PREPARE and ARRIVE:

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

norecopa.no/260124

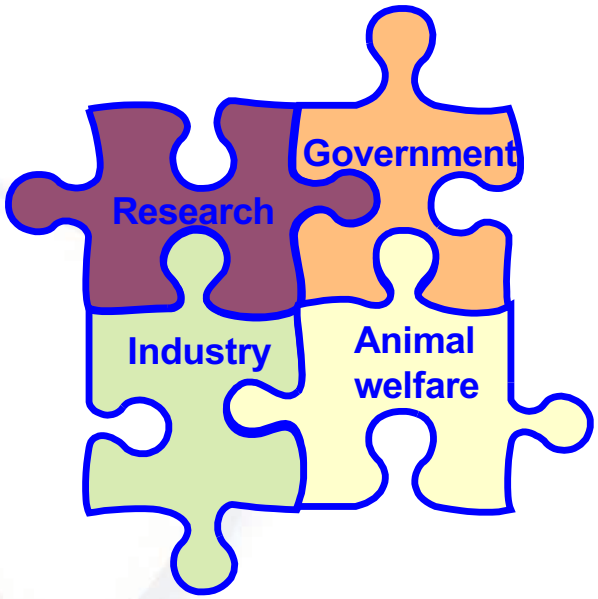
Adrian Smith
adrian.smith@norecopa.no

https://norecopa.no

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:

ecopa.eu

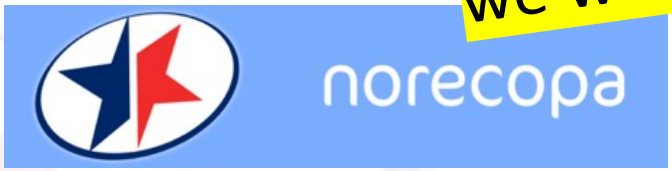


Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of *global* 3R resources

we welcome more from you!



https://norecopa.no

Established in 2007

Norecopa: PREPARE for better Science

40-slide powerpoint presentation about the 3Rs

ccac.ca

All three Rs of Russell and Burch:

Replacement, Reduction & Refinement

English, French and Spanish versions (soon German)

Free download from norecopa.no/3Rs

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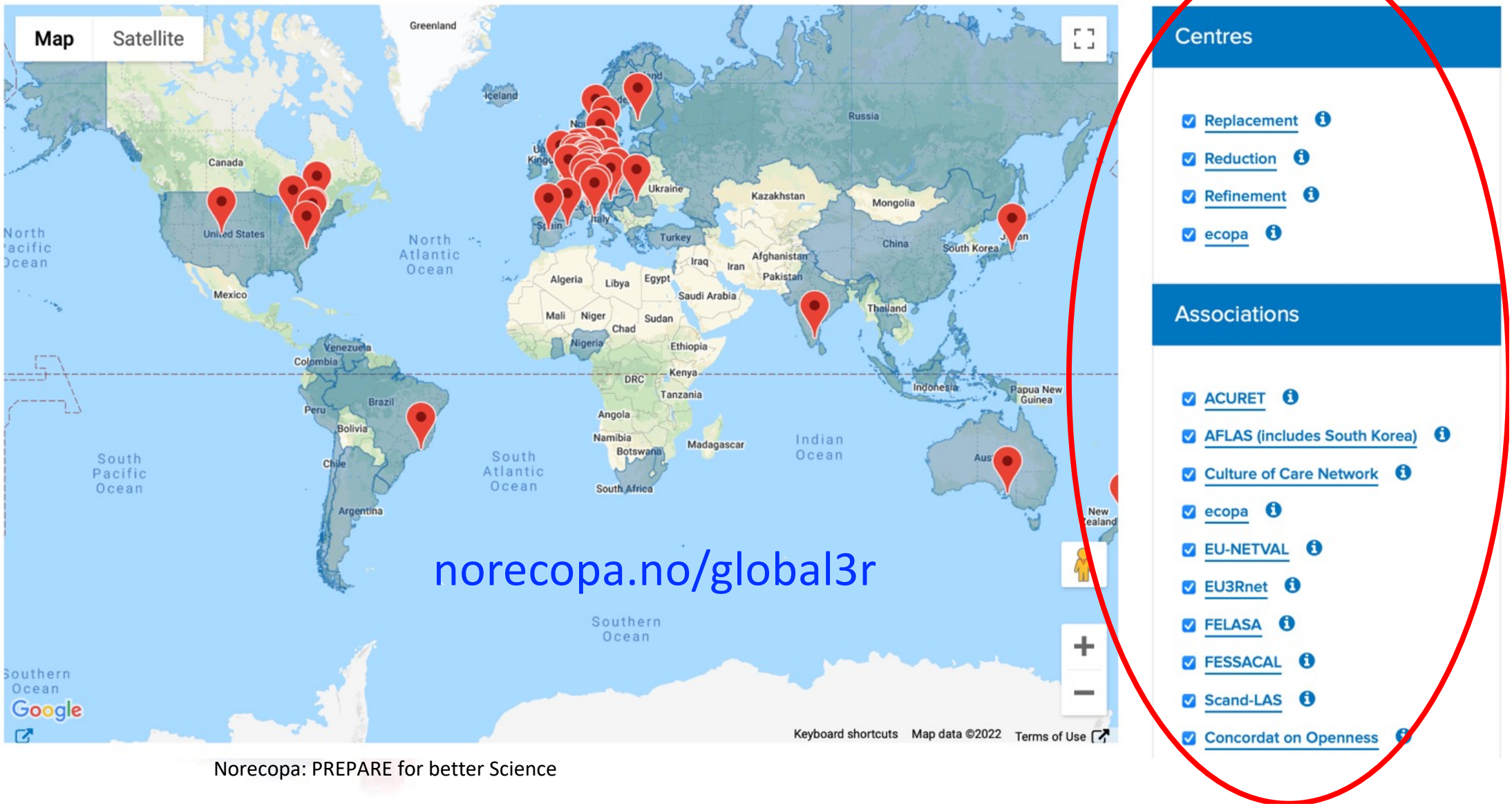


Centres

- Replacement
- Reduction
- Refinement
- ecopa

Associations

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

Norecopa: PREPARE for better Science

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

approx. 10,000 webpages

7-8 detailed newsletters per year

Norecopa: PREPARE for better Science

+ webpages for past meetings and recorded meetings

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 Heinl), 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
FRAME
WWW.FRAME.ORG.UK
University of Nottingham
UK | CHINA | MALAYSIA
TRAINING SCHOOL
IN EXPERIMENTAL DESIGN
Nottingham, UK
17-19 April 2024
FELASA Accredited
felasa
REGISTRATION OPEN SOON
SEE HERE TO SIGN UP FOR NOTIFICATIONS:


FOCUS ON FISH 2024
RSPCA
Practical refinements for fishes in research and testing
ONLINE 29 FEBRUARY 2024
FREE TO ATTEND

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

Databases & Guidelines

Published lists of resources are difficult to search and quickly become outdated. Lists on a website are easier to search, but do not enable the use of filters or intelligent search engines.
Norecopa has therefore constructed four databases, which together with all the text on this website can be searched simultaneously using the search field at the top of every page.

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

These databases are updated regularly. Please give us feedback if you discover errors or omissions.

The Norecopa website also includes four other collections:

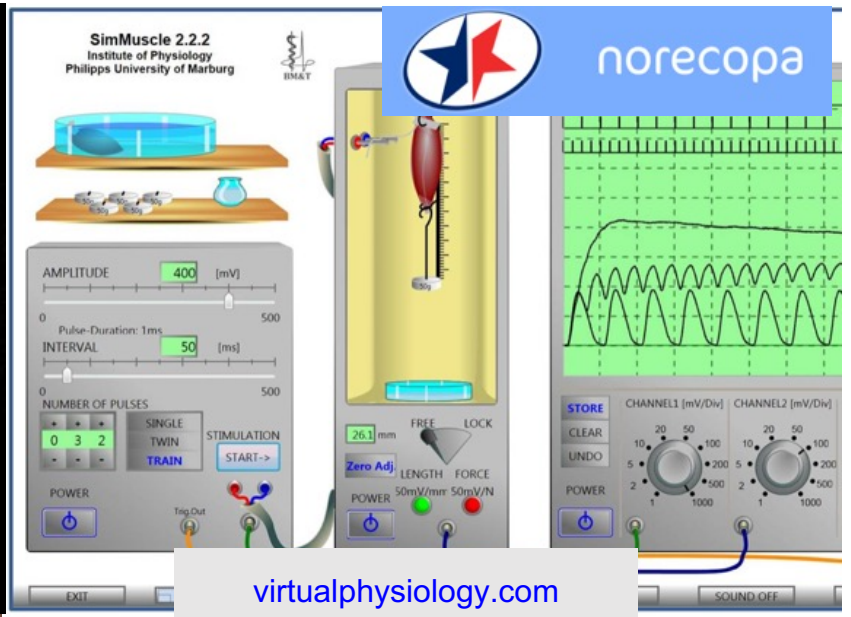
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal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

Here is an alphabetical global list of all the databases cited on the Norecopa website.

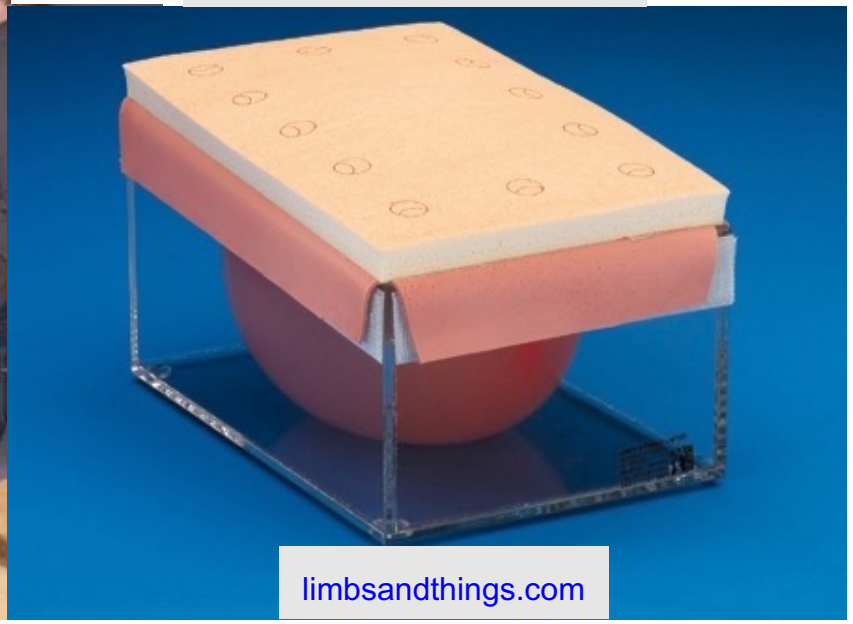
norecopa.no/databases-guidelines

links to over 70 other databases


norecopa.no/NORINA
3dglasshorse.com


SimMuscle 2.2.2
Institute of Physiology
Philipps University of Marburg
norecopa
AMPLITUDE
400
[mV]
Pulse-Duration: 1ms
INTERVAL
50
[ms]
NUMBER OF PULSES
SINGLE
TWIN
TRAIN
STIMULATION
START->
POWER
Zero Adj
LENGTH
FORCE
STORE
CLEAR
UNDO
CHANNEL1 [mV/Div]
CHANNEL2 [mV/Div]
EXIT
SOUND OFF
virtualphysiology.com


rescuecritters.com


limbsandthings.com

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

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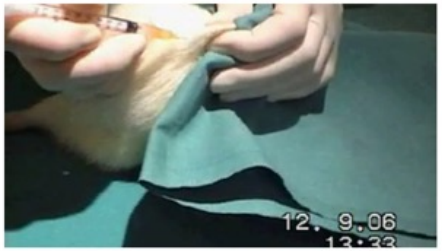
Rat s.c. injection
Norecopa | 1,380 views

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

Anatomia de la rata
Norecopa | 977 views

Testing anaesthetic depth in the chicken
Norecopa | 598 views

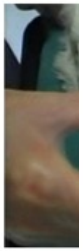
Blood collection from the saphenous vein in the mouse
Norecopa | 6,777 views



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

Blood san
Norecop

Blood san
Norecop



Blood san
Norecop

Blood sampling from the pig
Norecopa | 3,914 views

Intravenous injection in a rabbit
Norecopa | 2,025 views

Lifting a rabbit
Norecopa | 2,420 views

Subcutaneous injection in the rabbit
Norecopa | 1,479 views

Subcutaneous injection in the chicken
Norecopa | 1,806 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

Working Party Report

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

P Hawkins (Convenor)[1], N Dennison[2], G Goodman[3], S Hetherington[4], S Llywelyn-Jones[5], K Ryder[2] and A J Smith[6]

Abstract

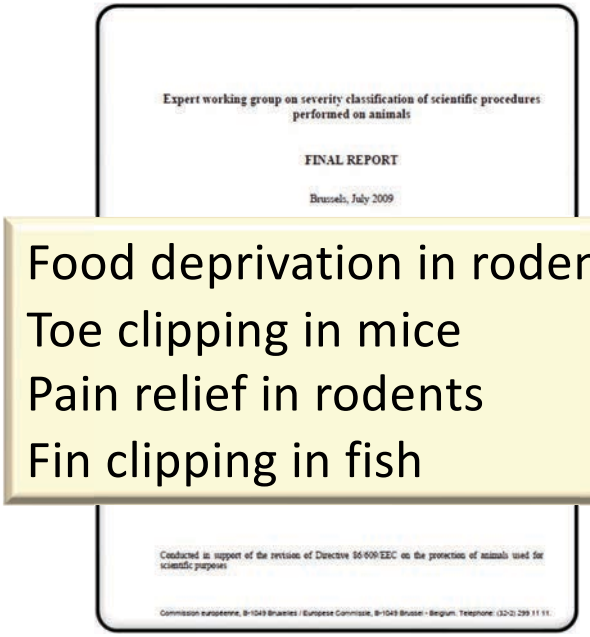
Keywords: Fish, harm–benefit assessment, humane endpoints, refinement, severity

Laboratory Animals 2011; 1–6. DOI: 10.1258/la.2011.010181

Background

Guidance on the severity classification of procedures involving fish

Report from a Working Group convened by Norecopa



Expert working group on severity classification of scientific procedures performed on animals

FINAL REPORT

Brussels, July 2009

Conducted in support of the revision of Directive 86/609/EEC on the protection of animals used for scientific purposes

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.

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

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

Laboratory Animals, 45: 219-224, 2011

norecopa.no/categories

TextBase:

1,500 books related to LAS:

norecopa.no/textbase

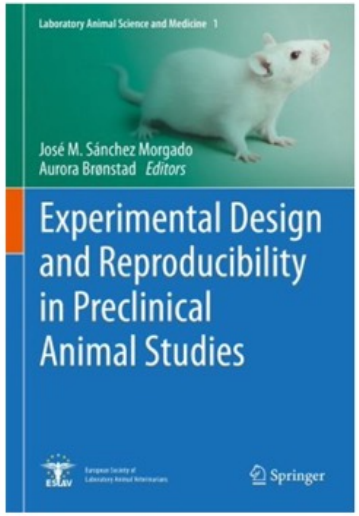
Experimental Design and Reproducibility in Preclinical Animal Studies

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

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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

nature human behaviour

Perspective | Open Access | Published: 10 January 2017

A manifesto for reproducible science

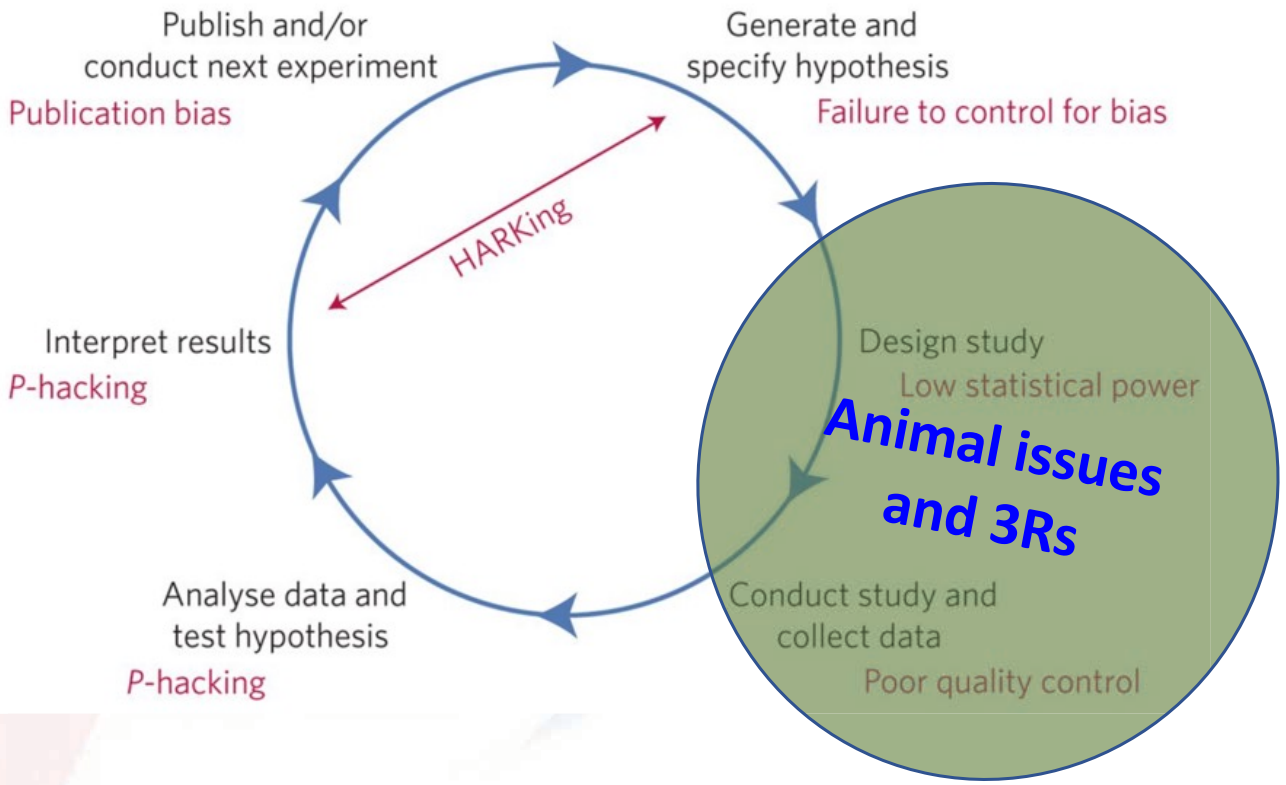
Marcus R. Munafò, Brian A. No
Button, Christopher D. Chambers,
Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



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

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The road to better research

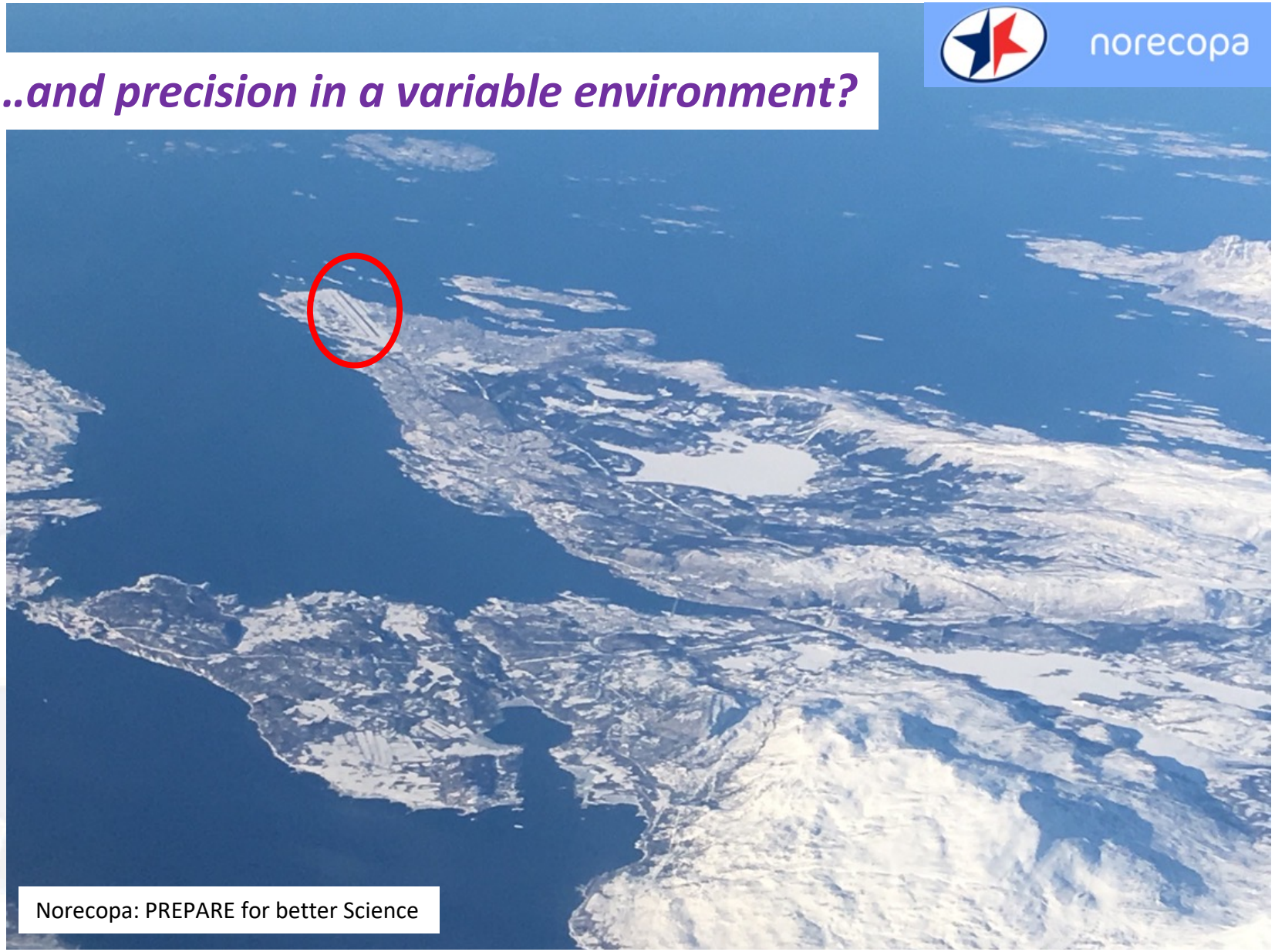
Norecopa: PREPARE for better Science

ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1

How do others achieve reproducibility?

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

…and precision in a variable environment?



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10-15 checklists even on short routine flights

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

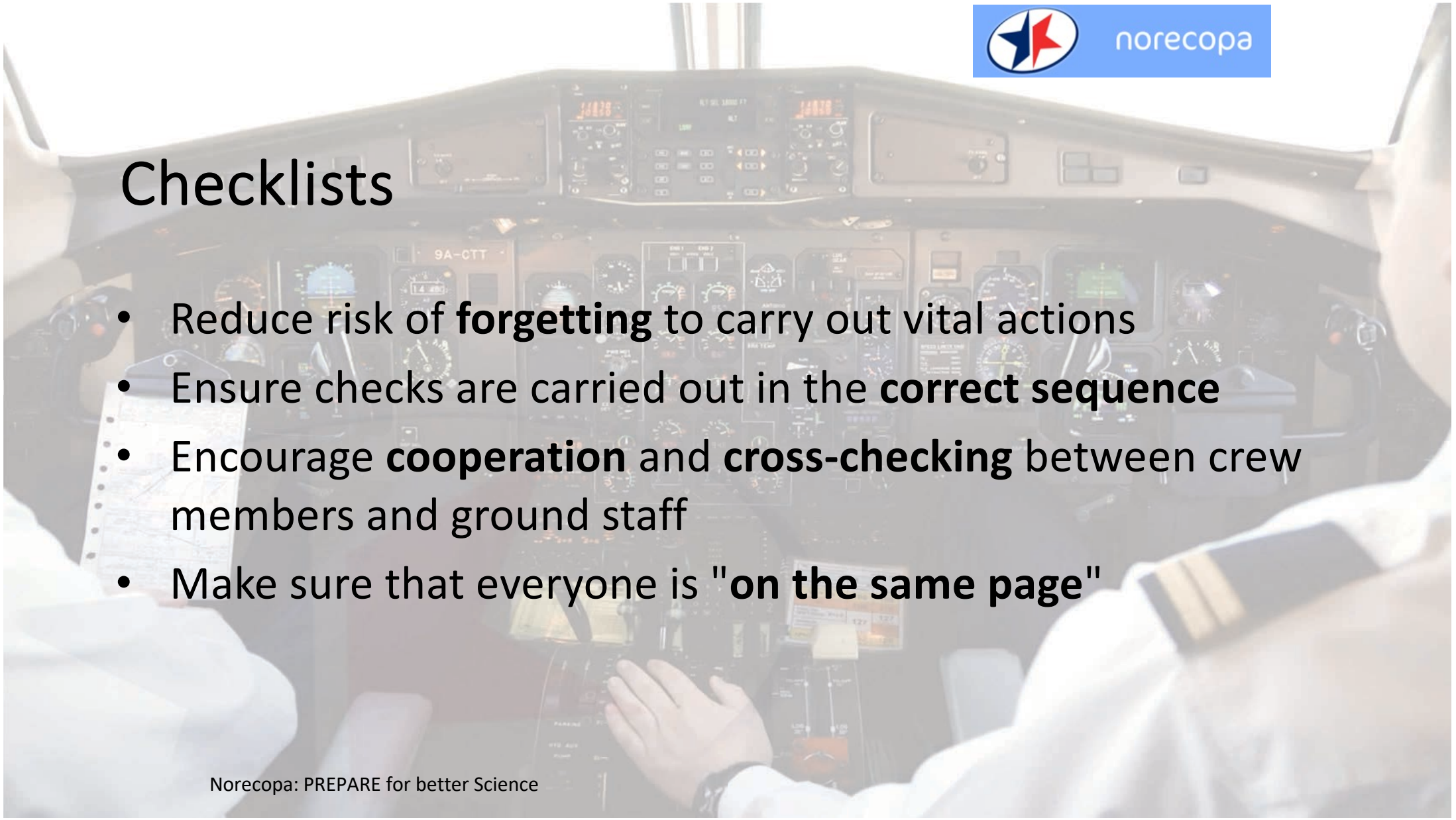
15.25.33	-01.38	Kaptein	Cockpit	V one, rotate
15.25.38	-01.33	Kaptein	Cockpit	positive rate
15.25.39	-01.32	Styrmann	Cockpit	Gear up please
15.25.39	-01.32	Kaptein	Cockpit	Gear up
15.26.37	-00.34	Kaptein	Cockpit	Uh what a view of the Hudson today
15.26.42	-00.29	Styrmann	Cockpit	Yeah
15.27.07	-00.04	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.

no.wikipedia.org/wiki/US_Airways_Flight_1549

en.wikipedia.org

Hudson River, 2009

All 155 passengers and crew saved

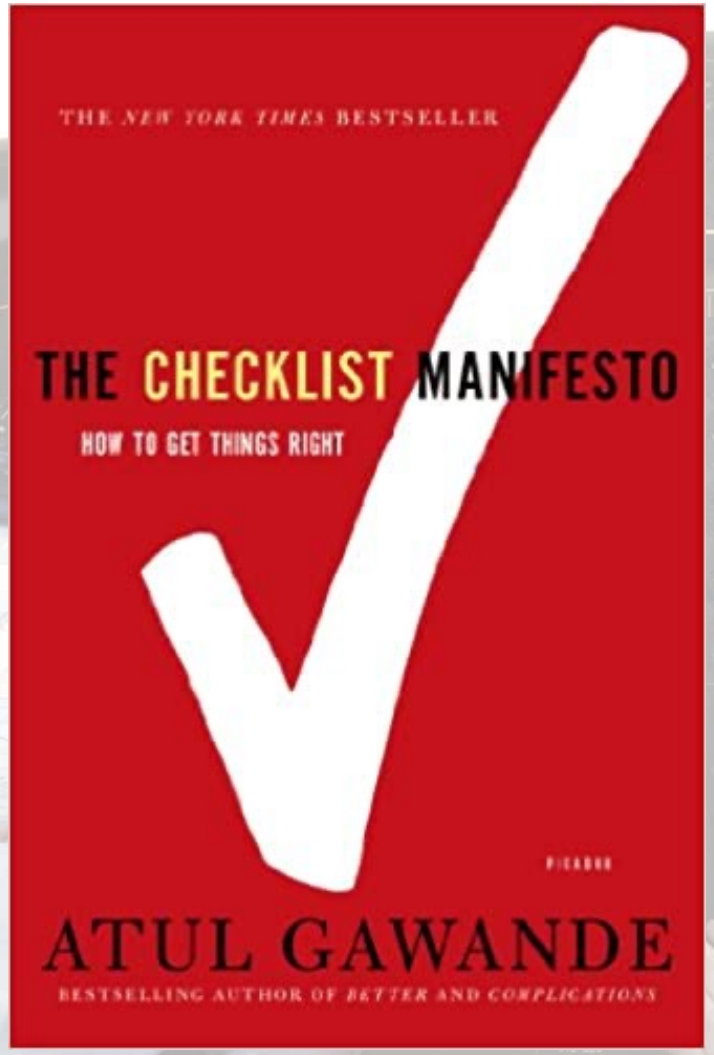


Checklists

- 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

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

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	☐ **Confirm all team members have introduced themselves by name and role.**	**Nurse Verbally Confirms:** ☐ The name of the procedure
Is the site marked? ☐ Yes ☐ Not applicable	☐ **Confirm the patient's name, procedure, and where the incision will be made.**	☐ Completion of instrument, sponge and needle counts
Is the anaesthesia machine and medication check complete? ☐ Yes	**Has antibiotic prophylaxis been given within the last 60 minutes?** ☐ Yes ☐ Not applicable	☐ Specimen labelling (read specimen labels aloud, including patient name)
Is the pulse oximeter on the patient and functioning? ☐ Yes	**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?	☐ Whether there are any equipment problems to be addressed
Does the patient have a: **Known allergy?** ☐ No ☐ Yes	**To Anaesthetist:** ☐ Are there any patient-specific concerns?	**To Surgeon, Anaesthetist and Nurse:** ☐ What are the key concerns for recovery and management of this patient?
Difficult airway or aspiration risk? ☐ No ☐ Yes, and equipment/assistance available	**To Nursing Team:** ☐ Has sterility (including indicator results) been confirmed? ☐ Are there equipment issues or any concerns?	
Risk of >500ml blood loss (7ml/kg in children)? ☐ No ☐ Yes, and two IVs/central access and fluids planned	**Is essential imaging displayed?** ☐ Yes ☐ Not applicable	

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

Revised 1 / 2009

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

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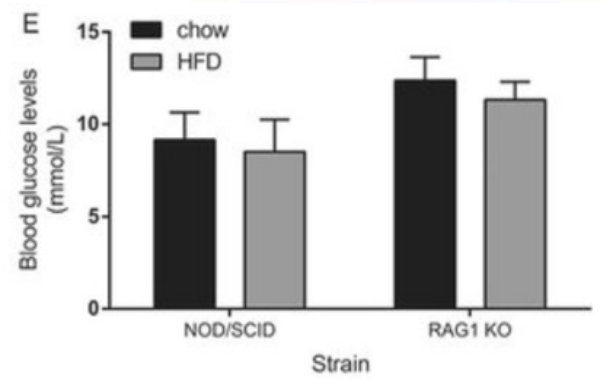
amazon.com/gp/product/0312430000

The scientist



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…

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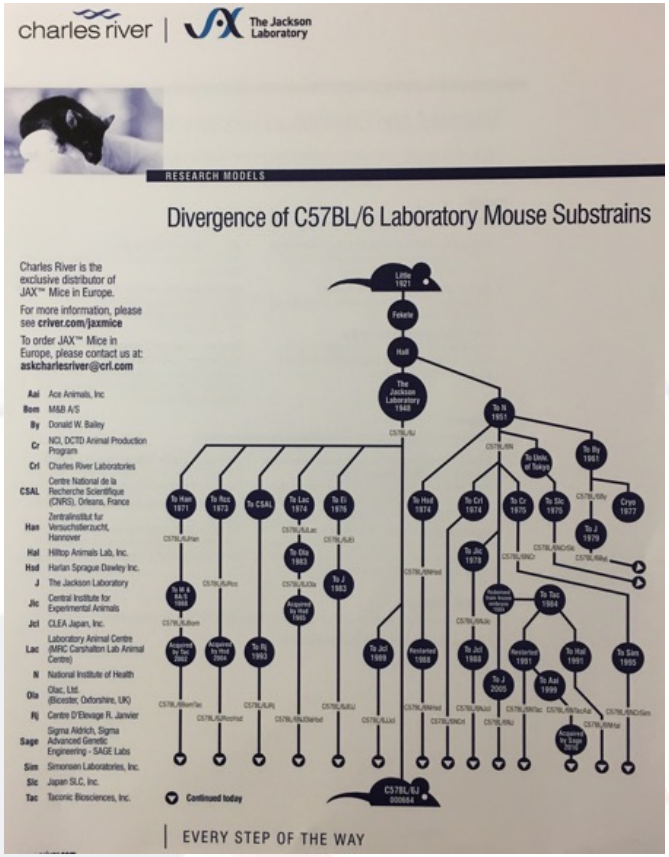
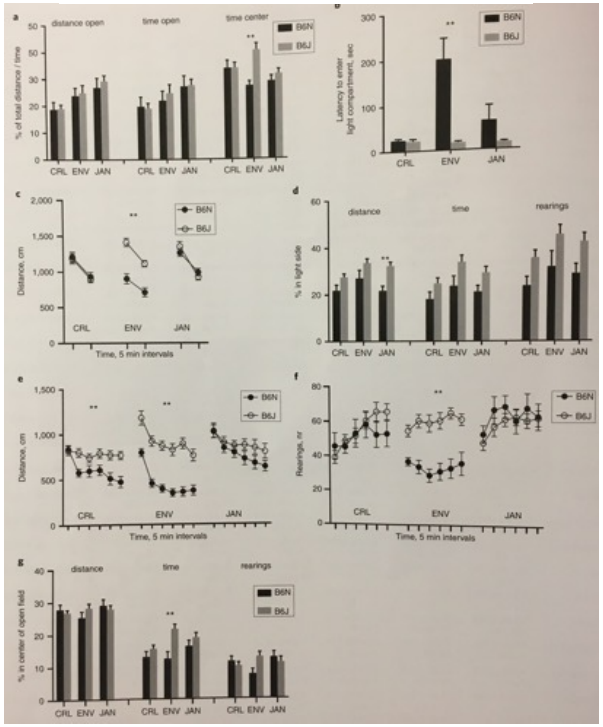
The C57BL/6 mouse



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

nature.com/articles/s41684-019-0288-8



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we are what we eat...

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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

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.

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

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

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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

photo: colourbox.com

Stress caused by capture and handling

INDEPENDENT

News › Science

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

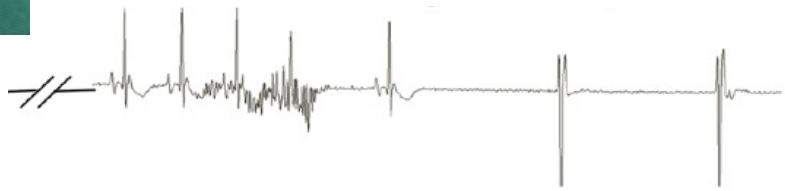
Mice picl
naturally

't act

Ian Johnstor

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

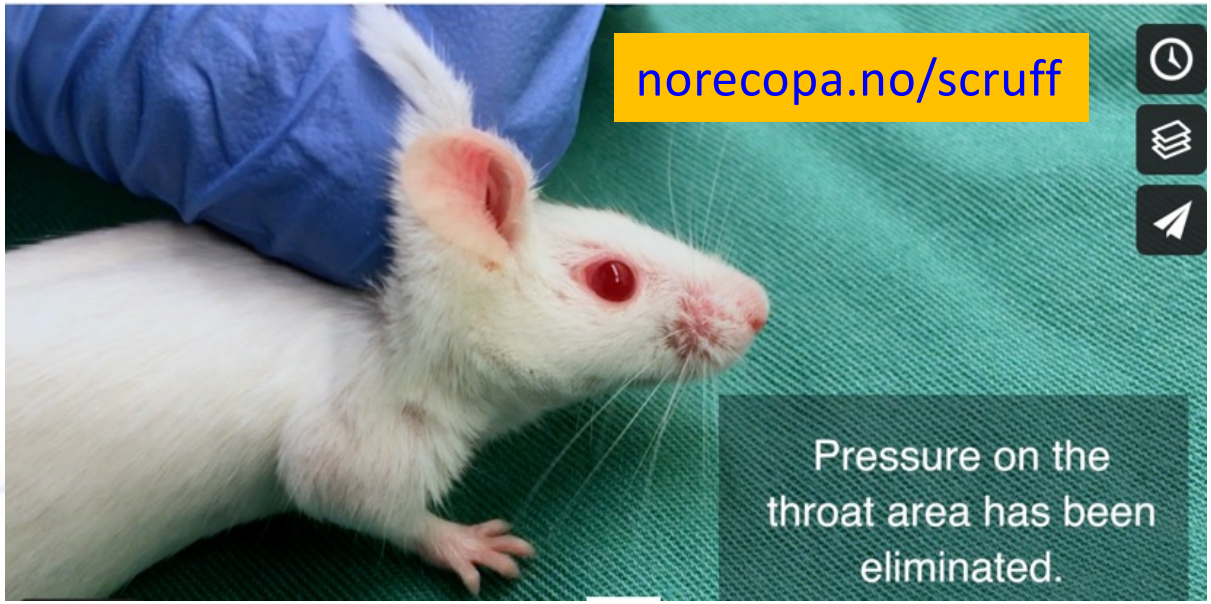
Sinus bradycardia
ventricular escape complexes

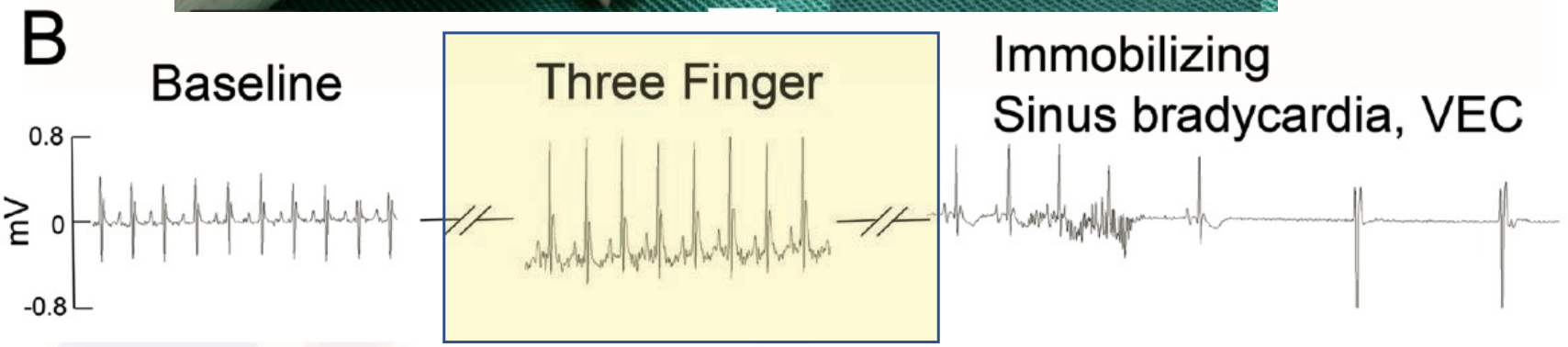


Labitt *et al.*, 26 February 2021

Both sexes and 4 strains of mice, 3 experienced handlers

Labitt RN, Oxford EM, Davis AK, Butler SD & Daugherity 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


norecopa.no/scruff
Pressure on the throat area has been eliminated.


B
Baseline
Three Finger
Immobilizing
Sinus bradycardia, VEC
0.8
mV
0
-0.8

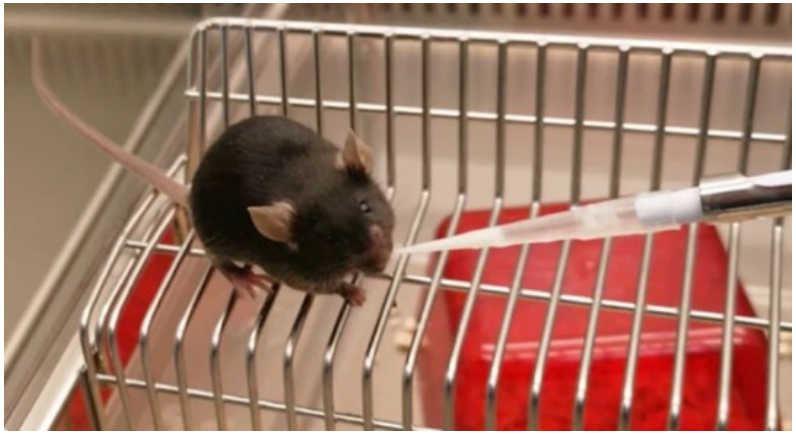
Artefacts caused by poor administration techniques

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.epdf

youtube.com/watch?v=bdtVZtrr69c

Disposable needles are designed to be used only once!

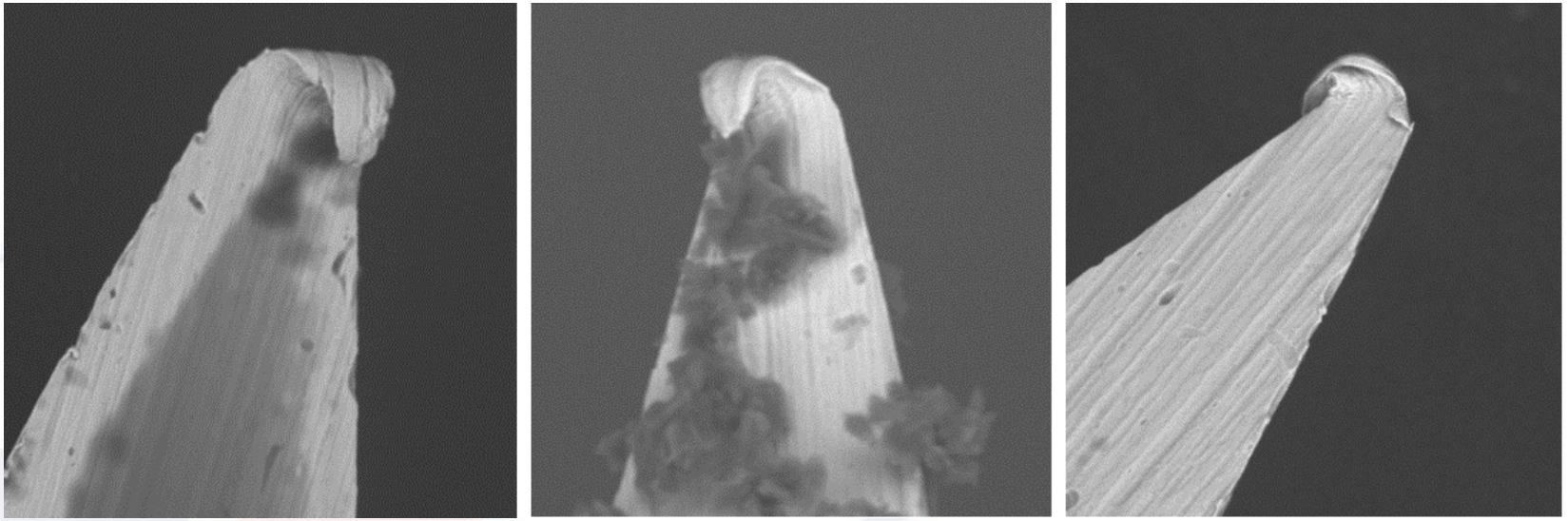


Photo: AstraZeneca

nc3rs.org.uk/news/re-use-needles-indicator-culture-care

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

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

medipoint.com/html/for_use_on_mice.html

theodora.com/rodent_laboratory/blood_collection.html

vimeo.com/486368886

photo:NMBU

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…

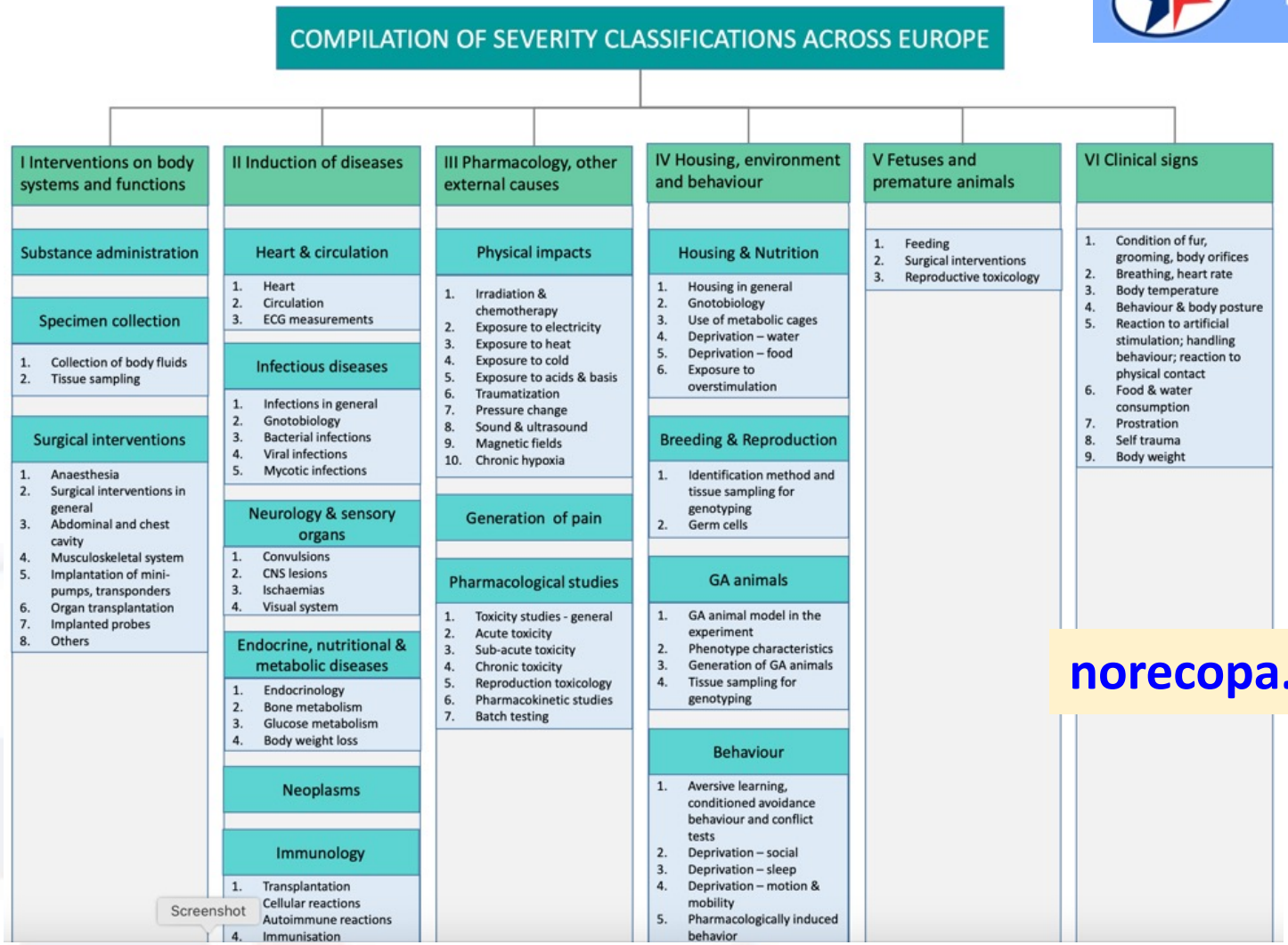
Carol M. Newton (1925-2014)

National Library of Medicine

The three S's

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

https://norecopa.no/3S

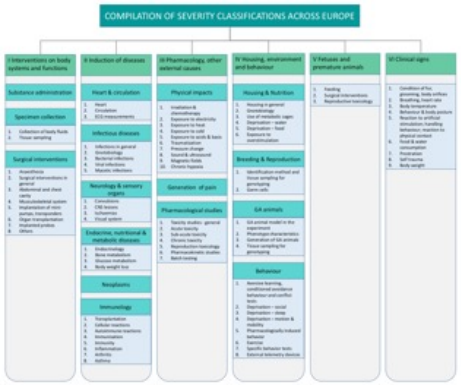


norecopa

norecopa.no/severity

Norecopa: PREPARE for better Science

Mild, Moderate or Severe? A compilation of severity classification



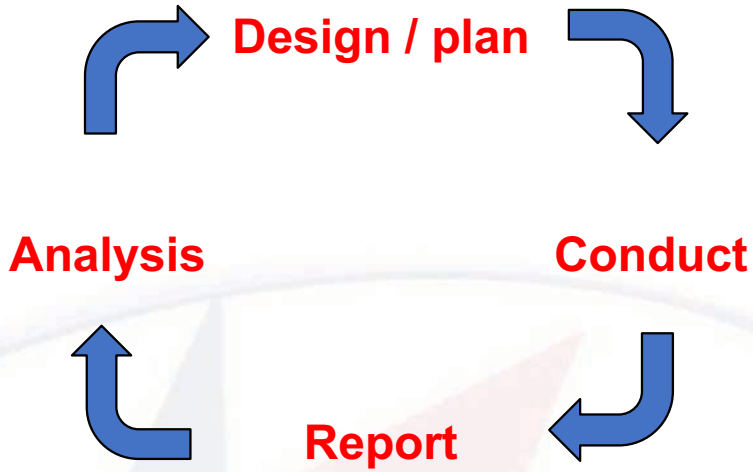
norecopa.no/severity

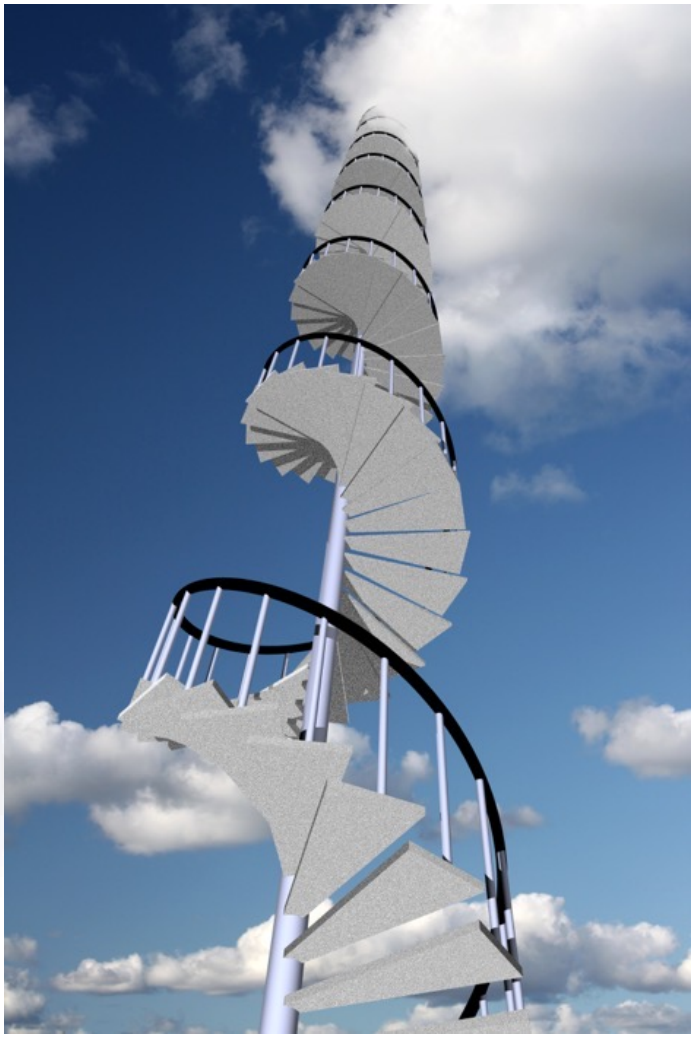
The compilation covers

- 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

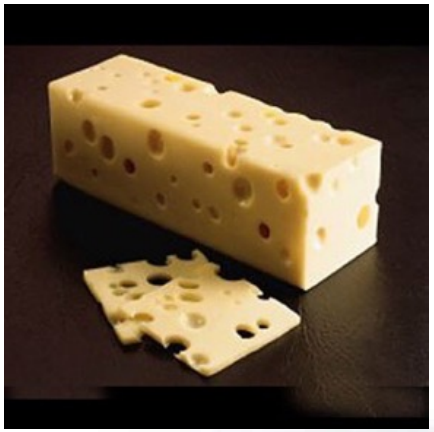
Source	Non-harmful / below threshold / severity degree 0	Mild / severity degree 1	Moderate / severity degree 2	Severe / severity degree 3
Directive 2010/63/EU, Annex VIII		Administration of substances by subcutaneous, intramuscular, intraperitoneal routes, gavage and intravenously via superficial blood 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.	
Home Office (2014 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.		
Federal Food Safety and Veterinary Office FSVO (2018)	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

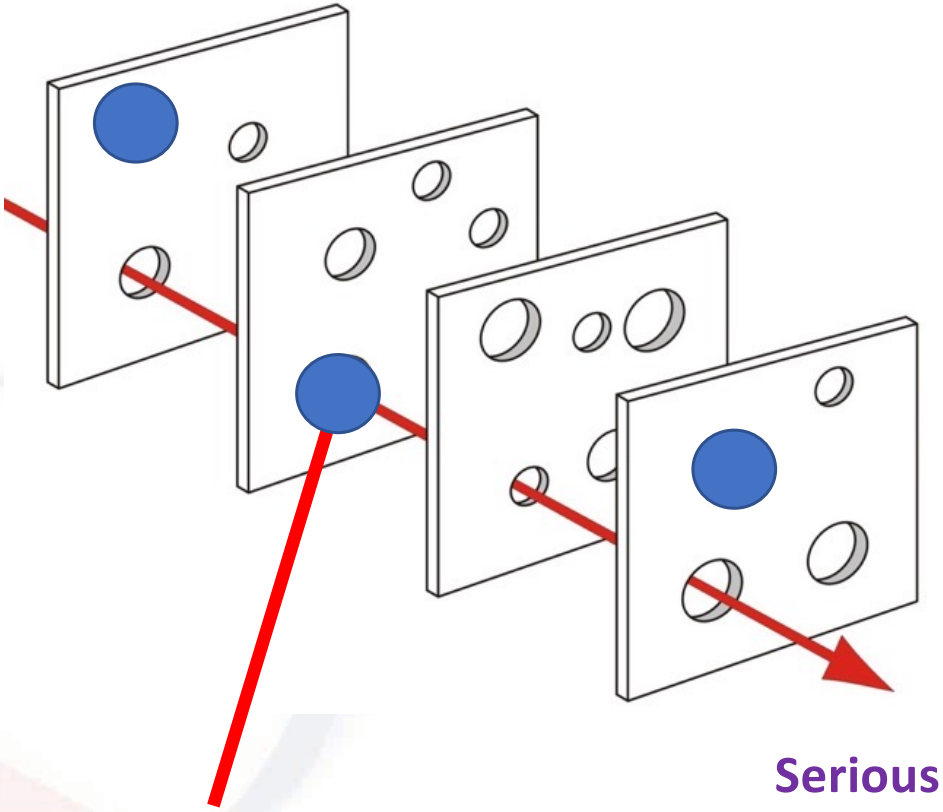




“Threat and Error Management”



eaugallecheese.com/Swiss-Cheese

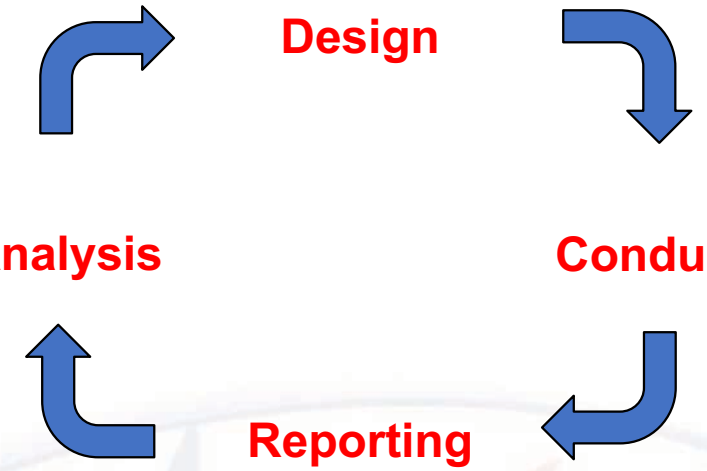


wikipedia.org/wiki/Swiss_cheese_model

Contingency and redundancy

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

Photo: NMBU



Identify and ensure the quality of (at least) the critical points in the experiment:

for scientific output and animal welfare

Space Shuttle, NASA

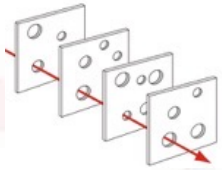
NASA

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 be appear insignificant
- until they occur simultaneously

We need a Culture of Care!



Culture of Care

The International Culture of Care Network

norecopa.no/coc

A demonstrable commitment, throughout the establishment, to improving:

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

It goes beyond simply complying with the law!

"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

CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

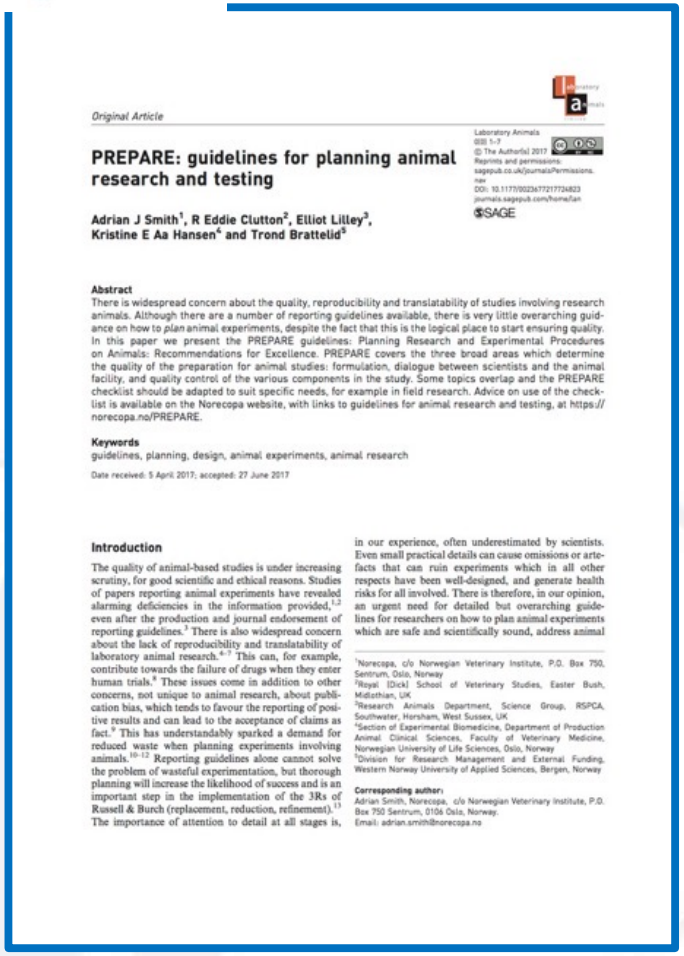
Refine - Reduce - Replace

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[1], R Eddie Clutton[2], Elliot Lilley[3], Kristine E Aa Hansen[4] and Trond Brattelid[5]

Laboratory Animals
0(0) 1–7

DOI: 10.1177/0023677217724823
journals.sagepub.com/home/lan
SAGE

Abstract

There is widespread concern about the quality, reproducibility and translatability of studies involving research animals. Although there are a number of reporting guidelines available, there is very little overarching guidance on how to plan animal experiments, despite the fact that this is the logical place to start ensuring quality. In this paper we present the PREPARE guidelines: Planning Research and Experimental Procedures on Animals: Recommendations for Excellence. PREPARE covers the three broad areas which determine the quality of the preparation for animal studies: formulation, dialogue between scientists and the animal facility, and quality control of the various components in the study. Some topics overlap and the PREPARE checklist should be adapted to suit specific needs, for example in field research. Advice on use of the checklist is available on the Norecopa website, with links to guidelines for animal research and testing, at https://norecopa.no/PREPARE.

Keywords

guidelines, planning, design, animal experiments, animal research

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

Introduction

The quality of animal-based studies is under increasing scrutiny, for good scientific and ethical reasons. Studies of papers reporting animal experiments have revealed alarming deficiencies in the information provided,[1,2] even after the production and journal endorsement of reporting guidelines.[3] There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research.[4–7] This can, for example, contribute towards the failure of drugs when they enter human trials.[8] These issues come in addition to other concerns, not unique to animal research, about publication bias, which tends to favour the reporting of positive results and can lead to the acceptance of claims as fact.[9] This has understandably sparked a demand for reduced waste when planning experiments involving animals.[10–12] Reporting guidelines alone cannot solve the problem of wasteful experimentation, but thorough planning will increase the likelihood of success and is an important step in the implementation of the 3Rs of Russell & Burch (replacement, reduction, refinement).[13] The importance of attention to detail at all stages is, in our experience, often underestimated by scientists. Even small practical details can cause omissions or artefacts that can ruin experiments which in all other respects have been well-designed, and generate health risks for all involved. There is therefore, in our opinion, an urgent need for detailed but overarching guidelines for researchers on how to plan animal experiments which are safe and scientifically sound, address animal

[1]Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750, Sentrum, Oslo, Norway
[2]Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, UK
[3]Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK
[4]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway
[5]Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

Corresponding author:
Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway.
Email: adrian.smith@norecopa.no

Norecopa: PREPARE for better Science

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Over 33,000 downloads from the journal website so far

PREPARE:

Planning **R**esearch and **E**xperimental **P**rocedures on **A**nimals: **R**ecommendations for **E**xcellence

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

norecopa.no/PREPARE/prepare-checklist

PREPARE

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The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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

PREPARE[1] består av retningslinjer for planlegging av dyreforsøk. Disse
som f.eks. ARRIVE[2]. 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 pr
PREPARE-sjekklisten kan endres for å ivareta spesielle behov, f.eks. ve
dyreavdelinger, fordi laboratorieforsøk er helt avhengige av deres kvalif
Norecopas nettsider, med lenker til globale ressurser, på **https://norec**
PREPARE-retningslinjene er et dynamisk sett som vil videreutvikles ette
produseres, og etterhvert som "best praksis" innenfor forsøksdyrmiljøet forbedres.

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

+ 2 online versions
35 languages

Tema	Anbefaling
(B) Dialogen mellom forskerne og dyreavdelingen	
5. Mål og tidshorisont, finansiering og arbeidsfordeling	☐ Arrangere møter med alle relevante personell når tidlige planer for prosjektet foreligger. ☐ Lag en omtrentlig tidsramme for prosjektet, som viser behovene for assistanse med forberedelser, dyrestell, prosedyrer og avfallshåndtering/dekontaminasjon. ☐ Diskutere og legge frem alle forventede og potensielle kostnader. ☐ Lage en detaljert plan for fordelingen av både arbeidsoppgavene og utgiftene, på alle stadiene i forsøket.
	fasilitetene, for å evaluere bygningsmassen, standarden på utstyret og
	ved perioder med ekstra risiko.
	tansen hos personalet og evaluere behovet for videreutdanning og
	en, foreta en risikoevaluering som omfatter alle personene og dyrene direkte, av studiet. dusere, spesifikke retningslinjer for alle stadiene av prosjektet. , dekontaminere og avhende alt utstyret som skal brukes i studiet.
(C) Kvalitetskontroll av de ulike komponentene i studiet	
9. Testsubstanser og -prosedyrer	☐ Oppgi så mye informasjon som mulig om testsubstansene. ☐ Evaluere gjennomførbarheten og validiteten av testprosedyrene, og de praktiske ferdighetene som er nødvendige for å gjennomføre dem.
10. Forsøksdyr	☐ Bestemme egenskapene til dyrene som er essensielle for studiet og som må rapporteres. ☐ Unngå produksjon av overskuddsdyr.
11. Karantene og helsemonitorering	☐ Diskutere dyrenes sannsynlige helsestatus, og eventuelle behov for transport, karantene og isolasjon, samt helsemonitorering og konsekvensene for personalet.
12. Oppstalling og stell	☐ Ta hensyn til dyrenes spesifikke instinkter og behov, i samråd med eksperter. ☐ Diskutere akklimatisering, optimale oppstallingsforhold og prosedyrer, miljøfaktorer og eventuelle begrensninger på disse (f.eks. fasting eller oppstalling i enebur).
13. Eksperimentelle prosedyrer	☐ Utvikle optimale metoder for fangst, immobilisering, merking og frisetting eller omplassering. ☐ Utvikle optimale metoder for å gi dyrene behandling, samt for prøvetaking, sedasjon og anestesi, kirurgi og andre inngrep.
14. Human avliving, frisettelse eller omplassering	☐ Konsultere relevant lovgivning og retningslinjer i god tid før studiet. ☐ Definere de primære metodene for avliving, samt metoder som kan brukes i en nødssituasjon. ☐ Evaluere kompetansen til personene som må foreta disse handlingene.
15. Obduksjon	☐ 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 & Brattelid T. PREPARE:Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
2. Kilkenny C, Browne WJ, Cuthill IC *et al.* Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PloS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

Mer informasjon
https://norecopa.no/PREPARE / *post@norecopa.no* / @norecopa

Norecopa: PREPARE for better Science

PREPARE

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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

PREPARE[1] consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE[2].
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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Nore

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.

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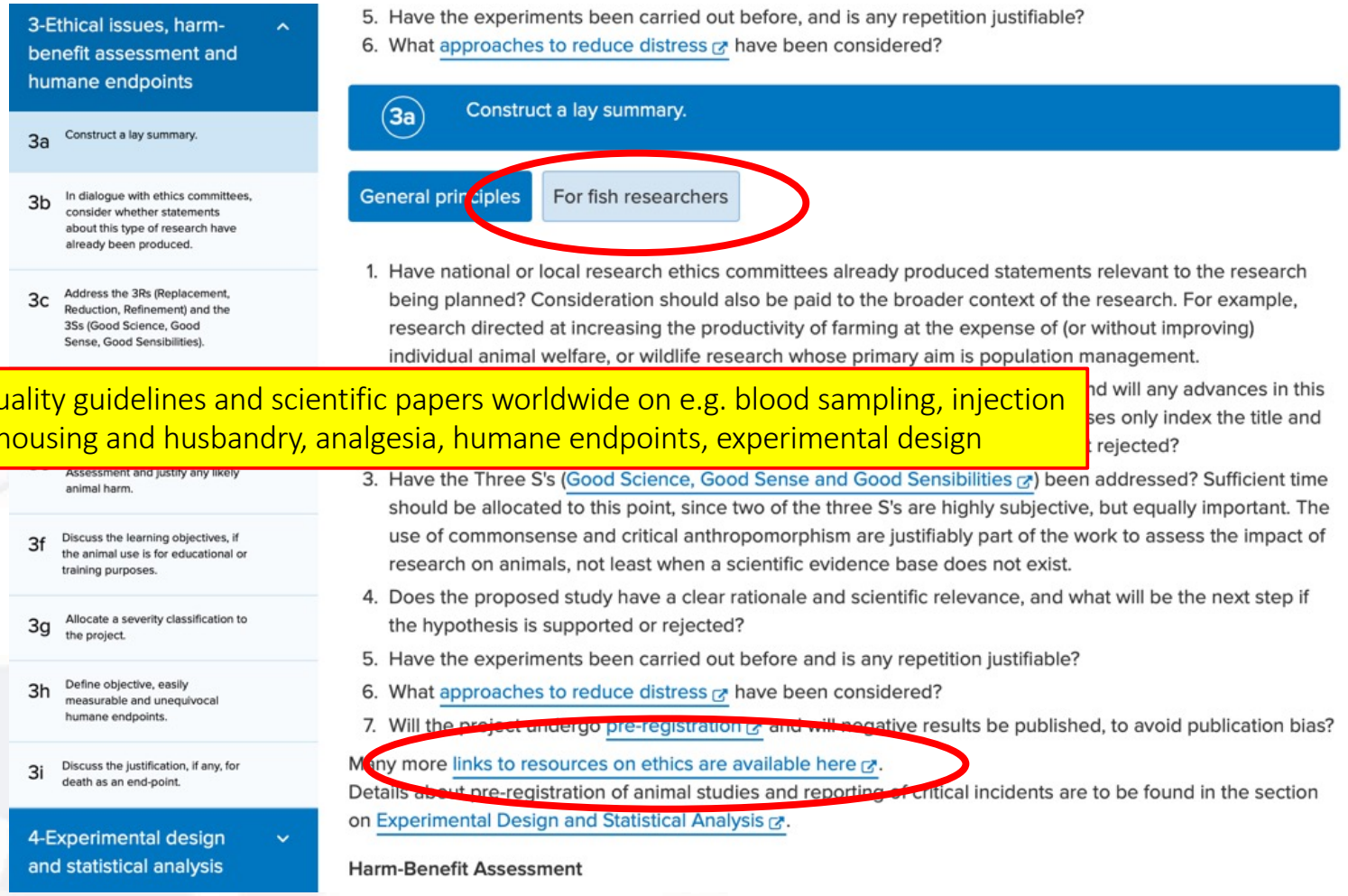
Topic	Recommendation
	(A) Formulation of the study
1. Literature searches	☐ Form a clear hypothesis, with primary and secondary outcomes. ☐ Consider the use of systematic reviews. ☑ Decide upon databases and information specialists to be consulted, and construct search terms. ☐ Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs. ☐ Assess the reproducibility and translatability of the project.
2. Legal issues	☐ Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety.

Nore

norecopa.no/PREPARE



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

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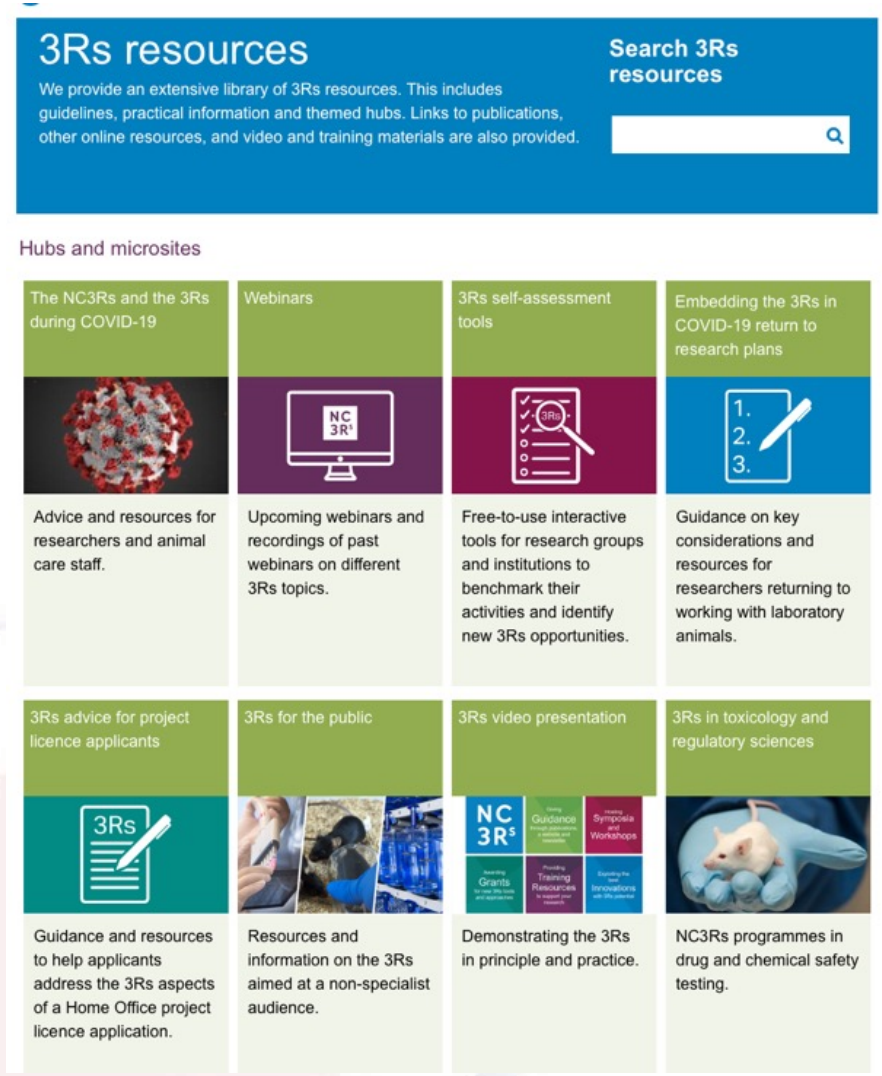
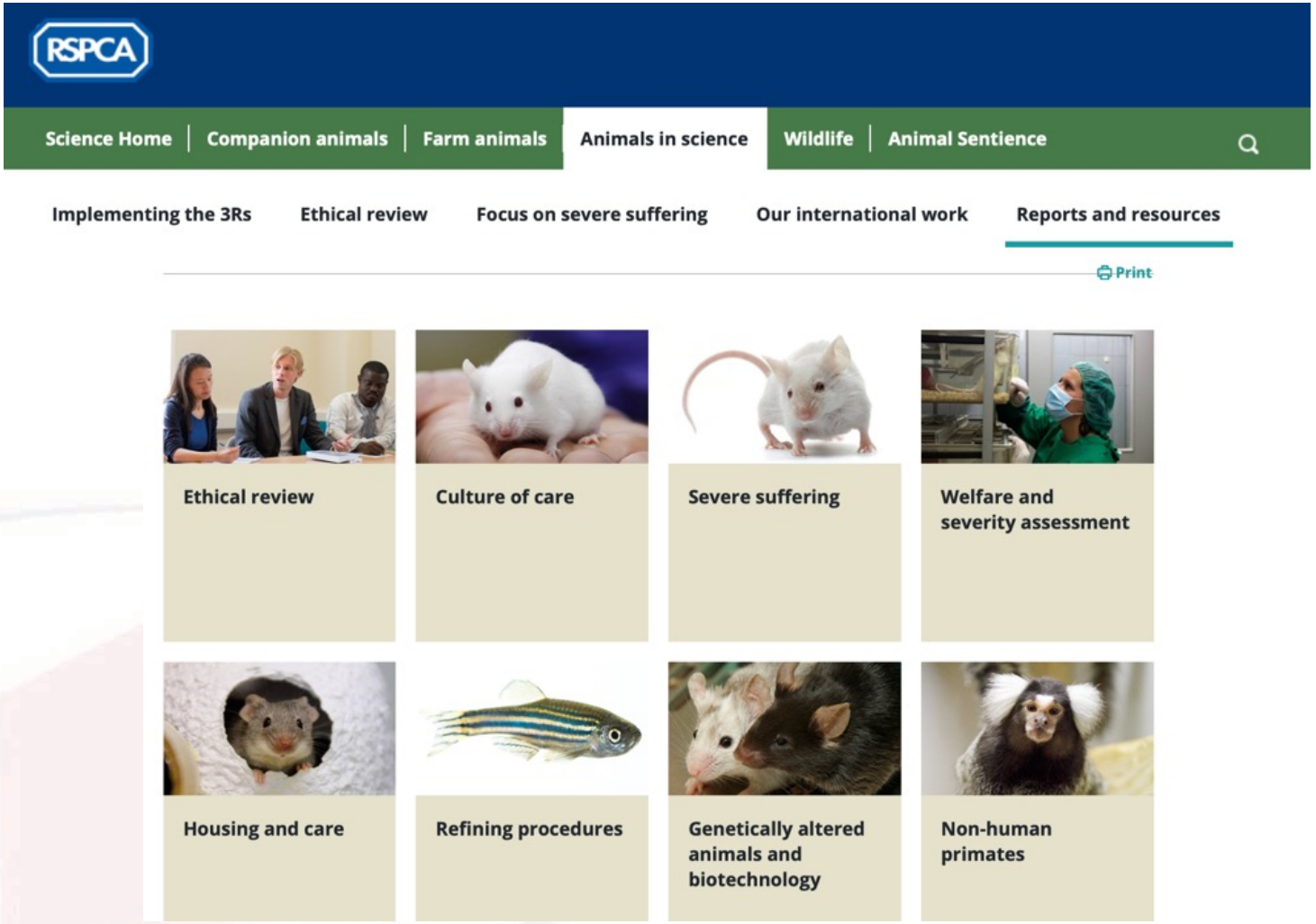
Resource hubs



nc3rs.org.uk/3rs-resources

Resource hubs



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

Program Description

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

63 pages

A simple but effective Master Plan

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A contract between the animal facility and the research group

Division of labour, responsibilities and cost

Clarifying all stages of the experiment

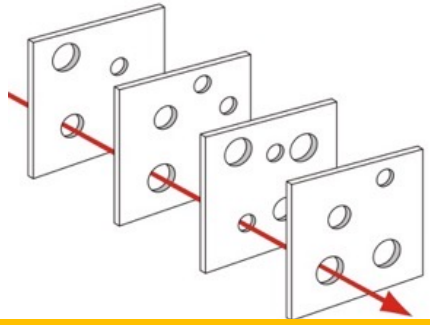
Ensuring that all necessary data are recorded

	Animal facility	Researcher	Not applicable
Animal:			
Arrival date			
Species			
Strain/stock and substrain			
Supplier (full name and address) or bred on the premises			
Number and sex			
Age, weight, stage of life cycle on arrival			
Pre-treatment (surgical or medical) from supplier			
Quality (e.g. SPF, germ-free, gnotobiotic, conventional)			
Acclimation time before the start of the experiment			
Time and duration of fasting (with/without water and bedding)			
Environment:			
Type of housing: barrier/conventional			
Temperature (mean ± variation)			
Light schedule			
Relative humidity (mean ± variation)			
Number of air changes in the animal room/cabinet per hour			
Environmental enrichment			
Housing:			
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			

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

These need to be revised or supplemented in the light of Covid-19
norecopa.no/be-prepared



Temporary staff at weekends and holidays

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

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

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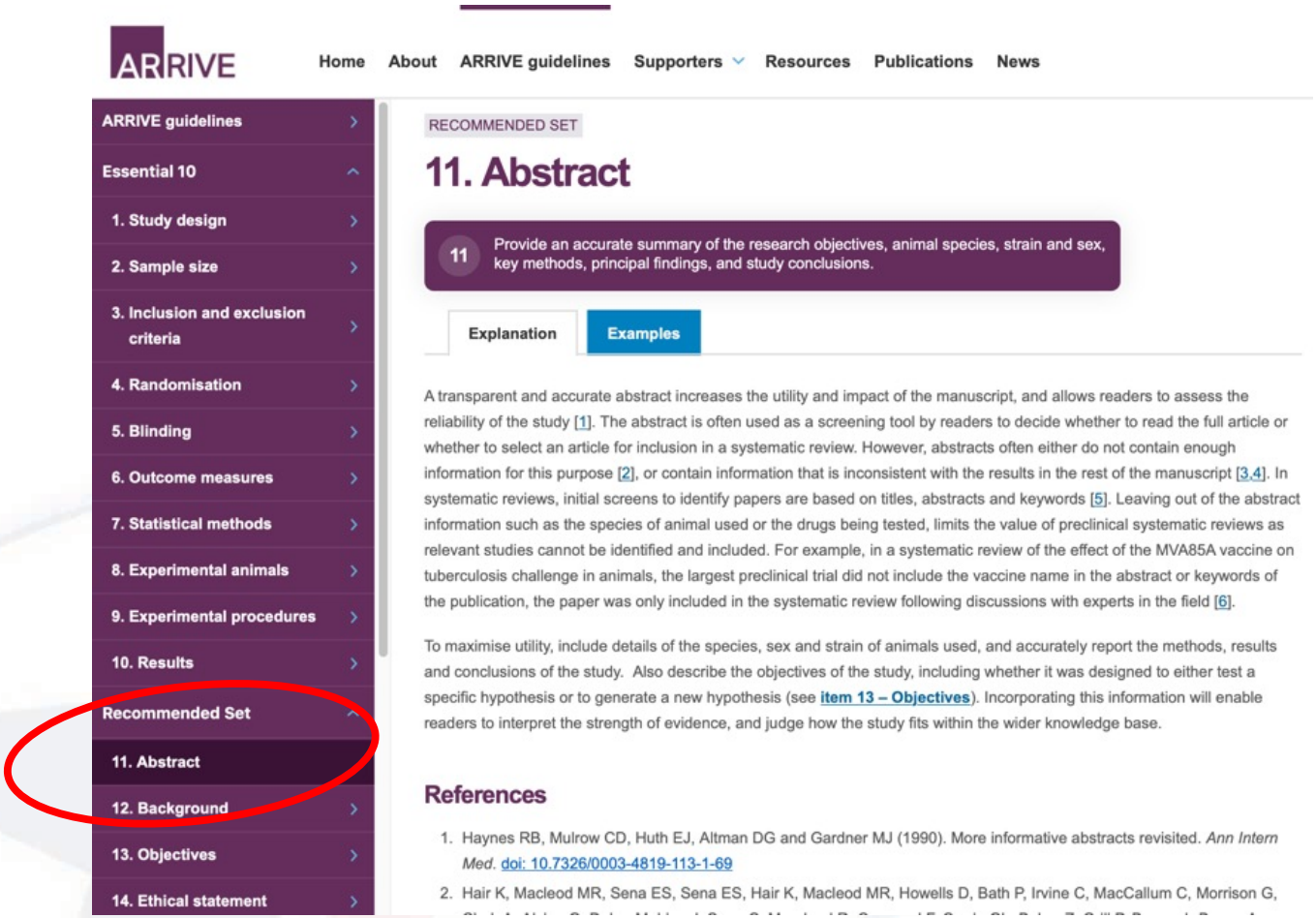
ARRIVE 2.0

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	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.
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	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study and the frequency of monitoring.
Interpretation /scientific implications	17	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.
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	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.

arriveguidelines.org



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, SP
   - Re-use of animals, which should be justified legislation
   - Any plans for release or re-homing, which m

More resources

- Examples and references from the NC3Rs
- Information on inbred strains of mice and rats
- Strategies to minimise genetic drift and maximise experimental reproducibility in mouse research
- Mouse Locator, UK
- The Collaborative Cross panel of inbred mouse strains
- Nude mice - more than what meets the eye
- The Rat Guide
- Rat Behavior and Biology

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"We ARRIVED, because we were PREPARED"

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

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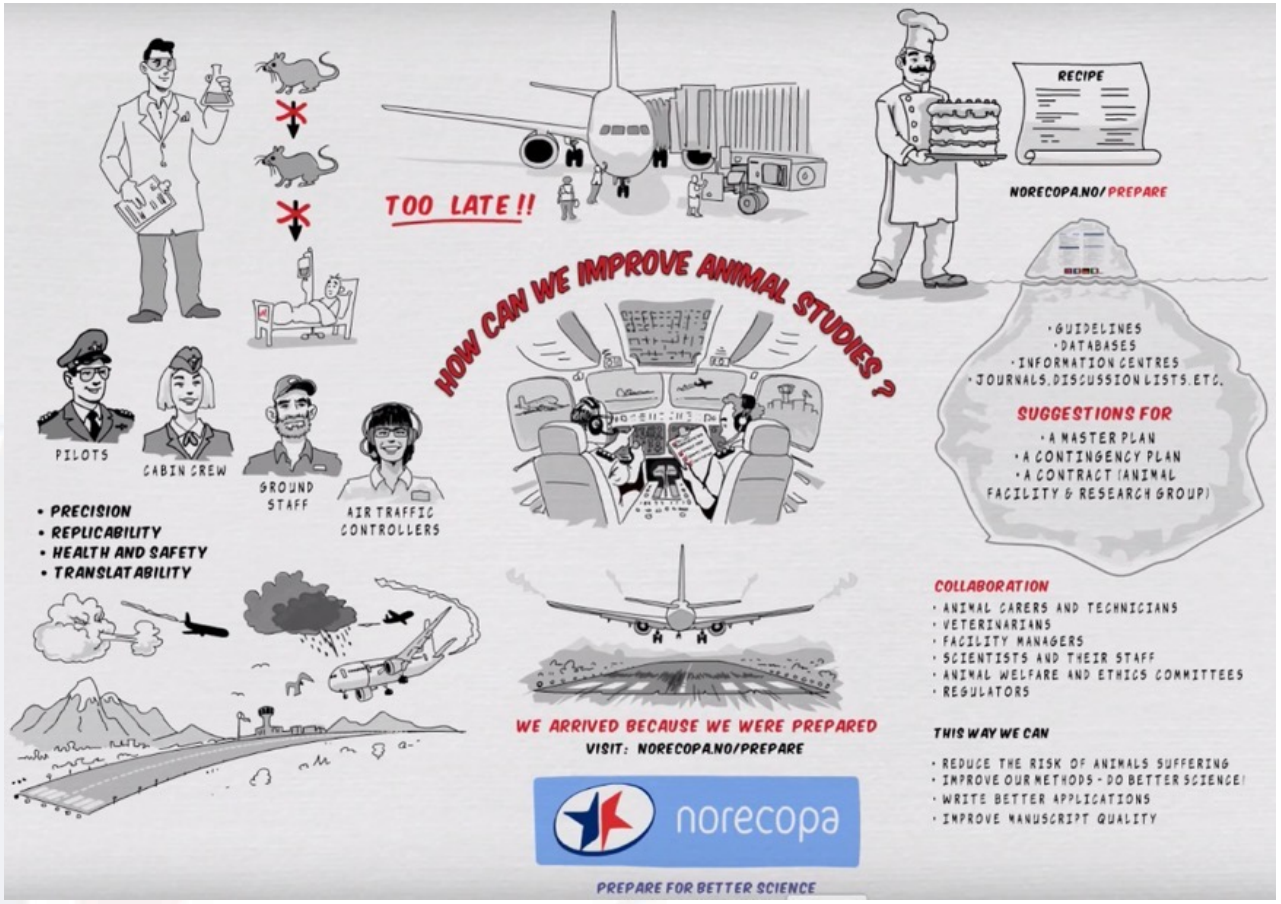
vimeo.com/358069203 or norecopa.no/PREPARE/film

3-minute cartoon film



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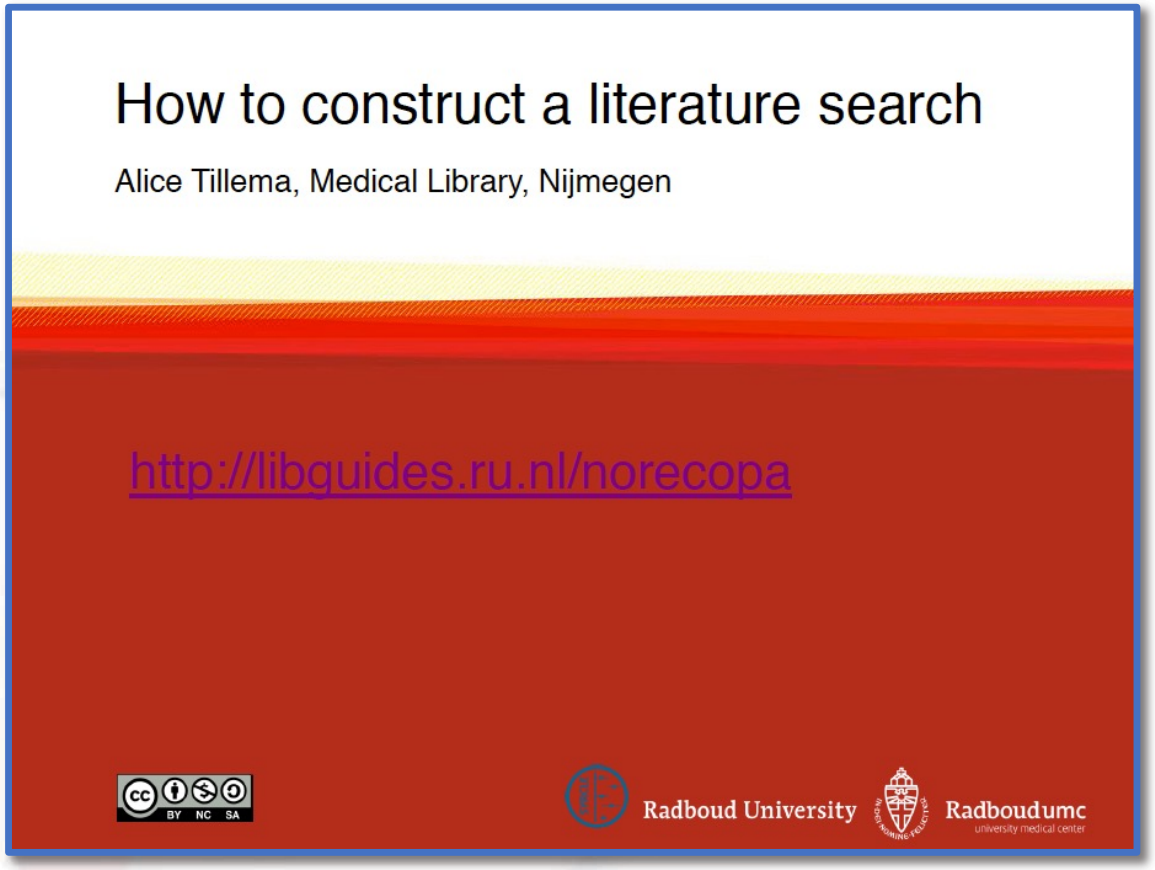
Why is 3R literature hard to find?

- 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



3R improvements are often not highlighted in the scientific literature

http://www.theodora.com/rodent_laboratory/blood_collection.html

photo:NMBU

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

3R Flag

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

Annelise Hem[1], Adrian J. Smith[2] & Per Solberg[1]

[1] ... PO Box 4404 Torshov, N-0403 Oslo and
[2] ... nce, PO Box 8146 Dep., N-0033 Oslo,

© Laboratory Animals Ltd. *Laboratory Animals* (1998) **32**, 364–368

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!

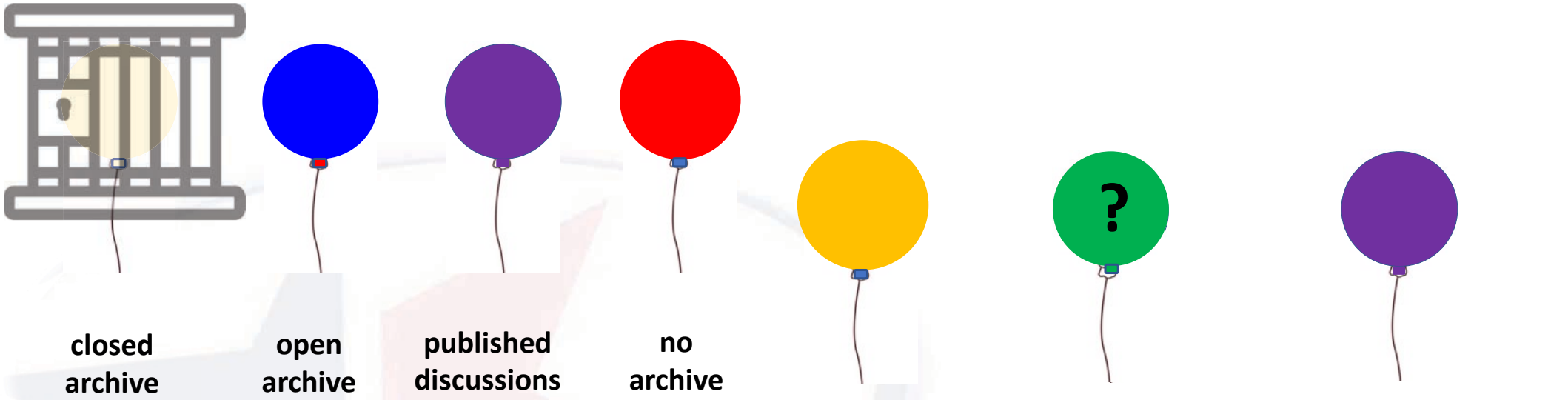
Not necessarily a high-impact journal.

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

The Waste of Good Ideas...



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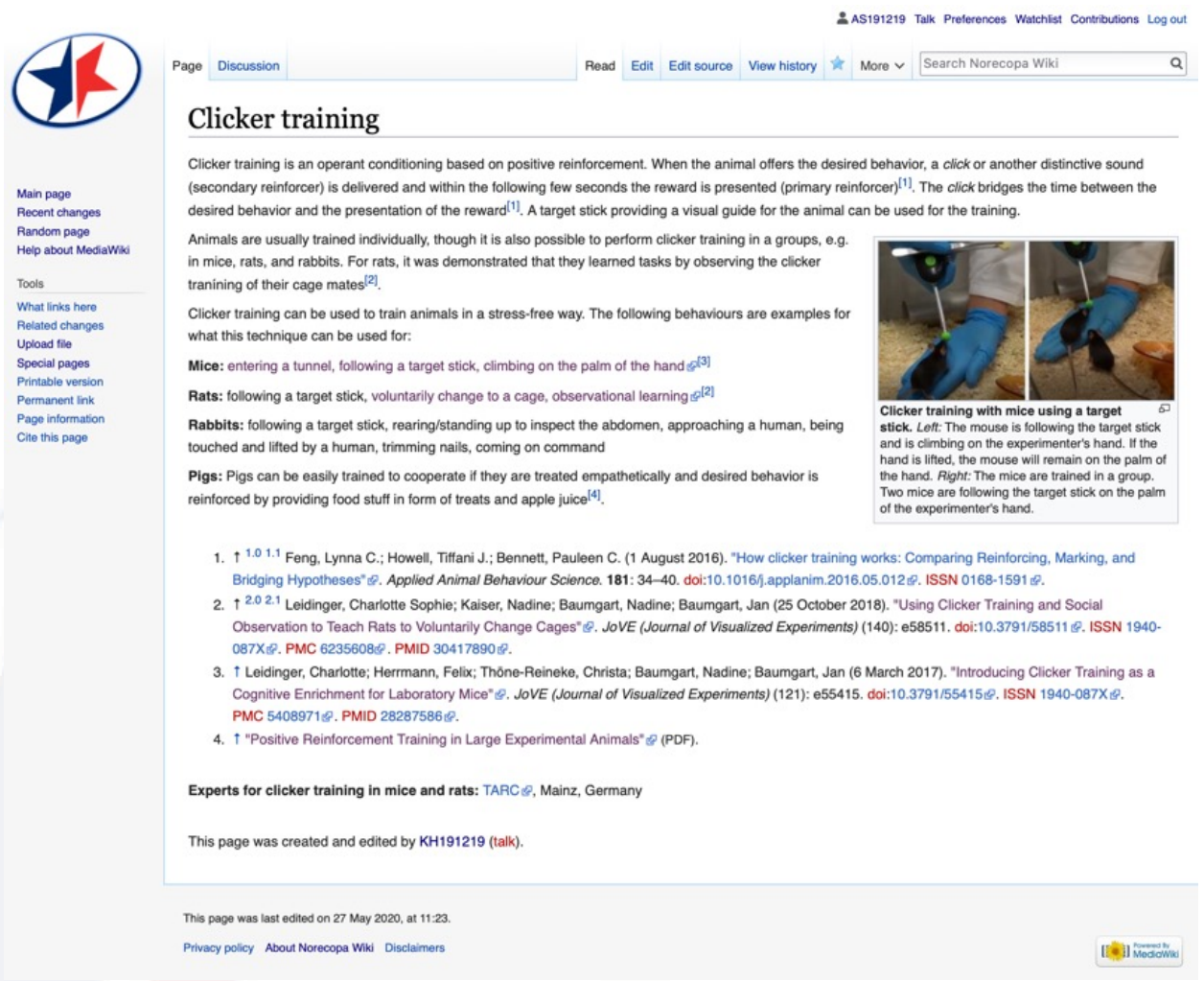

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Clicker training

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Clicker training is an operant conditioning based on positive reinforcement. When the animal offers the desired behavior, a *click* or another distinctive sound (secondary reinforcer) is delivered and within the following few seconds the reward is presented (primary reinforcer)[1]. The *click* bridges the time between the desired behavior and the presentation of the reward[1]. A target stick providing a visual guide for the animal can be used for the training.

Animals are usually trained individually, though it is also possible to perform clicker training in a groups, e.g. in mice, rats, and rabbits. For rats, it was demonstrated that they learned tasks by observing the clicker tranining of their cage mates[2].

Clicker training can be used to train animals in a stress-free way. The following behaviours are examples for what this technique can be used for:

Mice: entering a tunnel, following a target stick, climbing on the palm of the hand[3]

Rats: following a target stick, voluntarily change to a cage, observational learning[2]

Rabbits: following a target stick, rearing/standing up to inspect the abdomen, approaching a human, being touched and lifted by a human, trimming nails, coming on command

Pigs: Pigs can be easily trained to cooperate if they are treated empathetically and desired behavior is reinforced by providing food stuff in form of treats and apple juice[4].

Clicker training with mice using a target stick. *Left:* The mouse is following the target stick and is climbing on the experimenter's hand. If the hand is lifted, the mouse will remain on the palm of the hand. *Right:* The mice are trained in a group. Two mice are following the target stick on the palm of the experimenter's hand.

1. ↑ [1.0] [1.1] Feng, Lynna C.; Howell, Tiffani J.; Bennett, Pauleen C. (1 August 2016). "How clicker training works: Comparing Reinforcing, Marking, and Bridging Hypotheses". *Applied Animal Behaviour Science*. **181**: 34–40. doi:10.1016/j.applanim.2016.05.012. ISSN 0168-1591.
2. ↑ [2.0] [2.1] Leidinger, Charlotte Sophie; Kaiser, Nadine; Baumgart, Nadine; Baumgart, Jan (25 October 2018). "Using Clicker Training and Social Observation to Teach Rats to Voluntarily Change Cages". *JoVE (Journal of Visualized Experiments)* (140): e58511. doi:10.3791/58511. ISSN 1940-087X. PMC 6235608. PMID 30417890.
3. ↑ Leidinger, Charlotte; Herrmann, Felix; Thöne-Reineke, Christa; Baumgart, Nadine; Baumgart, Jan (6 March 2017). "Introducing Clicker Training as a Cognitive Enrichment for Laboratory Mice". *JoVE (Journal of Visualized Experiments)* (121): e55415. doi:10.3791/55415. ISSN 1940-087X. PMC 5408971. PMID 28287586.
4. ↑ "Positive Reinforcement Training in Large Experimental Animals" (PDF).

Experts for clicker training in mice and rats: TARC, Mainz, Germany

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

This page was last edited on 27 May 2020, at 11:23.

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Pages created (January 2024)

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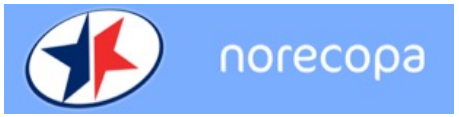

- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Dehydration
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- EMLA cream
- Embryo transfer
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- Food crunchers
- Forced swim test
- General discusson on use of analgesics
- Genotyping mice
- Habituation training
- Health monitoring
- High-fat diets
- Hot Bead Sterilisers
- Housing nude mice
- Housing research fish
- Humane endpoints
- Hydrodynamic gene delivery
- Intra-ocular injections
- Intranasal administration
- Intraperitoneal injection
- Intraperitoneal pentobarbitone
- Irradiation for haematology studies
- Ketamine and alpha-2 agonist combinations
- Long-term anaesthesia in rodents
- Lumpfish
- Main Page
- Marble Burying Test
- Metabolic cages
- Microchipping rats and mice
- Minipumps
- Montanide adjuvant
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Non-invasive genetic sampling in wildlife research
- Oestrus suppression in ferrets
- Pneumocystis murina
- Recapping needles
- Refinement of oral gavage
- Rotarod Test
- Screening cell lines
- Sedation of cattle
- Splenectomy
- Sterilisation of instruments
- TTEAM and TTouch
- Tail vein injection
- Tamoxifen
- Tamoxifen information sheet V4.pdf
- The use of DMSO
- Tramadol
- Transport stress
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing

wiki.norecopa.no

The Wiki is an integral part of Norecopa's website: 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

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?

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PREPARE for better Science

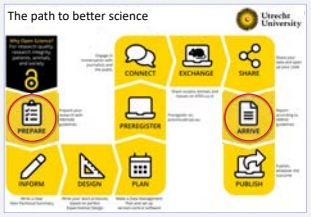
Norecopa: PREPARE for better Science

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

What's the problem?

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

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



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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
- 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*

norecopa.no/PREPARE

The Refinement Wiki
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 (NSMSD), Novo Nordisk, the Norwegian Animal Protection Alliance (Dyrevernalliansen), the Norwegian Society for Protection of Animals (Dyrebeskyttelsen 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

Thanks to Norecopa's main sponsors:

- Standing Committee on Business Affairs, Norwegian Parliament
- Norwegian Ministries of Agriculture and Fisheries
- Research Council of Norway (Forskningsrådet)
- 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)
- Novo Nordisk
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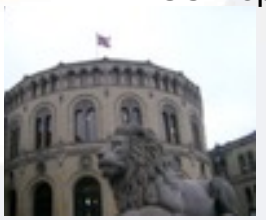
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture

Graphics: colourbox.com



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