

# Improving nonclinical research practices: way forward

2022. LAS webinar series organized by CroLASA in collaboration with SLAS

**How can NORECOPA help researchers PREPARE  
for better science?**

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16 February 2022

[norecopa.no/160222](https://norecopa.no/160222)



## ***"better science?"***

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





[journal.eahn.org/article/id/7475](http://journal.eahn.org/article/id/7475)



- Site work (excavation, waste & water, paths)
- Metal structures
- Concrete structures
- Masonry
- Carpentry (rough & visible)
- Waterproofing and insulation
- Escalators and lifts
- Heating, ventilation and air conditioning
- Plumbing
- Electrical systems
- Doors & windows
- Fire protection
- Painting
- Landscaping
- Rodent control

**From the Master Builder...**

**...to a coordinated effort from many experts**

# The path to better research



Norecopa: PREPARE for better Science

[norecopa.no/PREPARE](https://norecopa.no/PREPARE) and [ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1](https://ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1)

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

we welcome more from you!



norecoba

<https://norecoba.no>

*Established in 2007*

Norecoba: PREPARE for better Science

*EU3Rnet*

[norecopa.no/global3r](http://norecopa.no/global3r)



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**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](#) ⓘ

Norecopa: PREPARE for better Science

## 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 (a stylized star) and the text "norecopa". Below the header is a navigation menu with links: "About Norecopa", "Alternatives", "Databases & Guidelines", "Education & training", "Legislation", "Meetings", "More resources", "News", and "PREPARE".

The main content area features a grid of links for various topics: "Anaesthesia and analgesia", "Animal facilities", "Animal welfare organisations", "Blood sampling", "Culture", "Email discussion lists", "Environmental enrichment", "Ethics", "Experimental design and reporting", "Harmful", "Health and safety", "Health monitoring", "Humane endpoints", "Humane killing", "Journals", "Literature searches and systematic reviews", "Organisations", "Reporting guidelines", and "Severity classification".

Below the grid, there is a breadcrumb trail: "norecopa.no / More resources / Experimental design and reporting".

The main heading is "Design and reporting of animal experiments". Below it, a text block states: "This page supplements advice given in [Section 4 of the](#) covers all aspects of design (including animal and faci".

At the bottom left, it says "Norecopa: PREPARE for better Science".

On the right side, there is a "Search filters" sidebar. It includes:

- Search filters**
- Order by: Relevance (dropdown)
- Typo tolerance: Default (dropdown)
- Database** (dropdown menu)
- 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** (dropdown menu)
- 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** (dropdown menu)
- All Text
- Title
- Author
- Publisher
- Supplier
- Record Number

approx. 8,900 webpages  
320,000 hits annually

7-8 detailed newsletters per year





norecopa

NORSK [ENGLISH](#)

Search:

[About Norecopa](#) [Alternatives](#) [Databases & Guidelines](#) [Education & training](#) [Legislation](#) [Meetings](#) [More resources](#) [News](#) [PREPARE](#) [Species](#) [Wiki](#)



Fish



Farm animals



Laboratory animals



Wildlife and wild fish



Cephalopods



Other aquatic animals

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[Fish 2005](#) | [Wildlife 2008](#) | [Fish 2009](#) | [Agricultural animals 2010](#) | [Fish 2011](#) | [Fish 2012](#) | [Fish 2013](#) | [Fish 2014](#) | [Fish 2015](#) | [Fish 2016](#) | [Fish 2017](#) | [Past meetings](#) | [Meetings Calendar](#) | [An informal guide to the calendar](#)

+ webpages for past meetings and recorded meetings

[norecopa.no/meetings/meetings-calendar](https://norecopa.no/meetings/meetings-calendar)

## Webinar and Meetings calendar

### January 2022

- > [Guide to improving reproducibility by networking](#), webinar (Marcus Munafo), 19 January 2022
- > [Traumeforsøg og "den gode ansøgning"](#), miniseminar, 19 January 2022
- > [Refining mouse handling using tunnels or cupped hands: Why and How](#), NA3RsC webinar, 19 January 2022
- > [The Effects of Environmental Temperatures on Energy Expenditure in Mice](#), webinar (Marc Reitman & Oksana Gavrilova), 20 January 2022
- > [Evidence for pain in fishes: Implications for welfare](#), webinar (Lynne Sneddon), 25 January 2022
- > [FRAME Training School in Experimental Design](#), online, 25-28 January 2022 ([draft programme](#))
- > [How the pharmaceutical industry is tackling 'severe' suffering in animals used in science](#), RSPCA/EFPIA webinar, 26 January 2022
- > [2nd Next Generation Organ-on-Chip and Organoids workshop](#), Geneva, 26-27 January 2022
- > [ZEBREFINE - refinement opportunities for zebrafish anaesthesia](#), online meeting, 27 January 2022
- > [Injection or infusion? Insights for your next animal dosing investigation](#), Charles River webinar, 27 January 2022
- > [Demonstration of the Experimental Design Assistant \(EDA\)](#), webinar, 27 January 2022
- > [Statistical Analysis for In Vivo and In Vitro Scientists course](#), 31 January - 2 February 2022

## Pdf files of 80+ presentations held at Norecopa's meetings



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 [Wiki](#)

[Fish 2005](#) | 
 [Wildlife 2008](#) | 
 [Fish 2009](#) | 
 [Agricultural animals 2012](#) | 
 [Field research 2017](#) | 
 [Past meetings](#) | 
 [Meetings Calendar](#) | 
 [An informal guide to arranging a scientific meeting](#) | 
 [Presentations](#)

## [norecopa.no/meetings/presentations](https://norecopa.no/meetings/presentations)



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

They are grouped into

- > [General presentations](#)
- > [Care and use of animals in field research](#)
- > [Care and use of farm animals in research](#)
- > [Care and use of fish in research](#)

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

## Databases & Guidelines

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

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

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

These databases are updated regularly. [Please give us feedback](#) if you discover errors or omissions.

The Norecopa website also includes four other collections:

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

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

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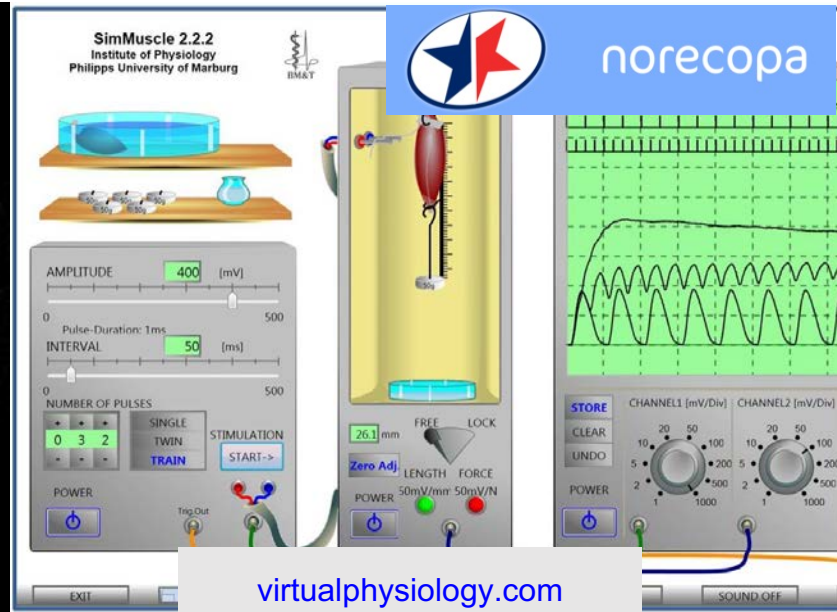
[norecopa.no/databases-guidelines](https://norecopa.no/databases-guidelines)

links to over 70 other databases

[norecopa.no/NORINA](http://norecopa.no/NORINA)



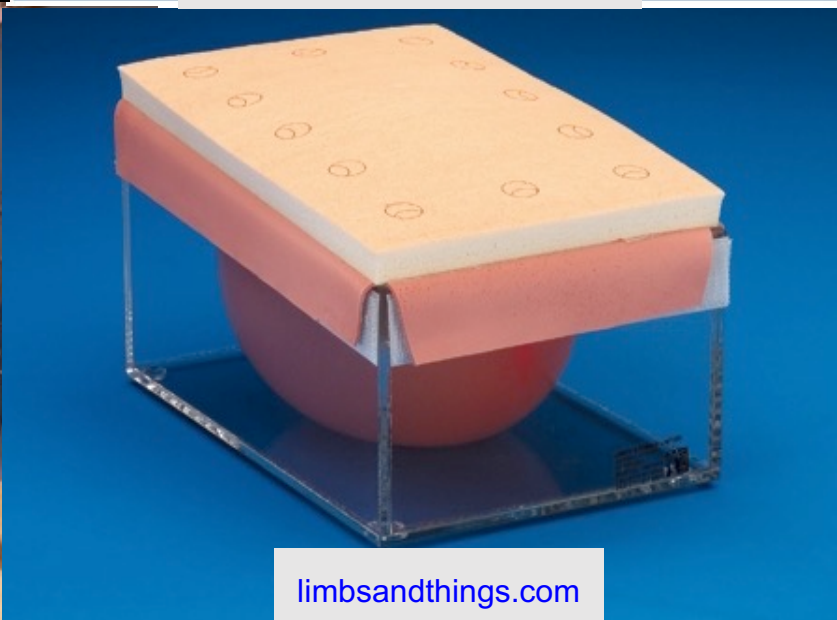
[3dglasshorse.com](http://3dglasshorse.com)



[virtualphysiology.com](http://virtualphysiology.com)

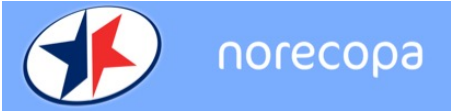


[rescuecritters.com](http://rescuecritters.com)



[limbsandthings.com](http://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



Blood sampling from the pig  
Norecopa | 3,914 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 Moriana  
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

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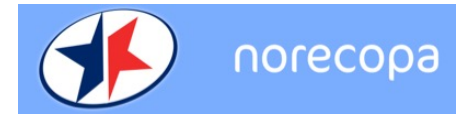
Training resources for animal research

|  |   |
|--|---|
|  <p><b>National Legislation (EU1)</b><br/>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><b>Ethics, Animal Welfare and the 3Rs (EU2)</b><br/>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><b>Basic and Appropriate Biology (EU3)</b><br/>Discover the basic principles of animal behaviour, care, biology and husbandry.</p>  |  <p><b>Animal Care, Health and Management (EU4)</b><br/>Examine information on various aspects of animal health, care and management including: environmental controls, husbandry practices, diet, health status and disease.</p>                          |
|  <p><b>Recognition of Pain, Suffering and Distress (EU5)</b><br/>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><b>Humane Methods of Killing (EU6.1)</b><br/>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><b>Minor Procedures without Anaesthesia (EU7)</b><br/>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><b>Anaesthesia for Minor Procedures (EU20)</b><br/>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><b>eModule – Recognition and Prevention of Pain, Suffering and Distress (EU5)</b><br/>ACCESS</p> |  <p><b>eModule – Humane Methods of Killing (EU6)</b><br/>ACCESS</p>  |  <p><b>eModule – Design of procedures and projects (level 1) (EU10)</b><br/>ACCESS</p>       |  <p><b>eModule – Design of procedures and projects (level 2) (EU11)</b><br/>ACCESS</p> |
|  <p><b>eModule – The Severity Assessment Framework (EU12)</b><br/>ACCESS</p>                         |  <p><b>eModule – Anaesthesia for Minor Procedures (EU20)</b><br/>ACCESS</p>  |  <p><b>eModule – Pre-Anaesthetic Preparations (EU21-1)</b><br/>ACCESS</p>                    |  <p><b>eModule – Choosing an Anaesthetic (EU21-2)</b><br/>ACCESS</p>                   |
|  <p><b>eModule – Anaesthetic Monitoring and Intraoperative Care (EU21-3)</b><br/>ACCESS</p>         |  <p><b>eModule – Anaesthetic Breathing Systems, Airway Management and Neuromuscular Blocking Agents (EU21-4)</b><br/>ACCESS</p> |  <p><b>eModule – Anaesthetic Management and Preventing Problems (EU21-5)</b><br/>ACCESS</p> |  <p><b>eModule – Post Anaesthetic Care (EU21-6)</b><br/>ACCESS</p>                    |
|  <p><b>eModule – Project Evaluation (EU25)</b></p>   |   |   |   |

From **3R-Guide** (380 guidelines for animal research and testing)  
[norecopa.no/3r-guide](http://norecopa.no/3r-guide)



## Guidance on the severity classification of procedures involving fish

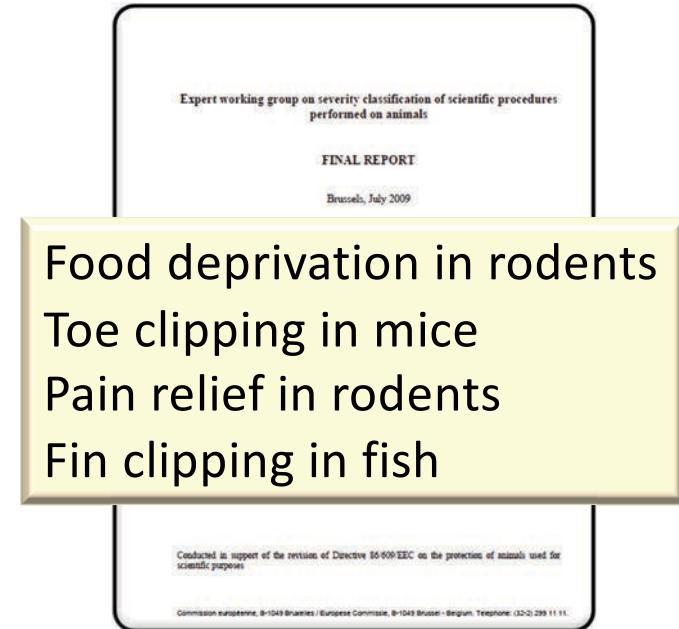
Report from a Working Group convened by Norecopa

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

Laboratory Animals, 45: 219-224, 2011

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[norecopa.no/categories](http://norecopa.no/categories)



[http://ec.europa.eu/environment/chemicals/lab\\_animals/pdf/report\\_ewg.pdf](http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf)



TextBase:

1,500 books related to LAS:

[norecopa.no/textbase](http://norecopa.no/textbase)

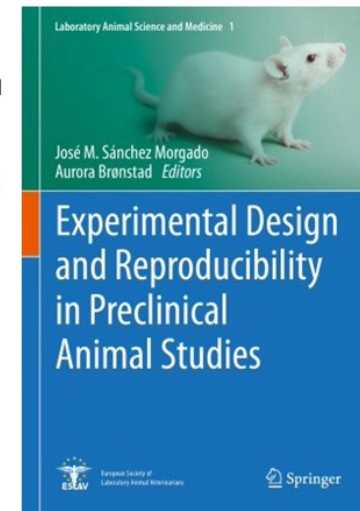
## Experimental Design and Reproducibility in Preclinical Animal Studies

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.

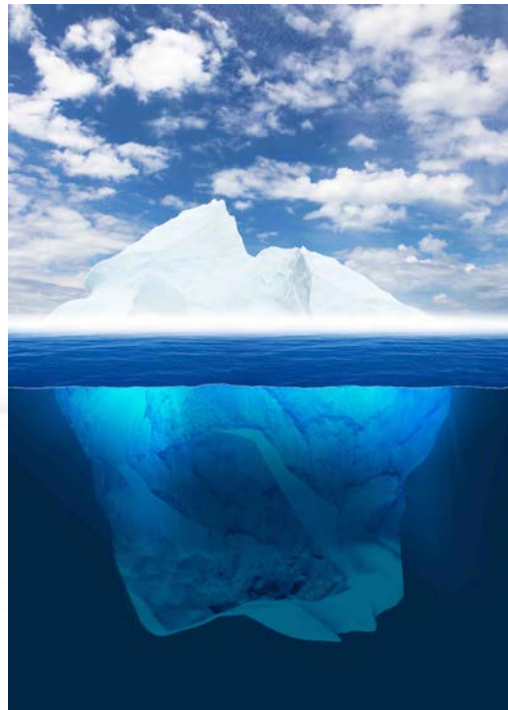


[norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies](http://norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies)

We have a "reproducibility crisis" in science...

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


[norecopa.no/concerns](https://norecopa.no/concerns)



Reporting

Planning

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



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



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The easy parts of design and reporting:

**WHAT THE NUMBERS MEAN**

Electric → 100 CC

|              |                               | OREGON |       |       |
|--------------|-------------------------------|--------|-------|-------|
|              |                               | .050"  | .058" | .063" |
| <b>.325"</b> | = $\leftarrow +2 \rightarrow$ | 95     |       |       |
| <b>3/8"</b>  | = $\leftarrow +2 \rightarrow$ | 72     | 73    | 75    |

[arborist101.com](http://arborist101.com)

- Chainsaw
  - Blade characteristics
  - Sparkplug type
  - Petrol/oil mixture
  - Service history
- Angle of cut in tree
- Length of tree logs



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## Critical issues behind the scenes that may not get reported:

- Experience of the workers
- Inspection for signs of rot and to decide felling direction
- Additional equipment (winch, chains, straps, wedges)
- Routines and equipment for sharpening the chain
- Clearing-up and transport of logs
- Health and safety precautions – clothing, onlookers
- **Division of labour and costs**

Starts long before the actual work.

## *How do others achieve reproducibility?*



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



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*...and precision in a variable environment?*



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## *10-15 checklists even on short routine flights*



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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**"

***Too late to read the checklists when you have ARRIVED!***



colourbox.com

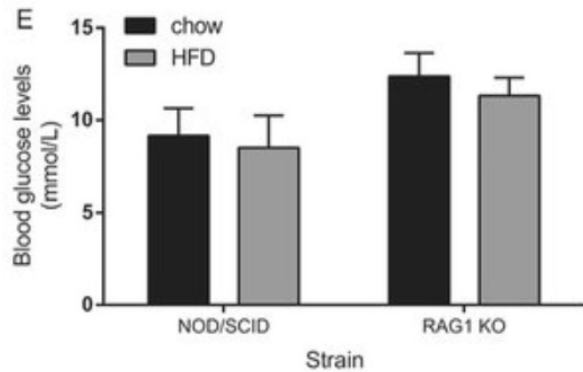
**Norecopa: PREPARE for better Science**

[norecopa.no/PREPARE/film](http://norecopa.no/PREPARE/film)  
3-minute cartoon film



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## The scientist



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## The mouse

Breeding

New social groups

Transportation

Acclimation to research facility

Allocation to experimental group

Adaptation to new diet

Handling and immobilisation

### Blood sampling

*often also:*

injections, gavaging, surgery

pain and distress

developing illness and death

## *Stress caused by capture and handling*



News > Science

# Scores of scientific studies based on mice thrown into doubt because they were

Mice pick naturally

Ian Johnstone



't act

[nc3rs.org.uk/3rs-resources/mouse-handling](https://nc3rs.org.uk/3rs-resources/mouse-handling)

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## *Artefacts caused by poor administration techniques*



Photo: NMBU

- *Are you sure that your injection ends up in the same place each time?*
- *Are the injections painful?*
- *Are they realistic? (intramuscular injections in small animals)*

*Disposable needles are designed to be used only once!*

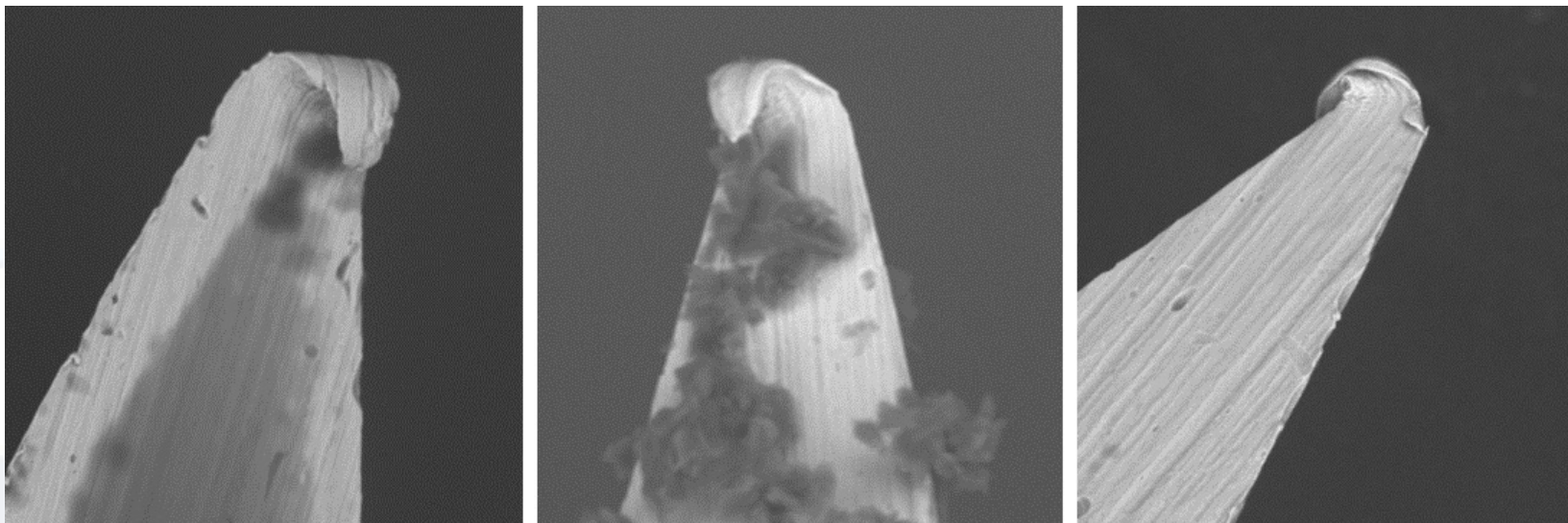
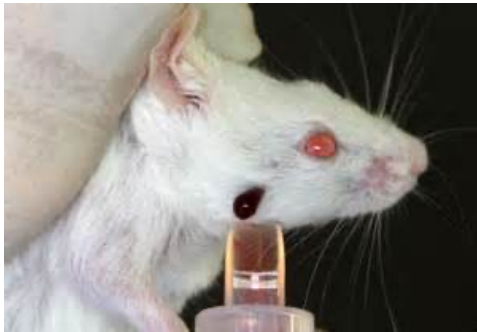


Photo: AstraZeneca

[nc3rs.org.uk/news/re-use-needles-indicator-culture-care](https://nc3rs.org.uk/news/re-use-needles-indicator-culture-care)



## *'A simple' case: a researcher wants a blood sample*



[medipoint.com/html/for\\_use\\_on\\_mice.html](http://medipoint.com/html/for_use_on_mice.html)



[theodora.com/rodent\\_laboratory/  
blood\\_collection.html](http://theodora.com/rodent_laboratory/blood_collection.html)



photo:NMBU

[vimeo.com/486368886](https://vimeo.com/486368886)

The best blood sampling techniques are those where you can:

- ✓ see the blood vessel
- ✓ regulate the amount of blood you remove
- ✓ stop the bleeding easily (including internal bleeding)
- ✓ avoid damage to the surrounding tissue
- ✓ collect samples rapidly, to avoid artefacts due to mechanical stress, temperature changes, differing lengths of sampling time

***While we are waiting for the scientific evidence...***

Carol M. Newton (1925-2014)



National Library of Medicine

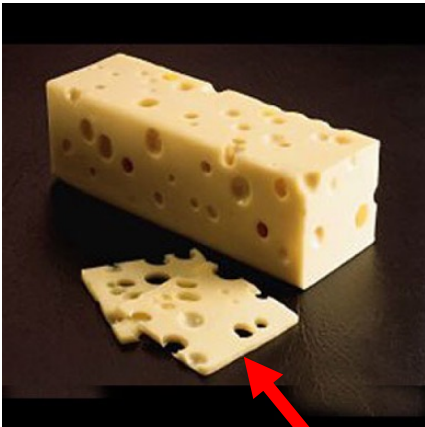
## ***The three S's***

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

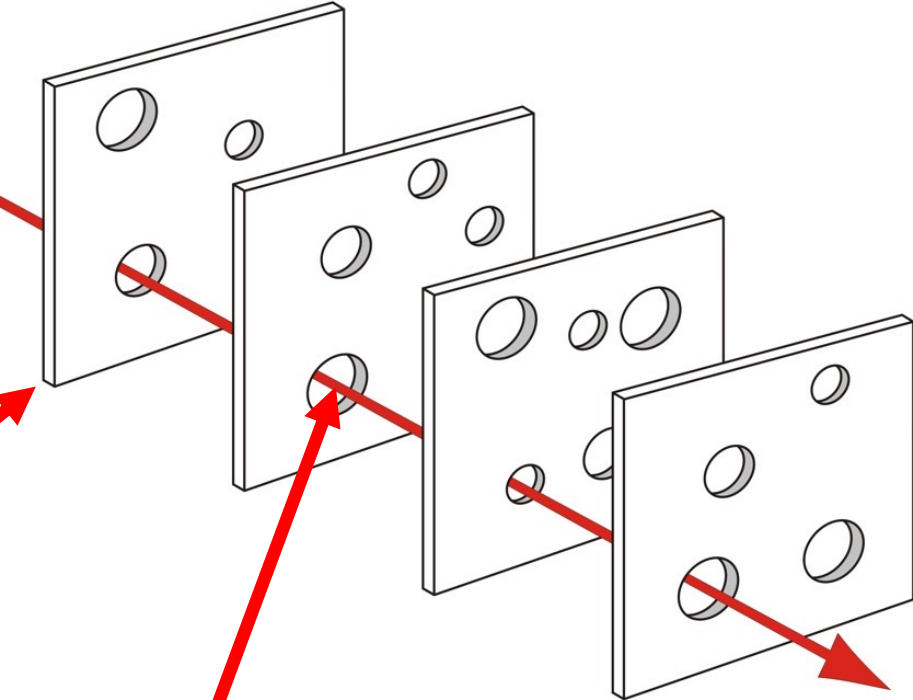
<https://norecopa.no/3S>

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# Threat and Error Management



[eaugallecheese.com/Swiss-Cheese](http://eaugallecheese.com/Swiss-Cheese)



"Layer of defence"  
or redundancy

Weakness / hazard

**Loss**

[wikipedia.org/wiki/Swiss\\_cheese\\_model](http://wikipedia.org/wiki/Swiss_cheese_model)

## Contingency and redundancy

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



Photo: NMBU



*Culture of Care*

The International Culture of Care Network  
[norecopa.no/coc](http://norecopa.no/coc)

A demonstrable commitment, throughout the establishment, to improving:

- animal welfare
- scientific quality
- care of staff
- transparency for all stakeholders, including the public

*It goes beyond simply complying with the law!*

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## Communication and the Culture of Care

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

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

### Regular meetings

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



Regular refresher/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](http://norecopa.no/culture-of-care)



Map

Satellite

Greenland



[norecopa.no/coc](http://norecopa.no/coc)

*Culture of Care Network*





"because we've always done it that way"

"as often as necessary"

"there are no alternatives"

Closely related to a culture of care is the concept of  
a **Culture of Challenge** (Louhimies, 2015).

Look for the acceptable, rather than choosing the accepted.

***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





# Prepare



Original Article

**PREPARE: guidelines for planning animal research and testing**

Adrian J Smith<sup>1</sup>, R Eddie Clutton<sup>2</sup>, Elliot Lilley<sup>3</sup>, Kristine E Aa Hansen<sup>4</sup> and Trond Brattelid<sup>5</sup>

**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,<sup>1,2</sup> even after the production and journal endorsement of reporting guidelines.<sup>3</sup> There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research.<sup>4-7</sup> This can, for example, contribute towards the failure of drugs when they enter human trials.<sup>8</sup> 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.<sup>9</sup> This has understandably sparked a demand for reduced waste when planning experiments involving animals.<sup>10-12</sup> 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).<sup>13</sup> 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

Adrian J. Smith<sup>1</sup>, R. Eddie Clutton<sup>2</sup>, Elliot Lilley<sup>3</sup>, Kristine E. Aa. Hansen<sup>4</sup> & Trond Bratteid<sup>5</sup>  
<sup>1</sup>Norecopia, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; <sup>2</sup>Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; <sup>3</sup>Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; <sup>4</sup>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; <sup>5</sup>Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE<sup>1</sup> consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE<sup>2</sup>. 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, as a checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidelines for facilities, since in-house experiments are dependent upon their quality. The full version of the checklist is available on the norecopia website, with links to global resources, at <https://norecopia.no/PREPARE>. The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

Three Rs!

| Topic   | Recommendation   |
|---|--|
| <b>(A) Formulation of the study</b>                             |  |
| 1. Literature searches  | <input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes.<br><input type="checkbox"/> Consider the use of systematic reviews.<br><input type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms.<br><input type="checkbox"/> Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering and to welfare needs.<br><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.<br><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.<br><input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced.<br><input type="checkbox"/> Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities).<br><input type="checkbox"/> Consider pre-Registration and the publication of negative results.<br><input type="checkbox"/> Perform a harm-benefit assessment and justify any likely animal harm.<br><input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes.<br><input type="checkbox"/> Allocate a severity classification to the project.<br><input type="checkbox"/> Define objective, easily measurable and unequivocal humane endpoints.<br><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.<br><input type="checkbox"/> Define the experimental unit and decide upon animal numbers.<br><input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.   |

| Topic  | Recommendation  |
|--|---|
| <b>(B) Dialogue between scientists and the animal facility</b> |   |
| 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.<br><input type="checkbox"/> Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination.<br><input type="checkbox"/> Discuss and disclose all expected and potential costs.<br><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.<br><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.<br><input type="checkbox"/> Assess, and if necessary produce, specific guidance for all stages of the project.<br><input type="checkbox"/> Discuss means for containment, decontamination, and disposal of all items in the study.   |
| <b>(C) Quality control of the components in the study</b>      |   |
| 9. Test substances and procedures                              | <input type="checkbox"/> Provide as much information as possible about test substances.<br><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.<br><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.<br><input type="checkbox"/> Discuss acclimatisation, 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.<br><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.<br><input type="checkbox"/> Define primary and emergency methods for humane killing.<br><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 & Bratteid T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.  
 2. Kilkenny C, Browne WJ, Cuthill IC et al. Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PLoS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

Further information  
<https://norecopia.no/PREPARE> | [post@norecopia.no](mailto:post@norecopia.no) | [@norecopia](https://twitter.com/norecopia)



## Three versions of the checklist:



### The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith<sup>1</sup>, R. Eddie Clutton<sup>2</sup>, Elliot Lilley<sup>3</sup>, Kristine E. Aa. Hanssen<sup>4</sup> & Trond Bratlie<sup>5</sup>  
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| Topic   | Recommendation   |
|---|--|
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1. plain pdf file

| Topic  | Recommendation  |
|--|---|
| <b>(B) Dialogue between scientists and the animal facility</b> |   |
| 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.<br><input type="checkbox"/> Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination.<br><input type="checkbox"/> Discuss and disclose all expected and potential costs.<br><input type="checkbox"/> Construct a detailed plan for division of labour and expenses at all stages of the study. |
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# PREPARE



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Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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### 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](https://norecopa.no/PREPARE/prepare-checklist)

*Three versions of the checklist:*

### 3. online version

[norecopa.no/PREPARE/Mychecklist](https://norecopa.no/PREPARE/Mychecklist)

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# PREPARE



## The PREPARE Guidelines Checklist

### Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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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   |
|-------------------------------------|--|
| <b>(A) Formulation of the study</b> |  |
| 1. Literature searches              | <input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes.<br><input type="checkbox"/> Consider the use of systematic reviews.<br><input checked="" type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms.<br><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.   |

text only stored on author's computer

[norecopa.no/prepare/mychecklist?id=deeb7d](http://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, and will any advances in this research only index the title and abstract, or will they 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



# The path to better research



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[norecopa.no/PREPARE](https://norecopa.no/PREPARE) and [ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1](https://ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1)

The screenshot shows the ARRIVE guidelines website. The top navigation bar includes 'Home', 'About', 'ARRIVE guidelines', 'Supporters', 'Resources', 'Publications', and 'News'. A left-hand sidebar lists various guideline sections, with '11. Abstract' highlighted under the 'Recommended Set' category. The main content area is titled '11. Abstract' and features a purple callout box with 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, there are tabs for 'Explanation' and 'Examples'. The 'Explanation' tab is active, containing 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 the explanation is a 'References' section with two entries: 1. Haynes RB, Mulrow CD, Huth EJ, Altman DG and Gardner MJ (1990). More informative abstracts revisited. *Ann Intern Med.* doi: 10.7326/0003-4819-113-1-69; 2. Hair K, Macleod MR, Sena ES, Sena ES, Hair K, Macleod MR, Howells D, Bath P, Irvine C, MacCallum C, Morrison G, ...



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*"We ARRIVED, because we were PREPARED"*

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

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3R improvements are often not highlighted in the scientific literature



[http://www.theodora.com/rodent\\_laboratory/blood\\_collection.html](http://www.theodora.com/rodent_laboratory/blood_collection.html)



photo:NMBU

*SCID-Hu mice immunized with a pneumococcal vaccine produce specific human antibodies and show increased resistance to infection.*



Flag



## Saphenous vein puncture for blood sampling of the mouse, rat, hamster, gerbil, guineapig, ferret and mink

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### Summary

A method is described for blood collection from the lateral saphenous vein. This enables rapid sampling, which if necessary can be repeated from the same site without a need for new puncture wounds. The method is a humane and practical alternative to cardiac and retro-orbital puncture, in species where venepuncture has traditionally been regarded as problematic.

**Keywords** Saphenous vein; blood sampling; mouse; rat; hamster; gerbil; guineapig; rodent; ferret; mink

The title and summary are critical, because they are often the only parts that are indexed by databases.

Not necessarily a high-impact journal.



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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)<sup>[1]</sup>. The *click* bridges the time between the desired behavior and the presentation of the reward<sup>[1]</sup>. 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<sup>[2]</sup>.

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<sup>[3]</sup>

**Rats:** following a target stick, voluntarily change to a cage, observational learning<sup>[2]</sup>

**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<sup>[4]</sup>.



**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.

- <sup>1</sup> <sup>1.0</sup> <sup>1.1</sup> Feng, Lynna C.; Howell, Tiffani J.; Bennett, Pauleen C. (1 August 2016). "How clicker training works: Comparing Reinforcing, Marking, and Bridging Hypotheses"<sup>?</sup>. *Applied Animal Behaviour Science*. **181**: 34–40. doi:10.1016/j.applanim.2016.05.012<sup>?</sup>. ISSN 0168-1591<sup>?</sup>.
- <sup>2</sup> <sup>2.0</sup> <sup>2.1</sup> 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"<sup>?</sup>. *JoVE (Journal of Visualized Experiments)* (140): e58511. doi:10.3791/58511<sup>?</sup>. ISSN 1940-087X<sup>?</sup>. PMC 6235608<sup>?</sup>. PMID 30417890<sup>?</sup>.
- <sup>3</sup> Leidinger, Charlotte; Herrmann, Felix; Thöne-Reineke, Christa; Baumgart, Nadine; Baumgart, Jan (6 March 2017). "Introducing Clicker Training as a Cognitive Enrichment for Laboratory Mice"<sup>?</sup>. *JoVE (Journal of Visualized Experiments)* (121): e55415. doi:10.3791/55415<sup>?</sup>. ISSN 1940-087X<sup>?</sup>. PMC 5408971<sup>?</sup>. PMID 28287586<sup>?</sup>.
- <sup>4</sup> "Positive Reinforcement Training in Large Experimental Animals"<sup>?</sup> (PDF).

**Experts for clicker training in mice and rats:** [TARC](#)<sup>?</sup>, Mainz, Germany

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


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