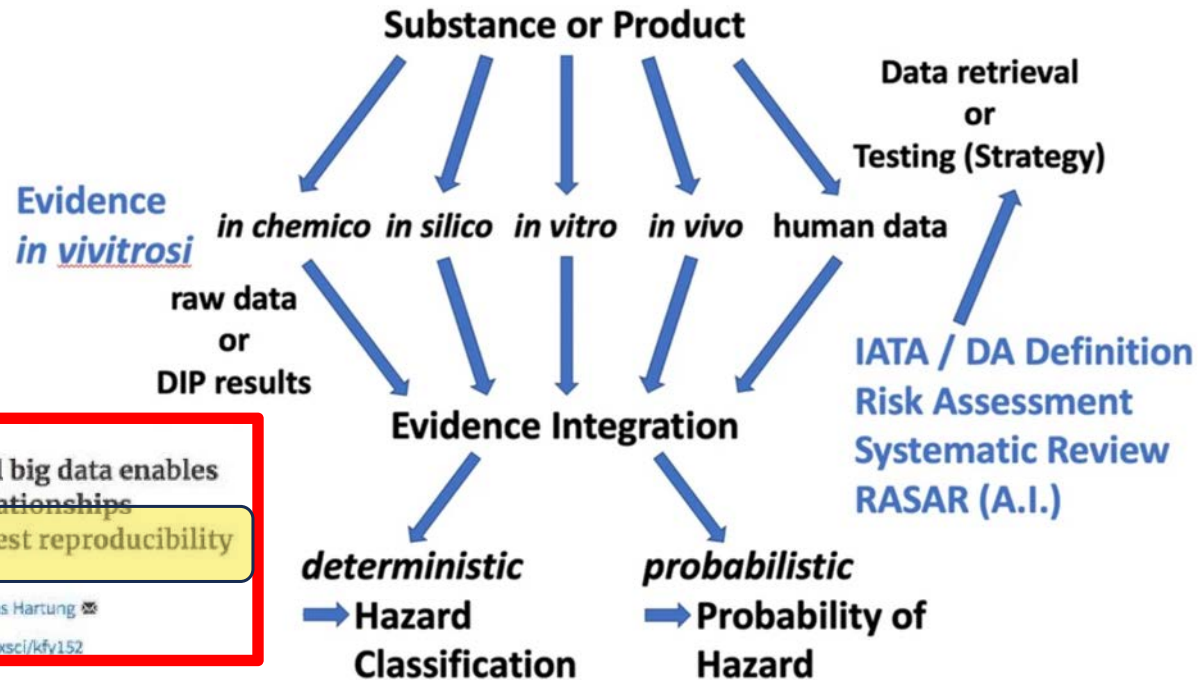
In vivitrosi

Replacement of animal testing by integrated approaches to testing and assessment (IATA): a call for in vivitrosi

Francesca Caloni¹ · Isabella De Angelis² · Thomas Hartung^{3,4} Arch Toxicol 2022

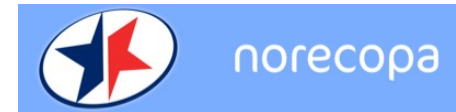



Aka Integrated Testing Strategies, IATA, Defined Approaches...



ACCEPTED MANUSCRIPT
Machine learning of toxicological big data enables read-across structure activity relationships (RASAR) outperforming animal test reproducibility
 Thomas Luechtefeld, Dan Marsh, Craig Rowlands, Thomas Hartung
 Toxicological Sciences, kfy152, <https://doi.org/10.1093/toxsci/kfy152>

The ARRIVE guidelines 2.0: Updated guidelines for reporting animal research



Nathalie Percie du Sert , Viki Hurst, Amrita Ahluwalia, Sabina Alam, Marc T. Avey, Monya Baker, William J. Browne, Alejandra Clark, Innes C. Cuthill, Ulrich Dirnagl, Michael Emerson, Paul Garner, Stephen T. Holgate, David W. Howells, Natasha A. Karp, Stanley E. Lazic, Katie Lidster, Catriona J. MacCallum, Malcolm Macleod, Esther J. Pearl, Ole H. Petersen, Frances Rawle, Penny Reynolds, Kieron Rooney, Emily S. Sena, Shai D. Silberberg, Thomas Steckler, Hanno Würbel

journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.3000410

Version 1 of ARRIVE (2010) was endorsed by more than a thousand journals but only a small number of journals actively enforce compliance

(Swiss study in 2016: 51% of researchers publishing in journals that had endorsed ARRIVE had never heard of them)

'Important information as set out in the ARRIVE guidelines is still missing from most publications sampled:

randomisation 30-30%

blinding 20%

sample size justification <10%

all basic animal characteristics <10%'

'It is likely that the level of resource required from journals and editors currently prohibits the implementation of all the items of the ARRIVE guidelines.'

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.

arriveguidelines.org

ARRIVE 2.0

ARRIVE Essential 10		
Study design	1	For each experiment, provide brief details of study design including: a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated. b. The experimental unit (e.g. a single animal, litter, or cage of animals).
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used. b. Explain how the sample size was decided. Provide details of any <i>a priori</i> sample size calculation, if done.
Inclusion and exclusion criteria	3	a. Describe any criteria established <i>a priori</i> for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. c. For each analysis, report the exact value of N in each experimental group.
Randomisation	4	Describe the methods used: a. To allocate experimental units to control and treatment groups. If randomisation was used, provide the method of randomisation. b. To minimise potential confounding factors such as the order of treatments and measurements, or animal/cage location.
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.
Statistical methods	7	a. Provide details of the statistical methods used for each analysis. b. Specify the experimental unit that was used for each statistical test. c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.
Experimental animals	8	a. Provide details of the animals used, including species, strain and substrain, sex, age or developmental stage, and weight. b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: a. What was done, how it was done and what was used. b. When and how often. c. Where (including detail of any acclimation periods). d. Why (provide rationale for procedures).
Results	10	For each experiment conducted, including independent replications, report: a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable. b. If applicable, the effect size with a confidence interval.

ARRIVE 2.0

		Recommended Set
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.
Background	12	<p>a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach.</p> <p>b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.</p>
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.
Animal care and monitoring	16	<p>a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress.</p> <p>b. Report any expected or unexpected adverse events.</p> <p>c. Describe the humane endpoints established for the study and the frequency of monitoring.</p>
Interpretation /scientific implications	17	<p>a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature.</p> <p>b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.</p>
Generalisability /translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.
Data access	20	Provide a statement describing if and where study data are available.
Declaration of interests	21	<p>a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated.</p> <p>b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.</p>

ARRIVE

Home About ARRIVE guidelines Supporters Resources Publications News

ARRIVE guidelines

Essential 10

1. Study design

2. Sample size

3. Inclusion and exclusion criteria

4. Randomisation

5. Blinding

6. Outcome measures

7. Statistical methods

8. Experimental animals

9. Experimental procedures

10. Results

Recommended Set

11. Abstract

12. Background

13. Objectives

14. Ethical statement

RECOMMENDED SET

11. Abstract

11 Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.

Explanation Examples

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.

References

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](https://doi.org/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](#)



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"We ARRIVED, because we were PREPARED"

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

Norecopa: PREPARE for better Science

Norecopa: PREPARE for better Science

Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 64, 1431 Ås, Norway
adrian.smith@norecopa.no

What's the problem?

Preclinical *in vivo* research needs to be reproducible and translatable, while maximising the animals' welfare and replacing them with alternatives wherever possible. This can be summed up in the 3Rs of Russell & Burch: **Replace, Reduce & Refine**.



Scientists are usually well aware of **reporting** guidelines when publishing research. These are important, but a sub-standard study, like a burnt cake, cannot be improved by a better description. Guidelines for **planning**, although not mandatory, are of great help in designing better experiments.



norecopa.no/PREPARE

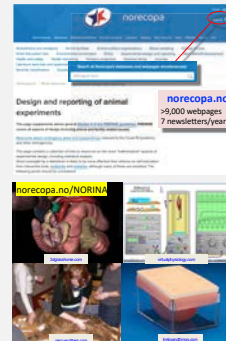
What can Norecopa offer?

Norecopa maintains a comprehensive database of resources for scientists, which include:

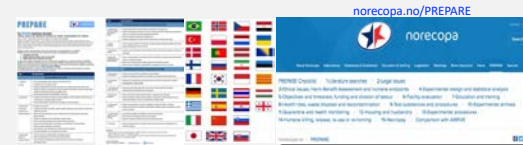


- over 9,000 searchable webpages of quality 3R resources, with filters to facilitate searching
- the PREPARE guidelines for planning animal experiments, with a checklist in over 30 languages
- links to recordings of webinars covering all aspects of animal research
- an International Webinars & Meetings Calendar
- a collection of over 400 guidelines for planning and conducting animal research
- an English-language newsletter with the latest developments within the 3Rs
- the NORINA database of alternatives to animal use in education and training
- a slide set describing the 3R concept in detail: norecopa.no/3Rs
- a Refinement Wiki

Examples of Norecopa's resources:



- PREPARE covers:**
- ✓ Formulation of a study
 - ✓ Dialogue between scientists and the animal facility
 - ✓ Quality control of the components in the study



The Refinement Wiki
wiki.norecopa.no

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Toolbox graphic: colourbox.com

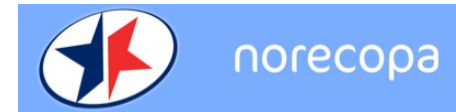
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and distribute!

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Thanks to Norecopa's main sponsors:

- Standing Committee on Business Affairs, Norwegian Parliament
- Norwegian Ministries of Agriculture and Fisheries
- Research Council of Norway
- Laboratory Animals Ltd.
- Architect Finn Rahn's Legacy
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Animal Protection Alliance's Research Fund
- Norwegian Society for the Protection of Animals
- Novo Nordisk
- Scanbur
- Scottish Accreditation Board
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture



Graphics: [colourbox.com](https://www.colourbox.com)



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Thank you for listening!