

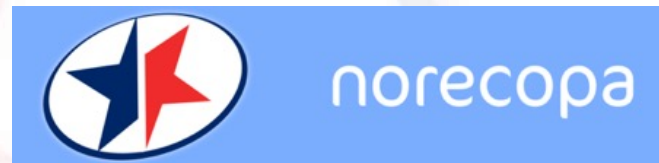
## PREPARE and ARRIVE:

How can we improve both our scientific output and animal welfare?

[norecopa.no/260124](https://norecopa.no/260124)

Adrian Smith

[adrian.smith@norecopa.no](mailto:adrian.smith@norecopa.no)



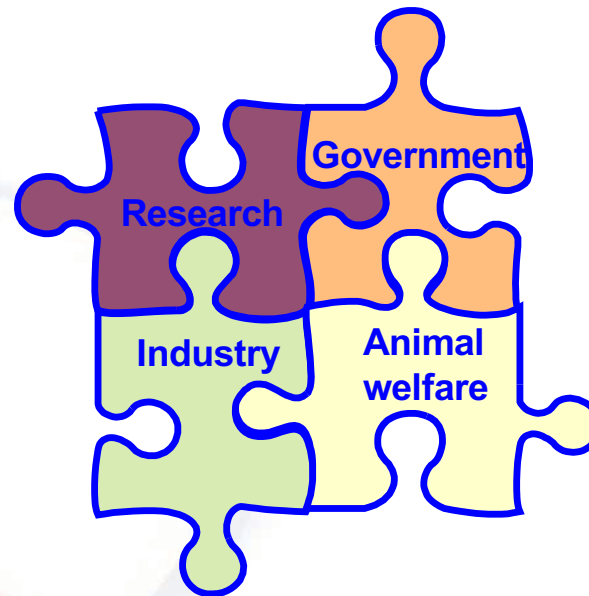
<https://norecopa.no>

Norecopa: PREPARE for better Science



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

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



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

*40-slide powerpoint presentation about the 3Rs*



ccac.ca

***All three Rs of Russell and Burch:***

**Replacement, Reduction & Refinement**

English, French and Spanish versions (soon German)

Free download from [norecopa.no/3Rs](http://norecopa.no/3Rs)





**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

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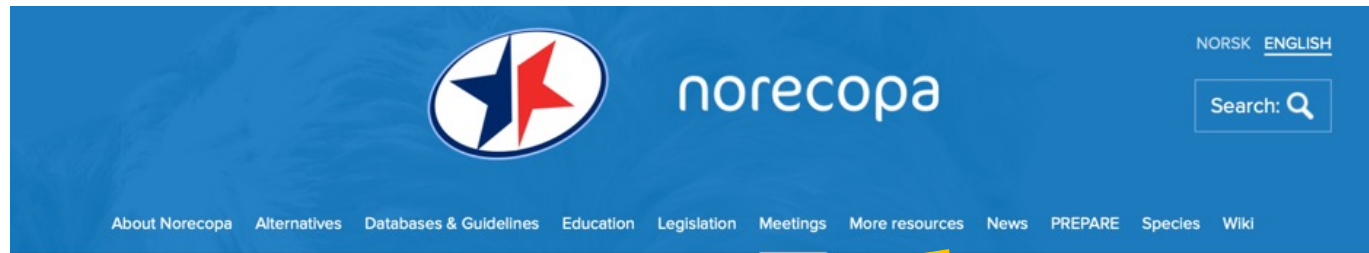
## norecopa.no : an updated overview of global 3R resources

The screenshot displays the norecopa.no website interface. At the top, the norecopa logo is visible. Below it, a navigation menu includes links such as 'About Norecopa', 'Alternatives', 'Databases & Guidelines', 'Education & training', 'Legislation', 'Meetings', 'More resources', 'News', and 'PREPARE'. A secondary menu lists various topics like 'Anaesthesia and analgesia', 'Animal facilities', 'Animal welfare organisations', 'Blood sampling', 'Culture', 'Email discussion lists', 'Environmental enrichment', 'Ethics', 'Experimental design and reporting', 'Harm-f', 'Health and safety', 'Health monitoring', 'Humane endpoints', 'Humane killing', 'Journals', 'Literature searches and systematic reviews', 'Organisations', 'Reporting guidelines', and 'Severity classification'. A breadcrumb trail shows the current page: 'norecopa.no / More resources / Experimental design and reporting'. The main content area features the title 'Design and reporting of animal experiments' and a sub-header 'approx. 10,000 webpages'. Below this, it states '7-8 detailed newsletters per year' and 'This page supplements advice given in Section 4 of the... covers all aspects of design (including animal and facility related issues)'. At the bottom, the text reads 'Norecopa: PREPARE for better Science'. On the right side, a search filters sidebar is visible, containing sections for 'Search filters' (with 'Order by' and 'Typo tolerance' dropdowns), 'Database' (listing various databases with counts), 'Browse the databases' (listing categories like eBooks, Free, Held at NMBU Oslo, etc.), and 'Search in the databases' (listing search criteria like All Text, Title, Author, etc.).

**Design and reporting of animal experiments**  
approx. 10,000 webpages  
7-8 detailed newsletters per year

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

Norecopa: PREPARE for better Science



+ webpages for past meetings and recorded meetings

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

## Webinar and Meetings calendar

### February 2024

- > [Annual meeting of Swedish animal technicians](#), online, 1 February 2024
- > [CLAST course on Application of the 3Rs to the severity assessment framework](#), 5-6 February 2024
- > [Animal experiments with cephalopods: The epistemic limits of legislation and administrative procedures out to the test](#), webinar (Klaus Gärditz), 6 February 2024 (Kenncode 467832)
- > [L'imagerie in vivo comme outil de réduction et de raffinement chez l'animal de laboratoire](#), webinar (Philippe Garrigue & Benjamin Guillet), 8 February 2024
- > [4th Italian Zebrafish Meeting](#), Palermo, 7-9 February 2024
- > [Integrating RAT resources into your training](#), webinar (Paul Flecknell & Jon Gledhill), 8 February 2024
- > [CLAST course on Managing and Developing Teams](#), hybrid, 13 February, 19 March, 16 April & 28 May 2024
- > [Preregistration and open science - maximizing the knowledge gain from animal research](#), webinar (Céline Heintz), 16 February 2024
- > [Social media and ethics](#), UKRIO webinar (Nicholas Gold), 21 February 2024
- > [CLAST course on Advanced animal husbandry, care and enrichment practices](#), Oxford/online, start 23 February 2024
- > [MRC course on Mouse Genetics and Colony Management for Researchers](#), Harwell, 26-28 February 2024
- > [World Organoid Research Day](#), Cambridge, 27-28 February 2024
- > [Young TPI Webinar Series \(II\): in vitro and in silico: match made in heaven?](#), webinar (Aurélie Carlier & Christian Maas), 28 February 2024
- > [Focus on Fish](#), RSPCA online event, 29 February 2024





**SAVE THE  
DATE  
APRIL  
2024**



**University of  
Nottingham**

UK | CHINA | MALAYSIA

# TRAINING SCHOOL IN EXPERIMENTAL DESIGN

Nottingham, UK

17-19 April 2024

FELASA  
Accredited



REGISTRATION OPEN SOON  
SEE HERE TO SIGN UP FOR  
NOTIFICATIONS:



**FOCUS ON FISH | 2024**

Practical refinements for fishes  
in research and testing

**RSPCA**

**FREE TO ATTEND**

**ONLINE 29 FEBRUARY 2024**

Norecopa: PREPARE for better Science

<https://norecopa.no/meetings>

## **International consensus meetings**

*Harmonisation of the Care and Use of:*

- *Fish (2005)*
- *Wildlife (2008)*
- *Fish (2009)*
- *Agricultural animals (2012)*
- *Wildlife (2017)*


**All the presentations and consensus statements  
on the web: a lasting resource**



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



Norecopa: PREPARE for better Science



norecopa

NORSK [ENGLISH](#)

Search:

[About Norecopa](#) [Alternatives](#) [Databases & Guidelines](#) [Education](#) [Legislation](#) [Meetings](#) [More resources](#) [News](#) [PREPARE](#) [Species](#) [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](http://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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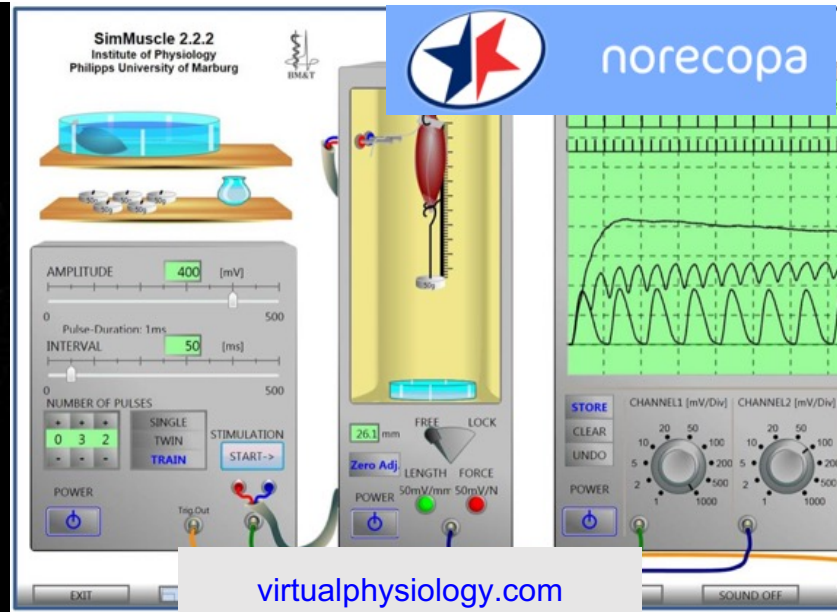
[norecopa.no/databases-guidelines](https://norecopa.no/databases-guidelines)

links to over 70 other databases

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



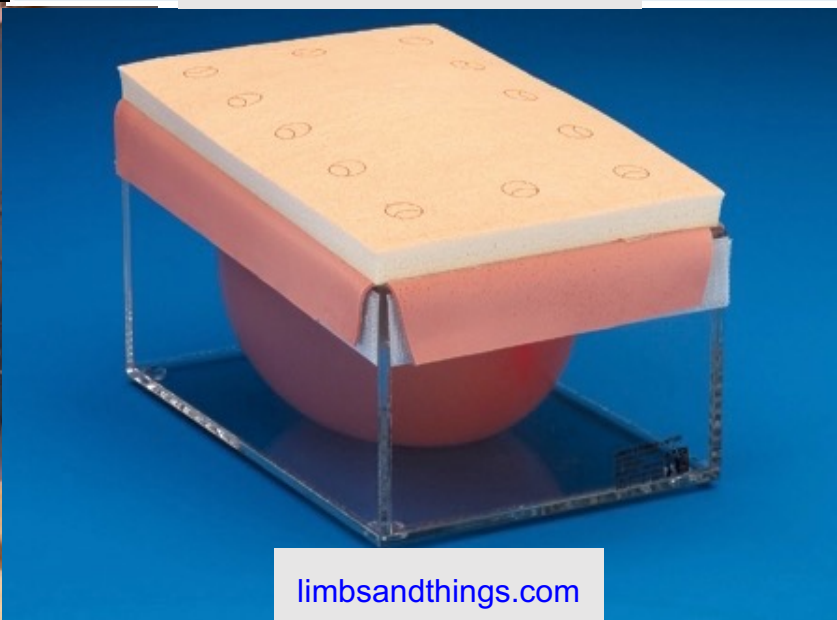
[3dglasshorse.com](http://3dglasshorse.com)



[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



Intravenous injection in a rabbit  
Norecopa | 2,025 views



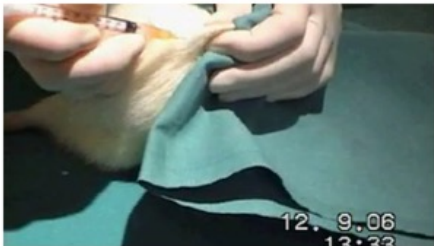
Subcutaneous injection in the chicken  
Norecopa | 1,806 views

**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

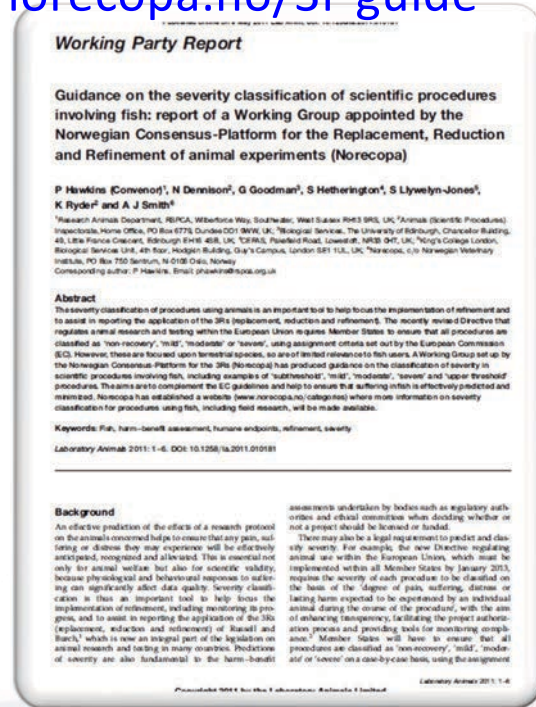


Immobilisation of the rabbit  
Norecopa | 2,072 views

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From **3R-Guide** (>400 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

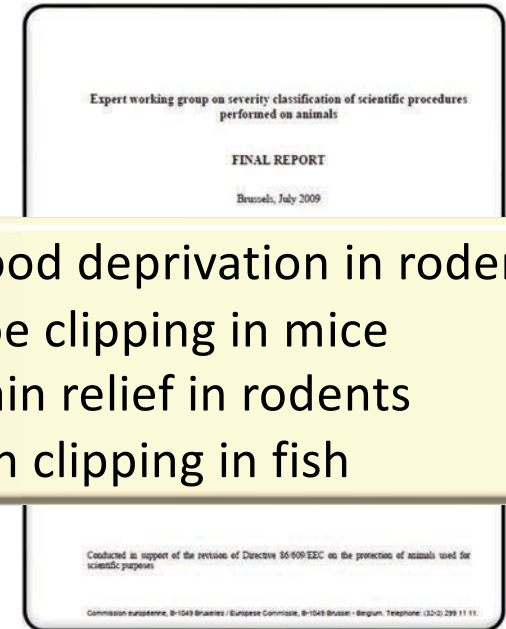
P Hawkins, N Dennison, G Goodman, S Hetherington, S Llywelyn-Jones, K Ryder and AJ Smith

Laboratory Animals, 45: 219-224, 2011

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

Food deprivation in rodents  
Toe clipping in mice  
Pain relief in rodents  
Fin clipping in fish



[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)

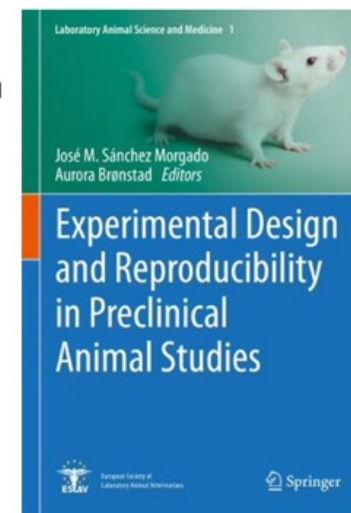
## Experimental Design and Reproducibility in Preclinical Animal Studies

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)



Scientists are becoming increasingly concerned about the validity of animal experiments

NATURE | NEWS

## Swiss survey highlights potential flaws in animal studies

Poor experimental design and statistical analysis could contribute to widespread problems in reproducing preclinical animal experiments

### Pain management in pigs undergoing experimental surgery; a literature review (2012–4) FREE

A. G. Bradbury, M. Eddleston, R. E. Clutton

Br J Anaesth (2016) 116 (1): 37–45. DOI: <https://doi.org/10.1093/bja/aev301>

Published: 03 October 2015

selection criteria. Most articles (193/233, 83%) described use of drugs with analgesic properties, but only 87/233 (37%) described postoperative analgesia. No article provided justification for the analgesic chosen, despite the lack of guidelines for analgesia in porcine surgical models and the lack of formal studies on this subject. Postoperative pain assessment was reported in only 23/233 (10%) articles. It was found that the reporting of postoperative pain management in the studies was remarkably low, reflecting either under-reporting or under-use. Analgesic description, when given, was frequently too limited to enable reproducibility. Development of a



NATURE | NEWS FEATURE

## 1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

25 May 2016 | Corrected: 28 July 2016

More than 70% of researchers have tried and failed to reproduce another scientist's experiments, and more than half have failed to reproduce their own experiments. Those are some of the telling figures that emerged from *Nature's* survey of 1,576 researchers who took a brief online questionnaire on reproducibility in research.

## Frequently highlighted causes of the "reproducibility crisis"

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

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

Perspective | Open Access | Published: 10 January 2017

## A manifesto for reproducible science

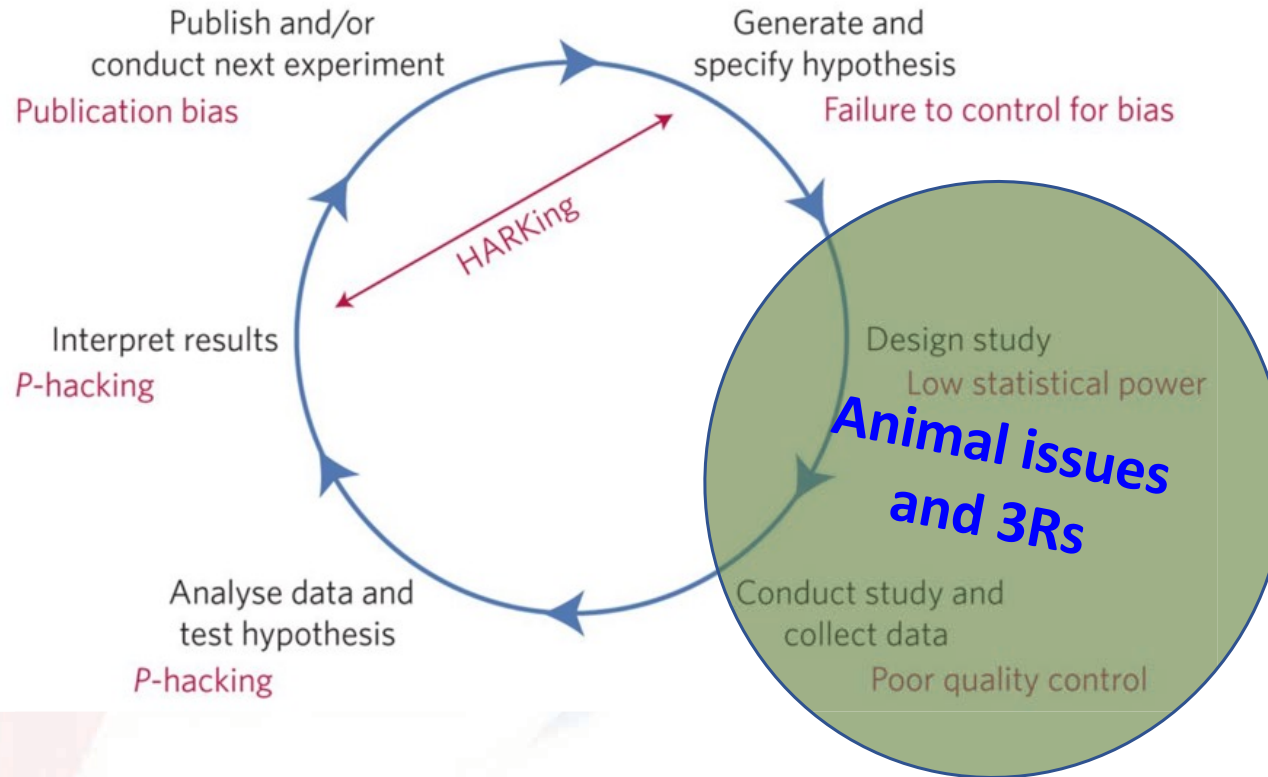
Marcus R. Munafò , Brian A. No-  
Button, Christopher D. Chambers,  
Jan Wagenmakers, Jennifer J. Wa

*Nature Human Behaviour* 1, Artic

33k Accesses | 518 Citations |

### Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



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Two frustrations:

'We can solve the reproducibility crisis by

- courses in Experimental Design that focus exclusively on the "mathematical" aspects (e.g. randomisation, experimental units, blinding, statistical methods) and ignore the animal/human-related issues”
- **better reporting**

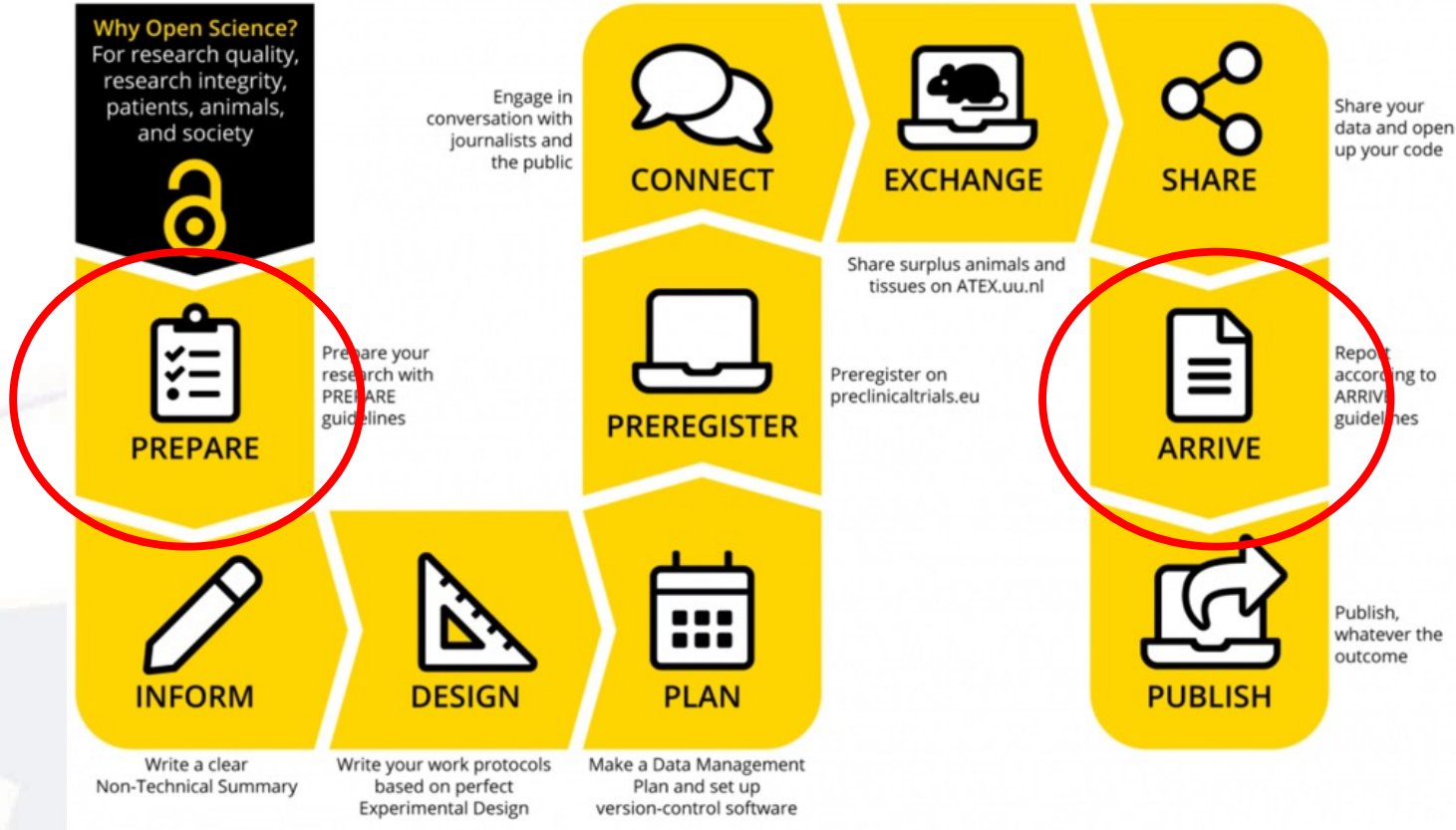


[reddit.com](https://www.reddit.com)





# The road to better research



## *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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[travelandleisure.com/airlines-airports/what-happens-when-planes-hit-birds](https://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. |



norecopa



***Hudson River, 2009***

[en.wikipedia.org](https://en.wikipedia.org)

***All 155 passengers and crew saved***

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

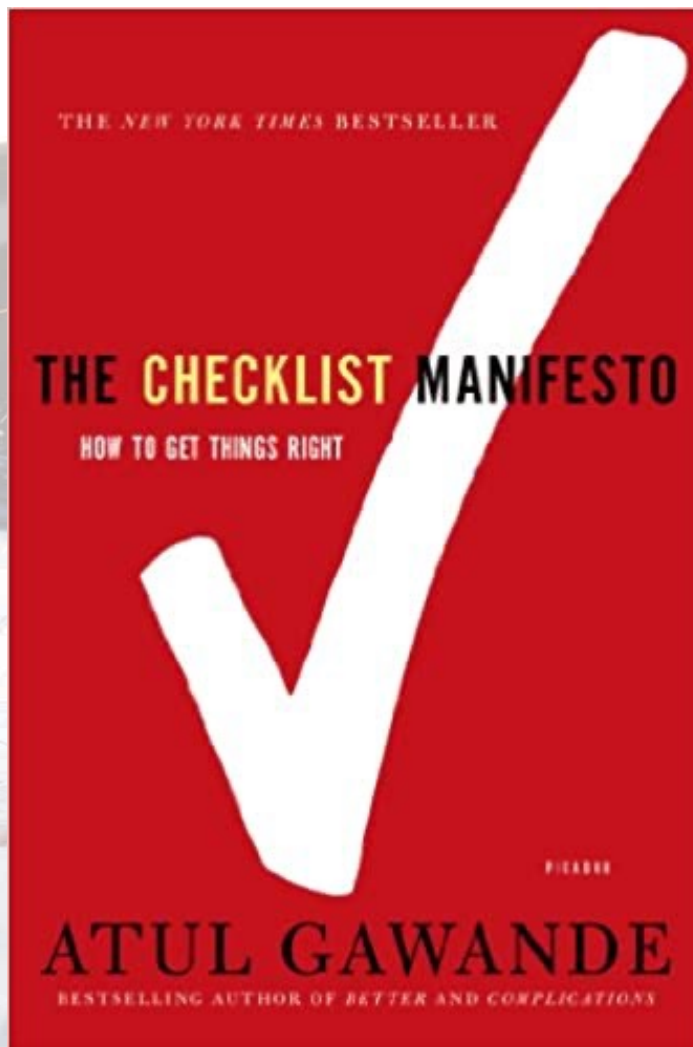


***Too late to read the checklists when you have ARRIVED!***



colourbox.com

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# Surgical Safety Checklist



- Before induction of anaesthesia** (with at least nurse and anaesthetist)
- Before skin incision** (with nurse, anaesthetist and surgeon)
- Before patient leaves operating room** (with nurse, anaesthetist and surgeon)

- Has the patient confirmed his/her identity, site, procedure, and consent?**
- Yes
- Is the site marked?**
- Yes  
 Not applicable
- Is the anaesthesia machine and medication check complete?**
- Yes
- Is the pulse oximeter on the patient and functioning?**
- Yes
- Does the patient have a:**
- Known allergy?**
- No  
 Yes
- Difficult airway or aspiration risk?**
- No  
 Yes, and equipment/assistance available
- Risk of >500ml blood loss (7ml/kg in children)?**
- No  
 Yes, and two IVs/central access and fluids planned

- Confirm all team members have introduced themselves by name and role.**
- Confirm the patient's name, procedure, and where the incision will be made.**
- Has antibiotic prophylaxis been given within the last 60 minutes?**
- Yes  
 Not applicable
- Anticipated Critical Events**
- To Surgeon:**
- What are the critical or non-routine steps?  
 How long will the case take?  
 What is the anticipated blood loss?
- To Anaesthetist:**
- Are there any patient-specific concerns?
- To Nursing Team:**
- Has sterility (including indicator results) been confirmed?  
 Are there equipment issues or any concerns?
- Is essential imaging displayed?**
- Yes  
 Not applicable

- Nurse Verbally Confirms:**
- The name of the procedure  
 Completion of instrument, sponge and needle counts  
 Specimen labelling (read specimen labels aloud, including patient name)  
 Whether there are any equipment problems to be addressed
- To Surgeon, Anaesthetist and Nurse:**
- What are the key concerns for recovery and management of this patient?

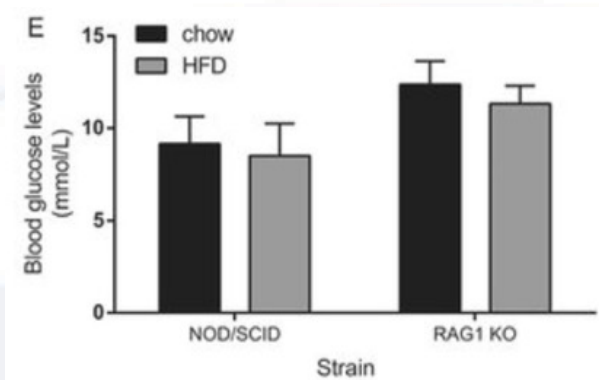
This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged. Revised 1 / 2009 © WHO, 2009

[who.int/patientsafety/topics/safe-surgery/checklist/en](http://who.int/patientsafety/topics/safe-surgery/checklist/en)

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[amazon.com/gp/product/0312430000](https://amazon.com/gp/product/0312430000)

## 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

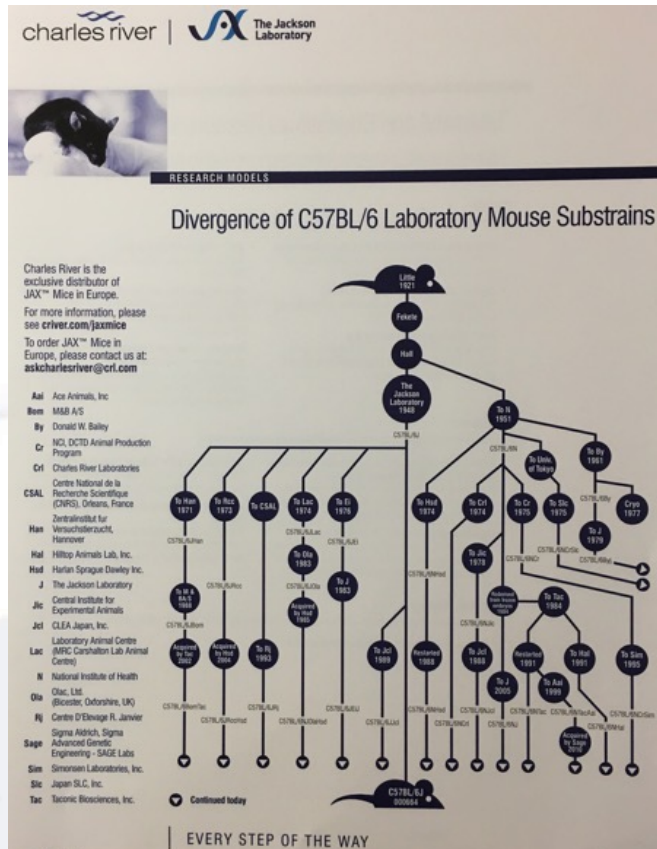
developing illness and death



# Some of the animal-related issues...

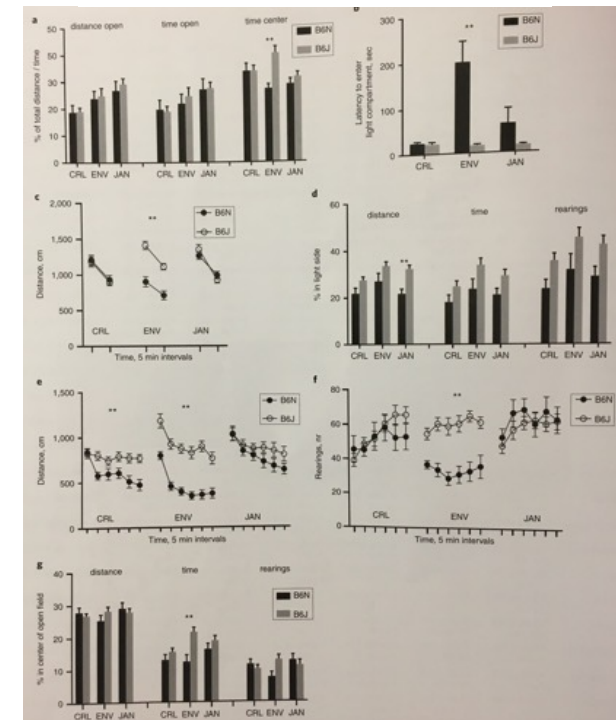


## The C57BL/6 mouse



Åhlgren & Voikar (2019): Behavioural differences between /6J and /6N mice

[nature.com/articles/s41684-019-0288-8](https://nature.com/articles/s41684-019-0288-8)



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*we are what we eat...*



## Diet-Induced Metabolic Syndrome in Rodent Models

A discussion of how diets made from purified ingredients influence the phenotypes of the MS in commonly used rodent models.

**Angela M. Gajda, MS, Michael A. Pellizzon, Ph.D.,  
Matthew R. Ricci, Ph.D. and Edward A. Ulman, Ph.D.**

Pellizzon and Ricci *Nutrition & Metabolism* (2018) 15:3  
DOI 10.1186/s12986-018-0243-5

Nutrition & Metabolism

PERSPECTIVE

Open Access

The common use of improper control diets in diet-induced metabolic disease research confounds data interpretation: the fiber factor



Michael A. Pellizzon\* and Matthew R. Ricci

[norecopa.no/prepare/12-housing-and-husbandry/12a/general-principles](https://norecopa.no/prepare/12-housing-and-husbandry/12a/general-principles)

Currently no FELASA guidance on nutrition (a working group has been convened)

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## Laboratory Animal Diets: A Critical Part of Your In Vivo Research

Most all of us are aware that certain dietary choices can increase or decrease the likelihood of developing certain diseases. Our diets can also change our metabolism as well the levels of circulating factors (hormones, lipids, etc.) which may be markers for disease risk. What is often overlooked is the fact that these concepts also apply to laboratory animals, making diet a critical part of study design.

**Matthew R. Ricci, Ph.D. and Edward A. Ulman, Ph.D.**

## Contingent suffering



animalcaresystems.com

(not just the direct suffering caused by the procedure)

Fear, boredom and discomfort

Caused by, for example:

Transport, or changes in housing, husbandry and social groups

Single-housed male mice show symptoms of what in humans would be characterised as depression

<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0111065>

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photo: colourbox.com

## *Stress caused by capture and handling*



News > Science

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

Mice pick naturally

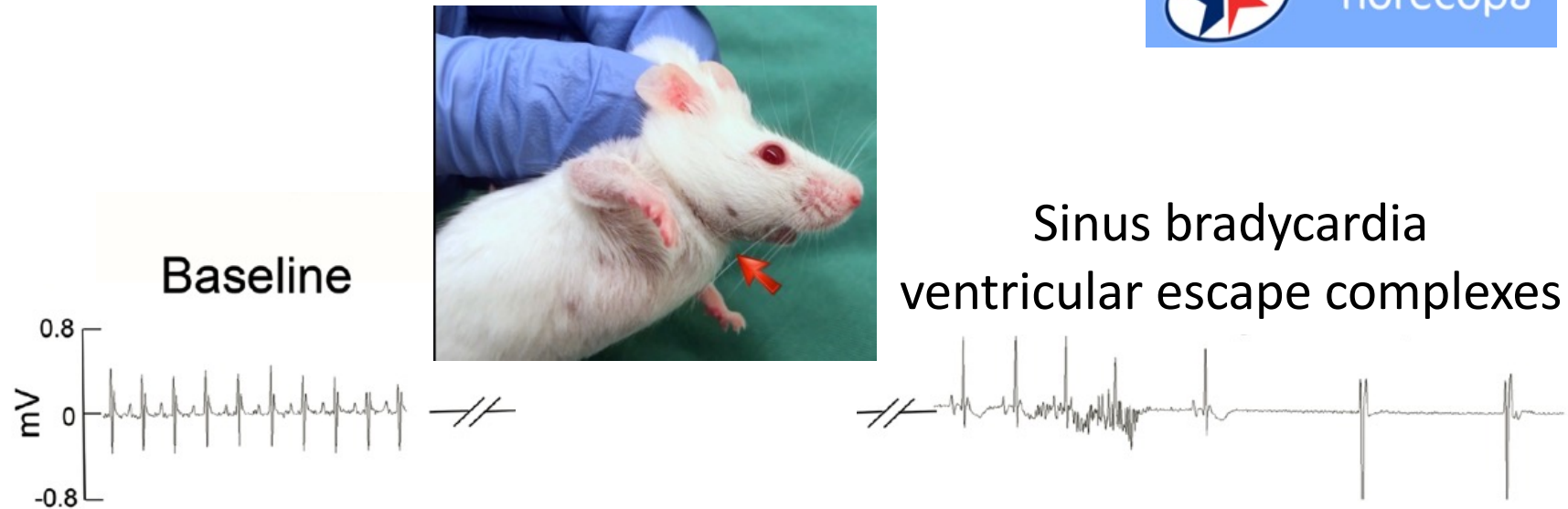
Ian Johnston



<https://www.nc3rs.org.uk/how-to-pick-up-a-mouse>

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Labitt *et al.*, 26 February 2021

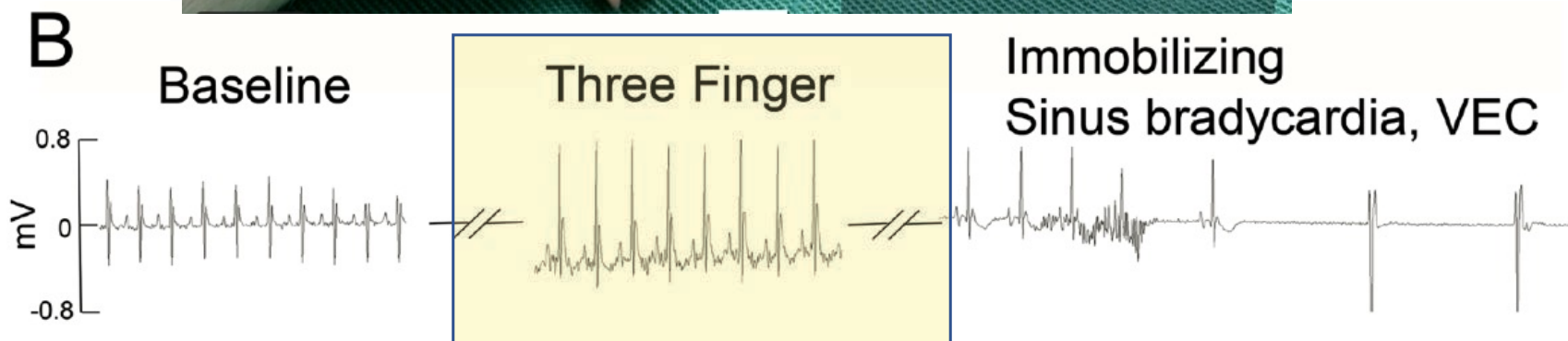
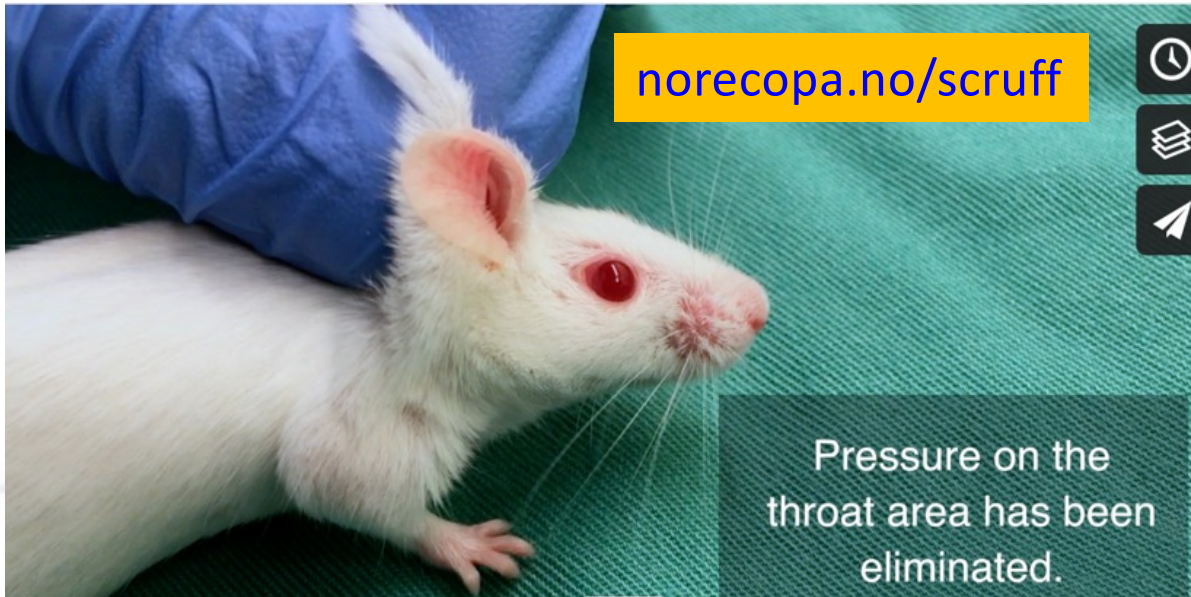
Both sexes and 4 strains of mice, 3 experienced handlers

Labitt RN, Oxford EM, Davis AK, Butler SD & Daugherty EK (2021): A Validated Smartphone-Based Electrocardiogram Reveals Severe Bradyarrhythmias during Immobilizing Restraint in Mice of Both Sexes and Four Strains. *J. Am. Assoc. Lab. Anim. Sci.*  
doi: 10.30802/AALAS-JAALAS-20-000069





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## *Artefacts caused by poor administration techniques*



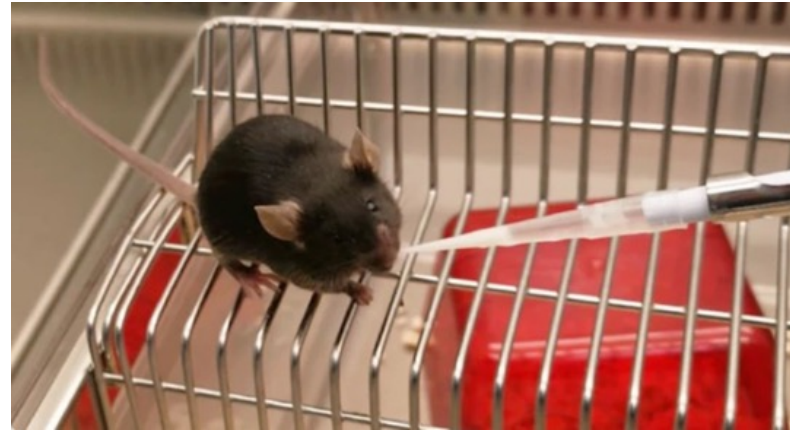
Photo: NMBU

- *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)*

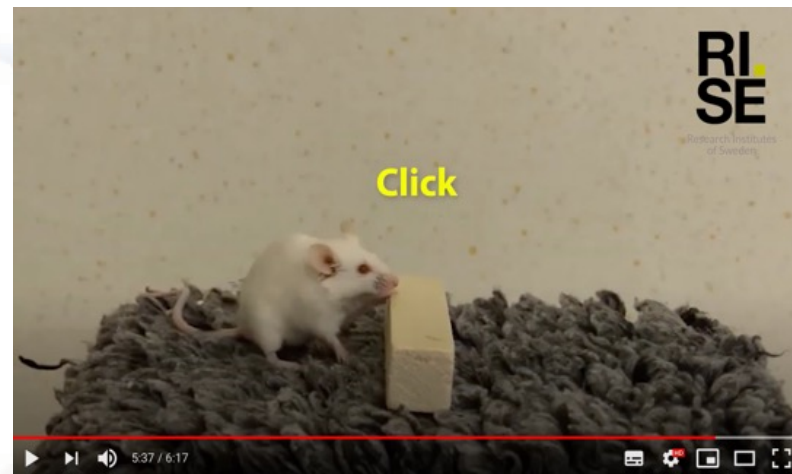
*'X was administered by gavage in 3 daily doses'*



photo: NMBU



[nature.com/articles/s41684-021-00723-0.pdf](https://www.nature.com/articles/s41684-021-00723-0.pdf)



[youtube.com/watch?v=bdtVZtrr69c](https://www.youtube.com/watch?v=bdtVZtrr69c)

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

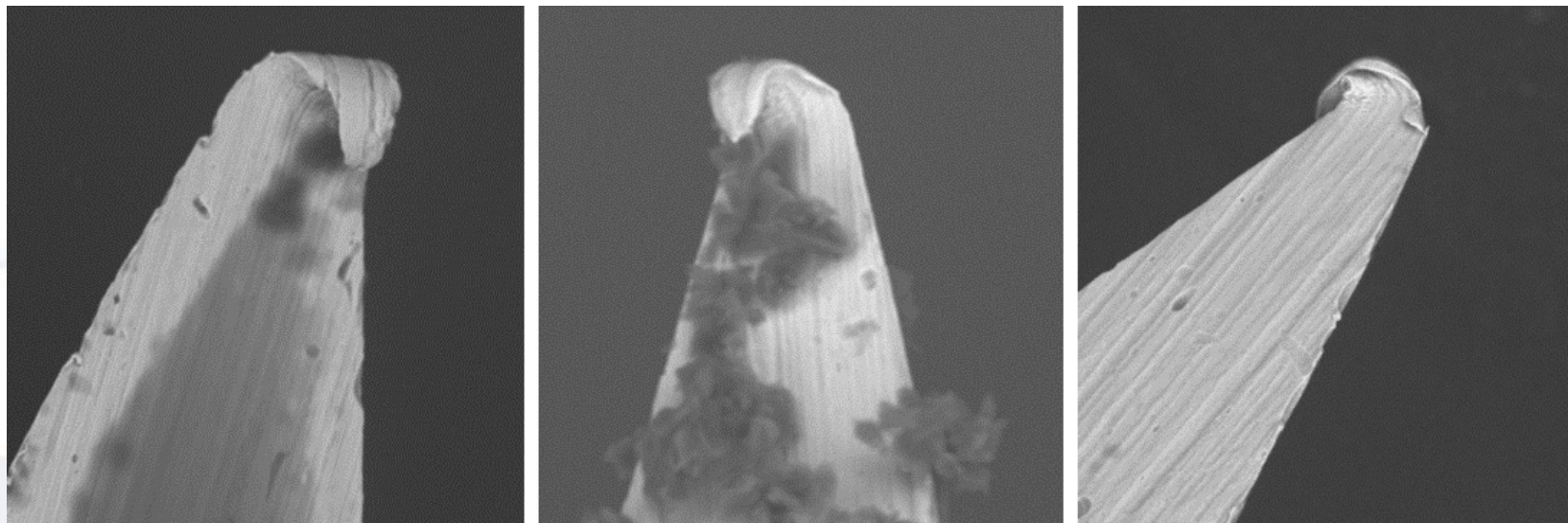


Photo: AstraZeneca

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



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[Home](#) > [News & Blog](#) > How serious are we about asepsis for rodent surgery?

# How serious are we about asepsis for rodent surgery?

**Monday 03 April 2017**

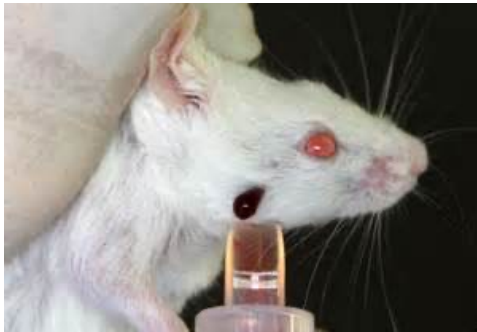
*As part of the [NC3Rs year of laboratory rodent welfare](#), our latest blog is from Professor Paul Flecknell, Newcastle University on the issue of aseptic surgery. Paul is a world renowned laboratory animal veterinarian who specialises in anaesthesia and analgesia.*

A rumour circulated recently amongst UK lab animal veterinarians that the Home Office Inspectorate (the UK regulator for animal



[nc3rs.org.uk/news/how-serious-are-we-about-asepsis-rodent-surgery](https://nc3rs.org.uk/news/how-serious-are-we-about-asepsis-rodent-surgery)

## *'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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## COMPILATION OF SEVERITY CLASSIFICATIONS ACROSS EUROPE

| I Interventions on body systems and functions   | II Induction of diseases   | III Pharmacology, other external causes  | IV Housing, environment and behaviour  | V Fetuses and premature animals                                       | VI Clinical signs  |
|---|--|--|--|---|--|
| <b>Substance administration</b>   | <b>Heart &amp; circulation</b>   | <b>Physical impacts</b>  | <b>Housing &amp; Nutrition</b>   | 1. Feeding<br>2. Surgical interventions<br>3. Reproductive toxicology | 1. Condition of fur, grooming, body orifices<br>2. Breathing, heart rate<br>3. Body temperature<br>4. Behaviour & body posture<br>5. Reaction to artificial stimulation; handling behaviour; reaction to physical contact<br>6. Food & water consumption<br>7. Prostration<br>8. Self trauma<br>9. Body weight |
| <b>Specimen collection</b>  | 1. Heart<br>2. Circulation<br>3. ECG measurements  | 1. Irradiation & chemotherapy<br>2. Exposure to electricity<br>3. Exposure to heat<br>4. Exposure to cold<br>5. Exposure to acids & basis<br>6. Traumatization<br>7. Pressure change<br>8. Sound & ultrasound<br>9. Magnetic fields<br>10. Chronic hypoxia | 1. Housing in general<br>2. Gnotobiology<br>3. Use of metabolic cages<br>4. Deprivation – water<br>5. Deprivation – food<br>6. Exposure to overstimulation   |   |  |
| 1. Collection of body fluids<br>2. Tissue sampling  | <b>Infectious diseases</b>   |  | <b>Breeding &amp; Reproduction</b>   |   |  |
| <b>Surgical interventions</b>   | 1. Infections in general<br>2. Gnotobiology<br>3. Bacterial infections<br>4. Viral infections<br>5. Mycotic infections | <b>Generation of pain</b>  | 1. Identification method and tissue sampling for genotyping<br>2. Germ cells   |   |  |
| 1. Anaesthesia<br>2. Surgical interventions in general<br>3. Abdominal and chest cavity<br>4. Musculoskeletal system<br>5. Implantation of mini-pumps, transponders<br>6. Organ transplantation<br>7. Implanted probes<br>8. Others | <b>Neurology &amp; sensory organs</b>  | <b>Pharmacological studies</b>   | <b>GA animals</b>  |   |  |
|   | 1. Convulsions<br>2. CNS lesions<br>3. Ischaemias<br>4. Visual system  | 1. Toxicity studies - general<br>2. Acute toxicity<br>3. Sub-acute toxicity<br>4. Chronic toxicity<br>5. Reproduction toxicology<br>6. Pharmacokinetic studies<br>7. Batch testing   | 1. GA animal model in the experiment<br>2. Phenotype characteristics<br>3. Generation of GA animals<br>4. Tissue sampling for genotyping   |   |  |
|   | <b>Endocrine, nutritional &amp; metabolic diseases</b>   |  | <b>Behaviour</b>   |   |  |
|   | 1. Endocrinology<br>2. Bone metabolism<br>3. Glucose metabolism<br>4. Body weight loss                                 |  | 1. Aversive learning, conditioned avoidance behaviour and conflict tests<br>2. Deprivation – social<br>3. Deprivation – sleep<br>4. Deprivation – motion & mobility<br>5. Pharmacologically induced behavior |   |  |
|   | <b>Neoplasms</b>   |  |  |   |  |
|   | <b>Immunology</b>  |  |  |   |  |
|   | 1. Transplantation<br>Cellular reactions<br>Autoimmune reactions<br>Immunisation<br>4.                                 |  |  |   |  |

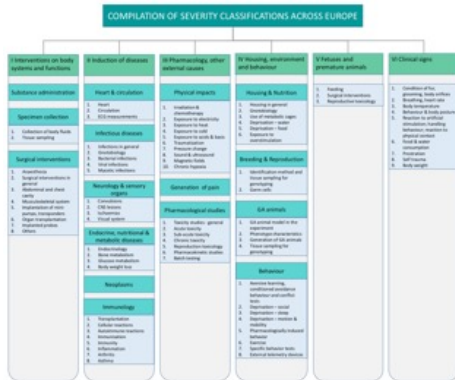
norecopa.no/severity



# Mild, Moderate or Severe? A compilation of severity classification



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



- The compilation covers
- > Interventions on body systems and functions
    - ▶ Substance administration
    - ▶ Specimen collection
    - ▶ Surgical interventions
  - > Induction of diseases
    - ▶ Heart and circulation
    - ▶ Infectious diseases
    - ▶ Neurology and sensory organs
    - ▶ Endocrine, nutritional and metabolic diseases
    - ▶ Neoplasms
    - ▶ Immunology
  - > Pharmacology and other external causes
    - ▶ Physical impacts
    - ▶ Generation of pain
    - ▶ Pharmacological studies
  - > Housing, environment and behaviour
    - ▶ Housing and nutrition
    - ▶ Breeding and Reproduction
    - ▶ GA animals
    - ▶ Behaviour
  - > Foetuses and premature animals
  - > Clinical signs

| Source  | Non-harmful / below threshold / severity degree 0  | Mild / severity degree 1  | Moderate / severity degree 2   | Severe / severity degree 3  |
|---|--|---|--|---|
| <a href="#">Directive 2010/63/EU, Annex VIII</a>                      |  | Administration of substances by subcutaneous, intramuscular, intraperitoneal routes, gavage and intravenously via superficial blood vessels, where the substance has no more than mild impact on the animal, and the volumes are within appropriate limits for the size and species of the animal.  | Frequent application of test substances which produce moderate clinical effects, and withdrawal of blood samples (> 10 % of circulating volume) in a conscious animal within a few days without volume replacement.  |   |
| <a href="#">Home Office (2014 a)</a>                                  |  | Injection by conventional routes, i.e. subcutaneous, intravenous, intraperitoneal or intramuscular (assuming competence of the person performing the procedure and that best practice guidelines for volume, pH, needle size, etc. are followed). Multiple injections by these routes may remain in the mild category if there are no cumulative effects.   |  |   |
| <a href="#">Federal Food Safety and Veterinary Office FSVO (2018)</a> | Single injection of small volumes s.c. and i.v. (species-specific), including repeated injections at long intervals (at least 24 hours). | I.v. or i.p. injections in sedated animals by catheter or tube and substances introduced into the body such as enemas. Implants and permanent accesses that can be created and used by means of a minimally invasive (superficial) procedure. Examples: Repeated iv or sc injection of small volumes (species-specific), insertion of cannulae into peripheral blood vessels. Subcutaneous injection of tumour tissue. Single subcutaneous implantations of osmotic minipumps and transponders. Subcutaneously channelled venous catheters. | Repeated injections at short intervals (several times within 24 hours). Implants and permanent accesses that have to be created by means of a deep surgical procedure or causing mild long-term constraint on an animal. Examples: Chronic iv catheters. Duodenal infusion cannula. Hepatic portal vein catheter. Gastric tube or chronic intragastric infusion cannula. Intraperitoneal or intravenous osmotic minipumps. Gavage. Telemetry transmitters. Implanted iv catheters with pumps in a jacket worn by dogs. Implantation of indwelling catheters in | Implants and permanent accesses that have to be created by means of a deep surgical procedure and causing severe long-term strain on an animal. Examples: Attachment of implants on the locomotor apparatus or other large implants that restrict movement (e.g. dorsal skinfold chamber in mice). Implantation of catheters in the abdominal aorta or bile duct. Implantation of an arterial blood-pressure catheter in the aortic arch via the left carotid artery or in the abdominal aorta via the femoral artery. Implantation of a combination of a venous and arterial catheter. |

## Quality assurance



Analysis

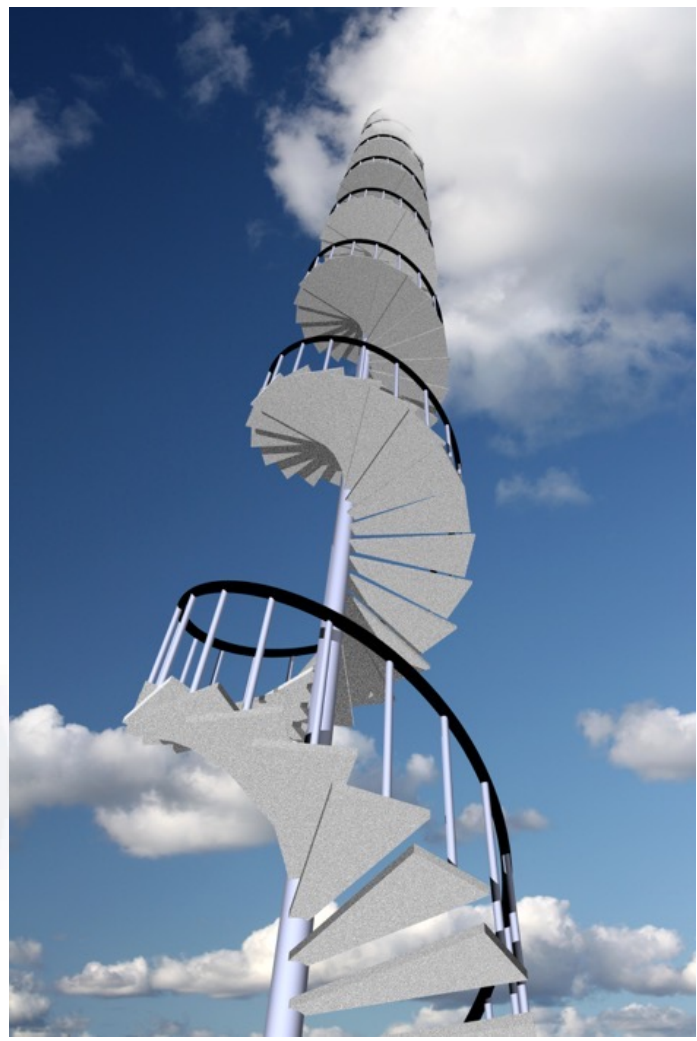
Conduct



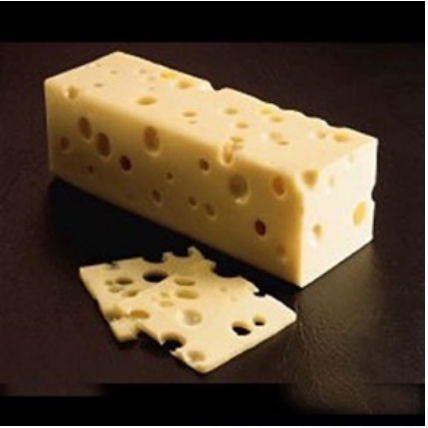
Report



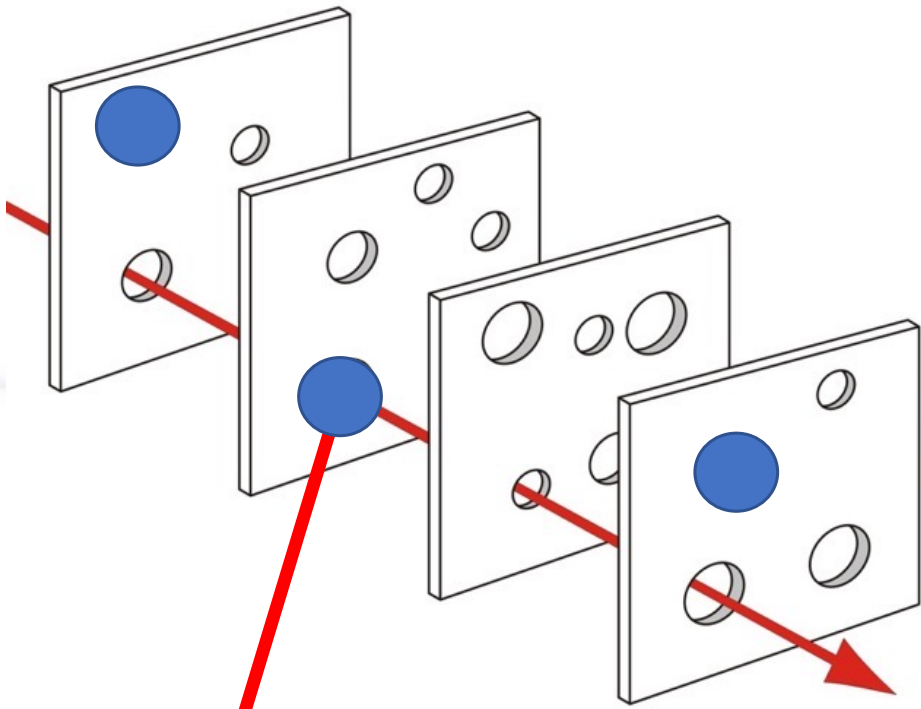
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# “Threat and Error Management”



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




Weaknesses / dangers

Serious incidents

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

## Contingency and redundancy

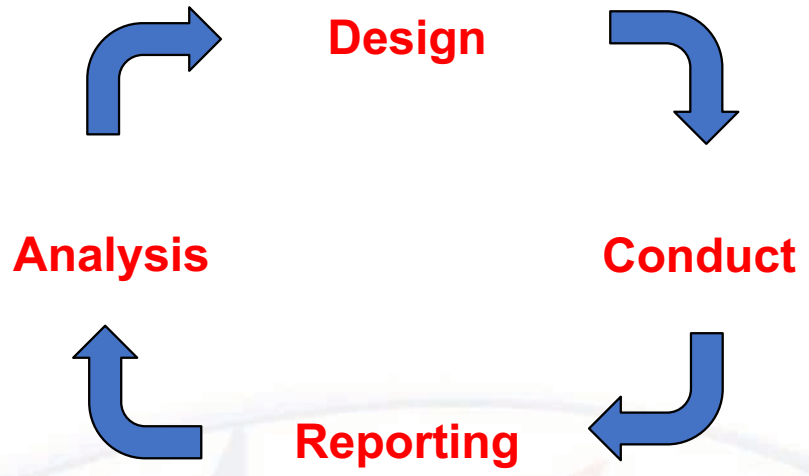
***Anything that can go wrong, will go wrong*** (Murphy's Law)  
***when it's least convenient*** (Sod's Law)



PREPARE draws on the authors' experience in managing accredited research facilities.

Photo: NMBU





**Identify and ensure the quality of (at least)  
the critical points in the experiment:  
for scientific output and animal welfare**



Space Shuttle, NASA



NASA



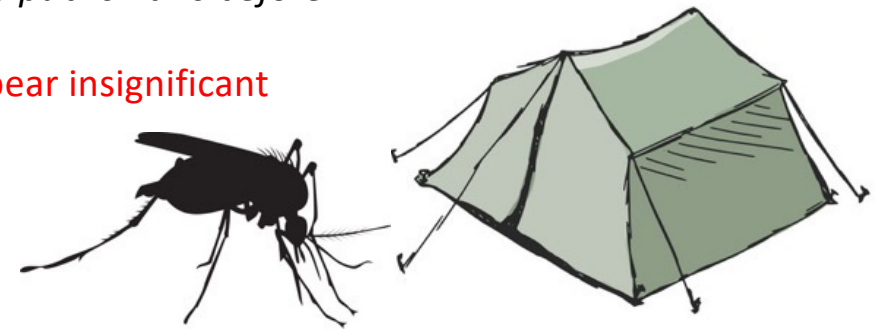
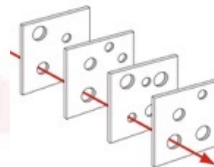
cbsnews.com



no.wikipedia.org

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

We need a Culture of Care!





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



"because we've always done it that way"

"as often as necessary"

"there are no alternatives"

*Shouldn't we as scientists be open for novel methods...?*

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.



<https://medium.com/the-composite/in-defence-of-the-emperors-new-clothes-dd23b1c04455>



***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

What if things go wrong?



[wikipedia](#)

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## CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

**Refine - Reduce - Replace**

Detect  
a critical  
incident

CIRS-LAS.de

Anonymous  
report

We all  
learn  
from it!

Get involved!

Expert  
analysis

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

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

**OPEN DIALOGUE** ensures transparency in laboratory animal science



# 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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<sup>3</sup>Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK  
<sup>4</sup>Section of Experimental Biomedicine, Department of Production Animal, Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway  
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Pre-published under Open Access on 3 August 2017, sponsored by the Universities Federation for Animal Welfare (UFAW), UK

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



Over 33,000 downloads from the journal website so far

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## **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. Hansens\* & Trond Bratteliid\*  
 \*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, Wilkesforden Way, Southwater, Horsham, West Sussex, GU14 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 dyreavdelingen  
 3. Kvalitetskontroll av de ulike komponentene i studiet  
 I praksis vil ikke temaene alltid behandles i den rekkefølgen som er på PREPARE-sjekklisten kan endres for å ivareta spesielle behov, f.eks. ved dyreavdelinger, fordi laboratorieforsøk er helt avhengige av deres kvalité Norecopas nettsider, med lenker til globale ressurser, på <https://morec>. PREPARE-retningslinjene er et dynamisk sett som vil videreutvikles etter produseres, og etter hvert som "best praksis" innføres for forskningsmiljøet forbedres.

+ 2 online versions  
35 languages

| Tema  | Anbefaling  |
|---|---|
| <b>(A) Designet av studiet</b>                                |   |
| 1. Litteratursøk  | <input type="checkbox"/> Formulere en klar hypotese, med primære og sekundære mål.<br><input type="checkbox"/> Vurdere å foreta en systematisk undersøkelse av litteraturen (Systematic Review).<br><input type="checkbox"/> Bestemme hvilke databaser og informasjonsspesialister som skal brukes, og konstruere søkebegrep.<br><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.<br><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.<br><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.<br><input type="checkbox"/> I dialog med etiske komitéer, vurdere om uttalelser om denne typen forsøk er allerede blitt produsert.<br><input type="checkbox"/> Adressere "de 3 R-ene" (Replacement, Reduction, Refinement) og "de 3 S-ene" (Good Science, Good Sense, Good Sensibillities).<br><input type="checkbox"/> Vurdere forhåndsregistrering av forsøket og publisering av negative resultater.<br><input type="checkbox"/> Foreta en kostnad-nytteanalyse ("Harm-Benefit Assessment") og diskutere eventuelle lidelser som kan oppstå under forsøket.<br><input type="checkbox"/> Diskutere læringsmålene dersom dyrene skal brukes i undervisnings- eller treningsøymed.<br><input type="checkbox"/> Klassifisere prosjektet etter belastningsgraden.<br><input type="checkbox"/> Definiere objektive, lett målbare og utvetydige humane endepunkter.<br><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.<br><input type="checkbox"/> Definiere den eksperimentelle enheten og bestemme antallet forsøksdyr.<br><input type="checkbox"/> Bestemme metodene for randomisering, fortlønde observasjonsskjemaer, og bestemme inklusjons- og eksklusjonskriterier.  |

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

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

| Tema  | Anbefaling   |
|---|--|
| <b>(C) Kvalitetskontroll av de ulike komponentene i studiet</b> |  |
| 9. Testsubstanser og -prosedyrer                                | <input type="checkbox"/> Oppgi så mye informasjon som mulig om testsubstansene.<br><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.<br><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.<br><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.<br><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.<br><input type="checkbox"/> Definiere de primære metodene for avlivning, samt metoder som kan brukes i en nødsituasjon.<br><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 & Bratteliid 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://morecopa.no/PREPARE> | [post@norecopa.no](mailto:post@norecopa.no) | [@norecopa](https://twitter.com/norecopa)

## The PREPARE Guidelines Checklist

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

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

<sup>a</sup>Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; <sup>b</sup>Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; <sup>c</sup>Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; <sup>d</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>e</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, 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.

Consider the use of systematic reviews.

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

# PREPARE



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## The PREPARE Guidelines Checklist

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

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

<sup>a</sup> Norecoba, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; <sup>b</sup> Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; <sup>c</sup> Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; <sup>d</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>e</sup> 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.

ecopa

| Topic                        | Recommendation   |
|------------------------------|--|
| (A) Formulation of the study |  |
| 1. Literature searches       | <p><input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes.</p> <p><input type="checkbox"/> Consider the use of systematic reviews.</p> <p><input checked="" type="checkbox"/> Decide upon databases and information specialists to be consulted, and construct search terms.</p> <p><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.</p> <p><input type="checkbox"/> Assess the reproducibility and translatability of the project.</p> |
| 2. Legal issues              | <p><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.</p>  |

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).
  - 3d Assessment and justify any likely animal harm.
  - 3f Discuss the learning objectives, if the animal use is for educational or training purposes.
  - 3g Allocate a severity classification to the project.
  - 3h Define objective, easily measurable and unequivocal humane endpoints.
  - 3i Discuss the justification, if any, for death as an end-point.
- 4-Experimental design and statistical analysis

5. Have the experiments been carried out before, and is any repetition justifiable?
6. What [approaches to reduce distress](#) have been considered?

## 3a Construct a lay summary.

- General principles
- For fish researchers**

1. Have national or local research ethics committees already produced statements relevant to the research being planned? Consideration should also be paid to the broader context of the research. For example, research directed at increasing the productivity of farming at the expense of (or without improving) individual animal welfare, or wildlife research whose primary aim is population management.

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

2. Will any advances in this research be published, and if so, will the publication only index the title and abstract, or will the full text be available? Will the project be rejected?
3. Have the Three S's ([Good Science, Good Sense and Good Sensibilities](#)) been addressed? Sufficient time should be allocated to this point, since two of the three S's are highly subjective, but equally important. The use of commonsense and critical anthropomorphism are justifiably part of the work to assess the impact of research on animals, not least when a scientific evidence base does not exist.
4. Does the proposed study have a clear rationale and scientific relevance, and what will be the next step if the hypothesis is supported or rejected?
5. Have the experiments been carried out before and is any repetition justifiable?
6. What [approaches to reduce distress](#) have been considered?
7. Will the project undergo [pre-registration](#) and will negative results be published, to avoid publication bias?

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

### Harm-Benefit Assessment

# Resource hubs

## 3Rs resources

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

Search 3Rs resources

### Hubs and microsites

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

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

# Resource hubs

The screenshot shows the RSPCA Science Home website. At the top is the RSPCA logo. Below it is a navigation bar with the following links: Science Home, Companion animals, Farm animals, Animals in science (highlighted), Wildlife, and Animal Sentience. A search icon is located on the right side of this bar. Below the navigation bar is a secondary menu with links: Implementing the 3Rs, Ethical review, Focus on severe suffering, Our international work, and Reports and resources (underlined). A 'Print' icon is visible on the right side of the page. The main content area features a grid of eight resource hubs, each with a representative image and a title:

- Ethical review**: Image of three people in a meeting.
- Culture of care**: Image of a white mouse being held in a person's hand.
- Severe suffering**: Image of a white mouse.
- Welfare and severity assessment**: Image of a person in a green lab coat and mask handling a mouse.
- Housing and care**: Image of a mouse in a cage.
- Refining procedures**: Image of a zebrafish.
- Genetically altered animals and biotechnology**: Image of two mice, one white and one black.
- Non-human primates**: Image of a monkey.

[science.rspca.org.uk/sciencegroup/researchanimals/reportsandresources](https://science.rspca.org.uk/sciencegroup/researchanimals/reportsandresources)





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

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

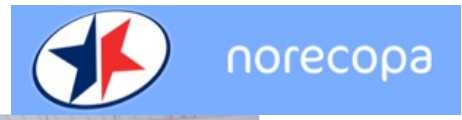


Photo: NMBU

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- III. Veterinary Care..... 29
  - A. Animal Procurement and Transportation ..... 29
    - 1. Animal Procurement..... 29
    - 2. Transportation of Animals ..... 29
  - B. Preventive Medicine..... 29
    - 1. Animal Biosecurity..... 29
    - 2. Quarantine and Stabilization ..... 30
    - 3. Separation by Health Status and Species ..... 30
  - C. Clinical Care and Management..... 30
    - 1. Surveillance, Diagnosis, Treatment and Control of Disease ..... 30
    - 2. Emergency Care ..... 31
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    - 3. Surgical Procedures ..... 33
    - 4. Aseptic Technique ..... 33
    - 5. Intraoperative Monitoring..... 34

63 pages



A simple but effective Master Plan



Norecopia: PREPARE for better Science

## A contract between the animal facility and the research group

Division of labour, responsibilities and cost

Clarifying all stages of the experiment

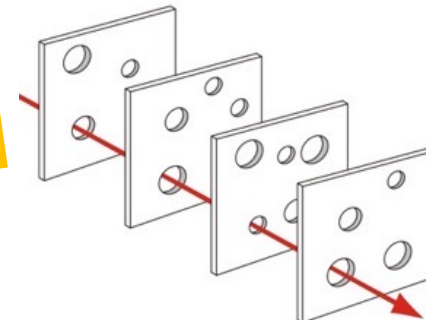
Ensuring that all necessary data are recorded

|   | Animal facility | Researcher | Not applicable |
|---|-----------------|------------|----------------|
| <b>Animal:</b>  |                 |            |                |
| 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) |                 |            |                |
| <b>Environment:</b>   |                 |            |                |
| 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                                      |                 |            |                |
| <b>Housing:</b>   |                 |            |                |
| Free-range, shelf, cabinet, isolator                          |                 |            |                |
| Cage type and size  |                 |            |                |
| Number and method of distribution of animals per cage         |                 |            |                |

## 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

These need to be revised or supplemented in the light of Covid-19  
[norecopa.no/be-prepared](https://norecopa.no/be-prepared)



Temporary staff at weekends and holidays

- 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>



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

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



## The ARRIVE guidelines 2019: updated guidelines for reporting animal research

Nathalie Percie du Sert<sup>1</sup>, Viki Hurst<sup>1</sup>, Amrita Ahluwalia<sup>2</sup>, Sabina Alam<sup>3</sup>, Marc T. Avey<sup>4</sup>, Monya Baker<sup>5</sup>, William J. Browne<sup>6</sup>, Alejandra Clark<sup>7</sup>, Innes C. Cuthill<sup>8</sup>, Ulrich Dirnagl<sup>8</sup>, Michael Emerson<sup>9</sup>, Paul Garner<sup>10</sup>, Stephen T. Holgate<sup>11</sup>, David W. Howells<sup>12</sup>, Natasha A. Karp<sup>13</sup>, Katie Lidster<sup>1</sup>, Catriona J. MacCallum<sup>14</sup>, Malcolm Macleod<sup>15</sup>, Ole Petersen<sup>16</sup>, Frances Rawle<sup>17</sup>, Penny Reynolds<sup>18</sup>, Kieron Rooney<sup>19</sup>, Emily S. Sena<sup>15</sup>, Shai D. Silberberg<sup>20</sup>, Thomas Steckler<sup>21</sup>, Hanno Würbel<sup>22</sup>

[biorxiv.org/content/10.1101/703181v1](https://doi.org/10.1101/703181v1)

Version 1 of ARRIVE (2010) '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%'

'Providing the level of journal or editorial input to ensure compliance with all the items of the ARRIVE guidelines is unlikely to be sustainable for most journals because of the resources needed'

arriveguidelines.org

## The ARRIVE guidelines 2.0

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

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

### **ARRIVE Essential 10**

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

### **Recommended Set**

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

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## ARRIVE 2.0

| ARRIVE Essential 10              |    |  |
|----------------------------------|----|--|
| Study design                     | 1  | For each experiment, provide brief details of study design including:<br>a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated.<br>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.<br>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.<br>b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why.<br>c. For each analysis, report the exact value of N in each experimental group. |
| Randomisation                    | 4  | Describe the methods used:<br>a. To allocate experimental units to control and treatment groups. If randomisation was used, provide the method of randomisation.<br>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).<br>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.<br>b. Specify the experimental unit that was used for each statistical test.<br>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.<br>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:<br>a. What was done, how it was done and what was used.<br>b. When and how often.<br>c. Where (including detail of any acclimation periods).<br>d. Why (provide rationale for procedures).   |
| Results                          | 10 | For each experiment conducted, including independent replications, report:<br>a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable.<br>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](#)



norecopa

*"We ARRIVED, because we were PREPARED"*

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



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[vimeo.com/358069203](https://vimeo.com/358069203) or [norecopa.no/PREPARE/film](https://norecopa.no/PREPARE/film)  
 3-minute cartoon film



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## *Why is 3R literature hard to find?*

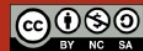
- Bibliographic databases are often not used adequately (poor overlapping between the databases)
- Too few scientists are aware of the specialist 3R-databases
- Scientists rarely use "3R" words when they write titles/abstracts/keywords for their papers
- Databases rarely flag 3R-papers with explicit thesaurus terms
- We have no single "Journal of Alternatives"

[norecopa.no/prepare/1-literature-searches](http://norecopa.no/prepare/1-literature-searches)

## How to construct a literature search

Alice Tillema, Medical Library, Nijmegen

<http://libguides.ru.nl/norecopa>



Radboud University



Radboudumc  
university medical center

3R improvements are often not highlighted in the scientific literature



[http://www.theodora.com/rodent\\_laboratory/blod\\_collection.html](http://www.theodora.com/rodent_laboratory/blod_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

Annelise Hem<sup>1</sup>, Adrian J. Smith<sup>2</sup> & Per Solberg<sup>1</sup>

<sup>1</sup> Norwegian Centre for Experimental Research in Animal Health, PO Box 4404 Torshov, N-0403 Oslo and  
© Laboratory Animals Ltd. *Laboratory Animals* (1998) 32, 364–368 <sup>2</sup> Centre for Experimental Research in Animal Health, PO Box 8146 Dep., N-0033 Oslo,

### 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 abstract are critical, because they are often the only parts that are indexed. They must contain 3R-terms that will be detected by indexers!

Not necessarily a high-impact journal.

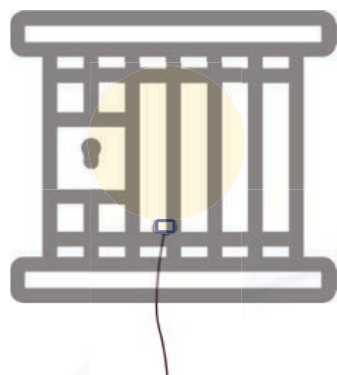
**A great source of 3R resources:  
Christine, Ontario**



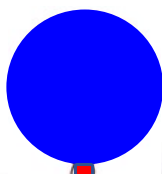
[speakingofresearch.com/2016/12/08/why-i-am-proud-to-be-a-registered-veterinary-technician-in-animal-research](http://speakingofresearch.com/2016/12/08/why-i-am-proud-to-be-a-registered-veterinary-technician-in-animal-research)

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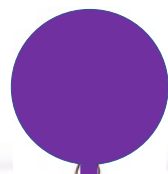
# The Waste of Good Ideas...



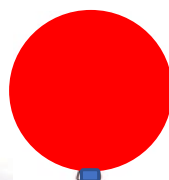
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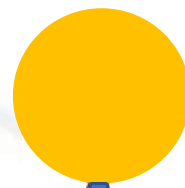
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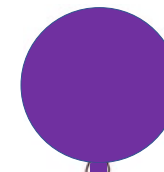
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## Clicker training

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>1.1</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>2.1</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

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- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Dehydration
- 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
- Forced swim test
- General discussion on use of analgesics
- Genotyping mice

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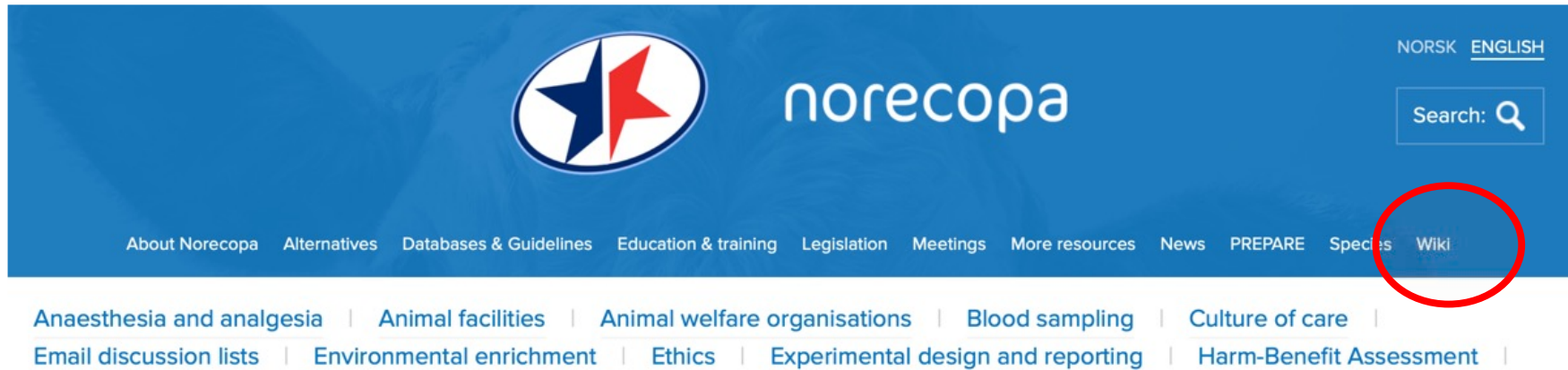
- Habituation training
- Health monitoring
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- Hot Bead Sterilisers
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- Metabolic cages
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- Mouse handling



- Nest building material
- Non-invasive genetic sampling in wildlife research
- Oestrus suppression in ferrets
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- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing

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wiki.norecopa.no



The Wiki is an integral part of Norecopa's website: [norecopa.no](http://norecopa.no)

All Wiki content is retrievable from Norecopa's search engine

In addition, the Wiki has its own internal search engine

A simple instruction manual to keep the threshold for adding new content as low as possible



## Acknowledgements

The idea of creating a Refinement Wiki came from Susanna Louhimies, EU Commission, whom we thank for her encouragement and valuable comments at all stages of this process



<https://norecopa.no/legislation/eu-directive-201063>

# English-language newsletters



[norecopa.no/news/newsletters](http://norecopa.no/news/newsletters)

1,400 international subscribers

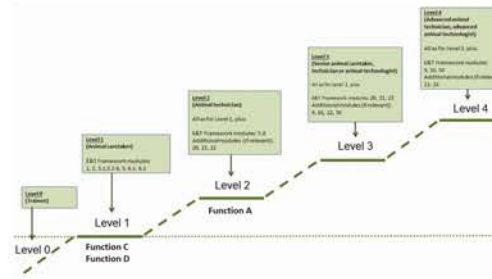
7-8 times a year

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



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

**Nordic zebrafish meeting 2023**  
 16 - 17 November, Stockholm



[www.thebehaviourforum.org](http://www.thebehaviourforum.org)

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

## TheBehaviourForum.org

Do you have questions on:

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

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

Post and find out:

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



## Norecopa: PREPARE for better Science

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



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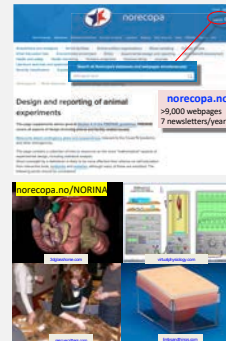
### What can Norecopa offer?

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

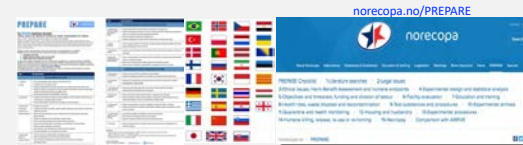


- over 9,000 searchable webpages of quality 3R resources, with filters to facilitate searching
- the PREPARE guidelines for planning animal experiments, with a checklist in over 30 languages
- links to recordings of webinars covering all aspects of animal research
- an International Webinars & Meetings 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](http://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](http://wiki.norecopa.no)

**Norecopa gratefully acknowledges financial support from:**  
The Norwegian Parliament, the Ministry of Agriculture & Food and the Ministry of Trade, Industry & Fisheries; the Nordic Society against Painful Experiments (NSMSE), Nava Nordisk, the Norwegian Animal Protection Alliance (Dyreværnsalliansen), the Norwegian Society for Protection of Animals (Dyreskytelsen Norge), the Research Council of Norway, Laboratory Animals Ltd., the Royal Society for the Prevention of Cruelty to Animals (RSPCA), Sanofi, the Scottish Accreditation Board, the Stiansen Foundation, the Universities Federation of Animal Welfare (UFAW) and the US Department of Agriculture (USDA).

Toolbox graphic: colourbox.com

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- Laboratory Animals Ltd.
- Architect Finn Rahn's Legacy
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Animal Protection Alliance's Research Fund (Dyrevernalliansen)
- Norwegian Society for the Protection of Animals (Dyrebeskyttelsen Norge)
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- Stiansen Foundation
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