

Can we improve our scientific quality and animal welfare?

Experiences with planning animal studies

norecopa.no/TUMS

Adrian Smith

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norecopa

<https://norecopa.no>

Many thanks to:

Dr. Ehsan Sharif-Paghaleh

Dr. Siavash Noorbakhsh

Mrs. Leila Ashrafi, Education Manager

Content of this webinar

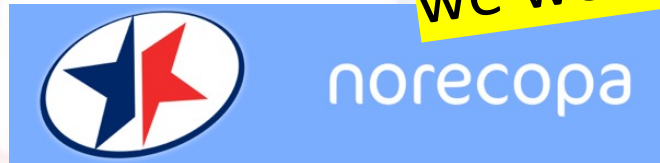
- practical tips for improving scientific quality and animal welfare – and also health & safety
- the PREPARE guidelines for planning animal research & testing
(Disclosure: lead author)
- where to find more resources

The views expressed in this webinar are my own and not necessarily those of Norecopa.

Norecopa

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

we welcome more from Iran!



<https://norecopa.no>

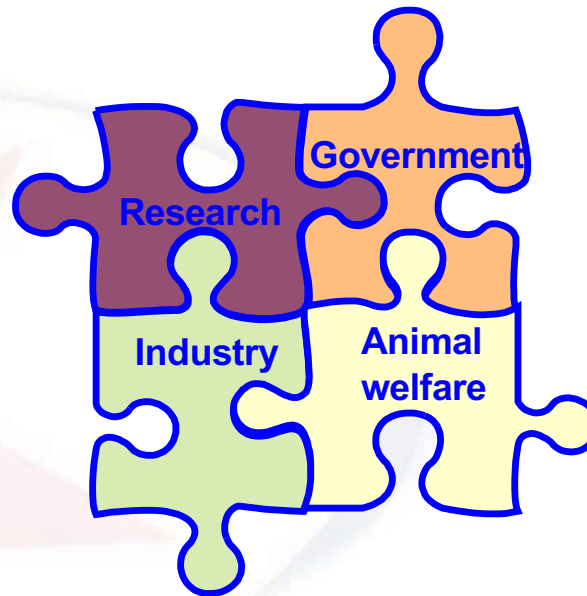
Norecopa: PREPARE for better Science

European Consensus-Platform for Alternatives

ecopa.eu



- Established in 2000
- Recognises **National Consensus Platforms** (NCPs) with **4 stakeholders** equally represented:



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



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About Norecopa | Alternatives | Databases & Guidelines | Education & training | Legislation | Meetings | More resources | News | PREPARE

Anaesthesia and analgesia | Animal facilities | Animal welfare organisations | Blood sampling | Culture
Email discussion lists | Environmental enrichment | Ethics | Experimental design and reporting | Harm-
Health and safety | Health monitoring | Humane
Literature searches and systematic reviews | Organi

norecopa.no / More resources / Experimental design

Design and reporting of animal experiments

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

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approx. 9,000 webpages
300,000 hits annually
7-8 detailed newsletters per year

Search filters

Order by:
Relevance

Typo tolerance:
Default

Database

- 3R Guide database (403)
- Classic AVs database (118)
- European Commission Inventory of 3Rs Education & Training Resources (567)
- European Commission Inventory of 3Rs Knowledge Sources (807)
- European Commission Inventory of NAMs for Respiratory tract diseases (280)
- NAL records (1688)
- NORINA database (3141)
- TextBase database (1501)
- Website (761)

Browse the databases

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

Search in the databases

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

+ webpages for past meetings and recorded meetings

norecopa.no/meetings/meetings-calendar

Webinar and Meetings calendar

- > Application of cardiac myocyte cell lines as models for heart disease, July 2021
- > Berlin 3R seminar series: Refinement and Reduction [↗](#), 8 July 2021
- > How to perform a systematic review in biomedical research and rigour [↗](#), webinar (Shona Lang), 9 July 2021
- > Zebrafish as experimental model for research [↗](#), webinar series, 10 July 2021
- > VetBioNet Summer School: Animal Infectious Disease Research: Ethics & 3Rs by Design [↗](#), 12-14 July 2021
- > KALAS International Symposium [↗](#), Jeju Island, 14-17 July 2021
- > Berlin 3R seminar series: Replacement and Refinement [↗](#), 15 July 2021
- > Norecopa: A National Consensus Platform working to advance animal research, 19 July 2021
- > Animal Research: Critical, Challenging & Creative Thinking [↗](#), 20 July 2021

August 2021

- > Course in Animal, General, and Plant Biosafety and Biosecurity, 2-4 August 2021
- > ISAE2020 (54th Congress of the International Society for Animal Ethics), 10-12 August 2021
- > **4th International TCPF Preclinical Imaging Symposium [↗](#), Virtual Meeting, 11-12 August 2021**
- > EFRA Satellite Training on Skin Sensitisation - Case Studies, 16-18 August 2021
- > 11th World Congress on Alternatives and Animal Use in the Life Sciences, 22-25 August 2021
- > ASAB Summer Virtual Meeting [↗](#), 23-25 August 2021

4th International Preclinical Imaging Symposium
(11-12) August 2021
Tehran University of Medical Sciences

Submission Articles Deadline: 22 July 2021

FREE

Symposium topics
 Pharmacy, Nano and drug delivery, Preclinical oncology, Cancer treatments, Perfusion and heart, Dental studies and materials, Material Science, Zoology, Ethics in preclinical research, Image processing methods and tools and other related areas

ONLINE

TEHRAN UNIVERSITY OF MEDICAL SCIENCES
 TUMS Preclinical core Facility

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



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The screenshot shows the Norecopa website header with the logo (a blue and red star) and the text 'norecopa'. There are language options for 'NORSK' and 'ENGLISH', and a search bar. The navigation menu includes: About Norecopa, Alternatives, Databases & Guidelines, Education, Legislation, Meetings, More resources, News, PREPARE, Species, and Wiki. Below the menu, there are links for 'Fish 2005', 'Wildlife 2008', 'Fish 2009', 'Agricultural animals 2012', 'Field research 2017', 'Past meetings', 'Meetings Calendar', 'An informal guide to arranging a scientific meeting', and 'Presentations'. The URL 'norecopa.no/meetings/presentations' is displayed in large blue text, along with social media icons for Facebook, Twitter, Email, and a plus sign.

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

Koenig 101017.pdf

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

norecopa.no/global3R



Centres

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

Associations

- [AFLAS \(includes South Korea\)](#) ⓘ
- [Culture of Care Network](#) ⓘ
- [EU3Rnet](#) ⓘ
- [FELASA](#) ⓘ
- [FESSACAL](#) ⓘ
- [Scand-LAS](#) ⓘ

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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

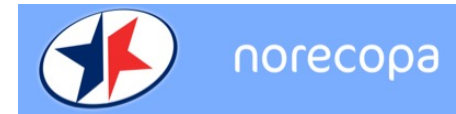
Here is [an alphabetical global list of all the databases](#) cited on the Norecopa website.

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norecopa.no/databases-guidelines

links to over 70 other databases

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



Guidance on the severity classification of procedures involving fish

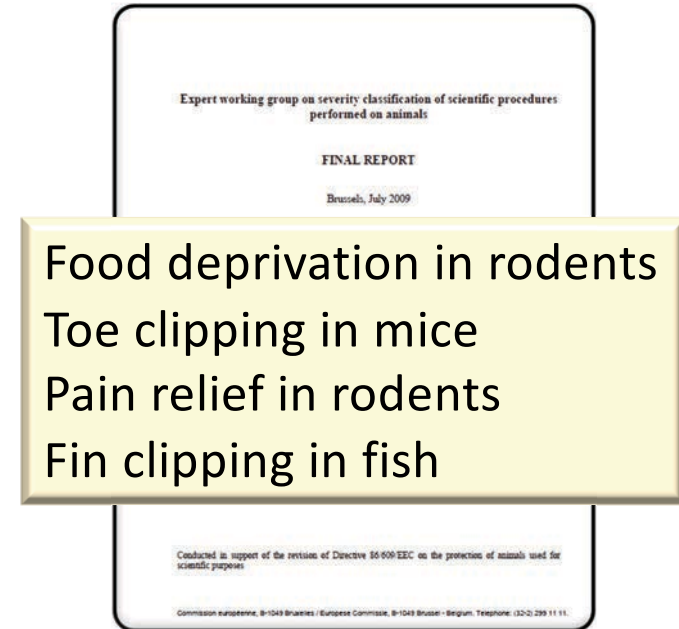
Report from a Working Group convened by Norecopa

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

Laboratory Animals, 45: 219-224, 2011

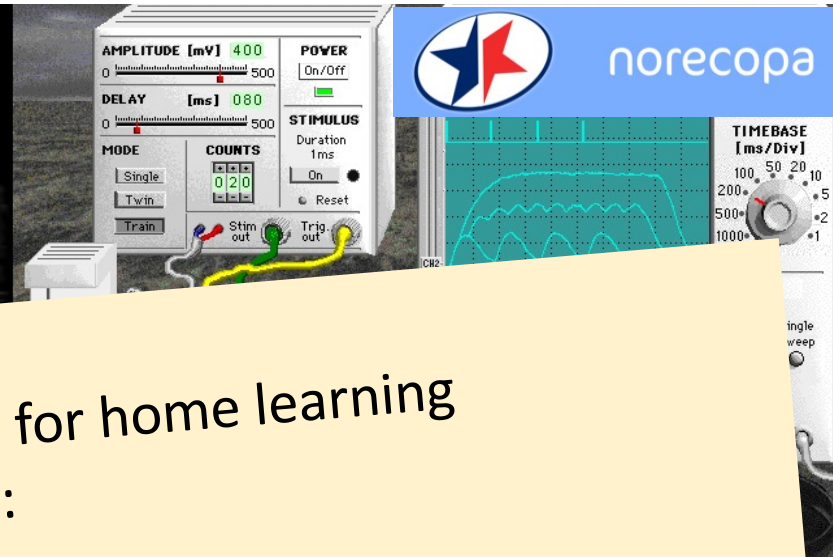
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norecopa.no/categories



http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf

norecopa.no/NORINA



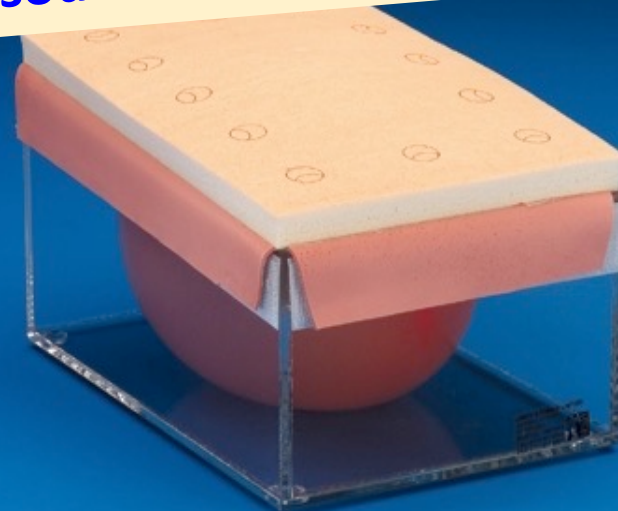
NEW:

overview of resources suitable for home learning during the Covid-19 pandemic:

norecopa.no/norina-database/resources-for-home-learning



rescuecritters.com



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 sam
Norecop



Blood sampling from the pig
Norecopa | 3,914 views



Subcutaneous injection in the rabbit
Norecopa | 1,479 views



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



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



Blood sam
Norecop



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 Moriana
Centro de Experimentación Animal, CAI Medicina-Biología, Universidad de Alcalá
122610000@uclm.es | 1226100100

Anatomía de la rata
Norecopa | 977 views



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



Blood sam
Norecop



Lifting a rabbit
Norecopa | 2,420 views



Immobilisation of the rabbit
Norecopa | 2,072 views

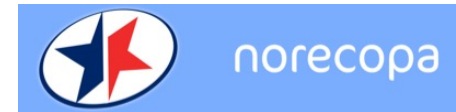
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norecopa.no/education-training/homemade-educational-materials



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The "reproducibility crisis"



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/aev3>

Published: 03 October 2015

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.

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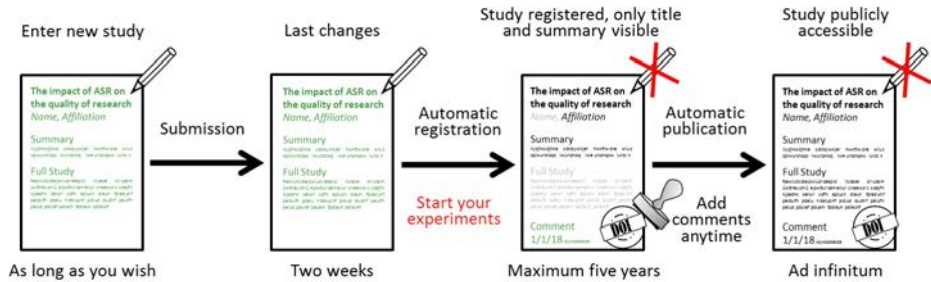
Frequently highlighted causes of the "reproducibility crisis"

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

Preregistration of a study





- Prevents p-hacking and HARKING
- Encourages the publication of negative results
- Ensures a detailed description of the study



<https://norecopa.no/prepare/4-experimental-design-and-statistical-analysis>

Pre-registration of animal research

The pre-registration of protocols for animal research is gaining momentum, enabling peer review and as part of the work to reduce bias:

- > [Preclinicaltrials.eu](https://preclinicaltrials.eu) 
- > [The Animal Study Registry \(animalstudyregistry.org\)](https://www.animalstudyregistry.org) , Germany (see also [Bert et al., 2019](#) )
- > [PROSPERO](#) : An international prospective register of systematic reviews, established by the National Institute for Health Research (NIHR) in the UK
- > [Should preclinical studies be registered?](#)  (Anderson & Kimmelman, 2015)
- > [Further advice on protocol registration](#) 

Depositories for online protocols

- > [Protocol Exchange](#)  from Nature.com
- > protocols.io 
- > protocol-online.org 
- > [Open Wetware](#) 

Perspective | Open Access | Published: 10 January 2017

A manifesto for reproducible science

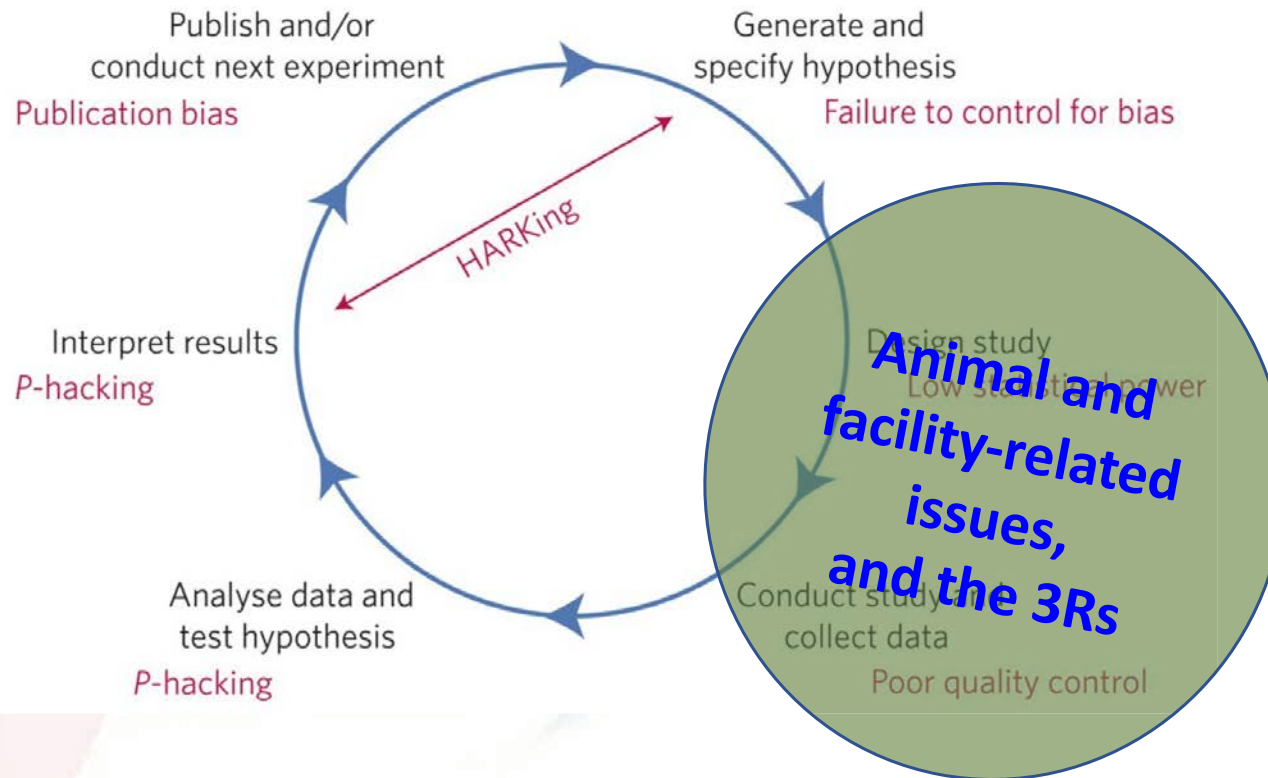
Marcus R. Munafò , Brian A. No-
Button, Christopher D. Chambers,
Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



My personal view

- The greatest source of variability lies within the animals and the way in which they are used
- I suspect that many scientists are unaware of the size of this, or they assume that the animal facility is dealing with it

"An injection is an injection, do we need to discuss that?"

Two frustrations

"We can solve the reproducibility crisis by

- courses in Experimental Design that focus primarily on the "mathematical" aspects (e.g. randomisation, experimental units, blinding, statistical methods)
- **better reporting"**



reddit.com



Reporting

Planning

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Reporting guidelines are not new...

e.g.

- Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments, 1985 (GV-SOLAS)
- Reporting animal use in scientific papers, 1997 (Smith *et al.*)
- Animal definition: a necessity for the validity of animal experiments (Rehbinder)
- Guidelines for reporting animal experiments, 2000 (Smith & Brattelid)
- **+ reporting guidelines in the journal itself**
- Standard Publication Checklist (GSPC), 2010 (SYRCLE)
- Institute for Laboratory Animal Research, 2011 (NRC)
- Instructions to authors, in many journals
- **ARRIVE 2.0 Guidelines, 2019 (Percie du Sert *et al.*)**



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The easy parts of reporting:

WHAT THE NUMBERS MEAN

Electric → 100 CC

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

arborist101.com

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



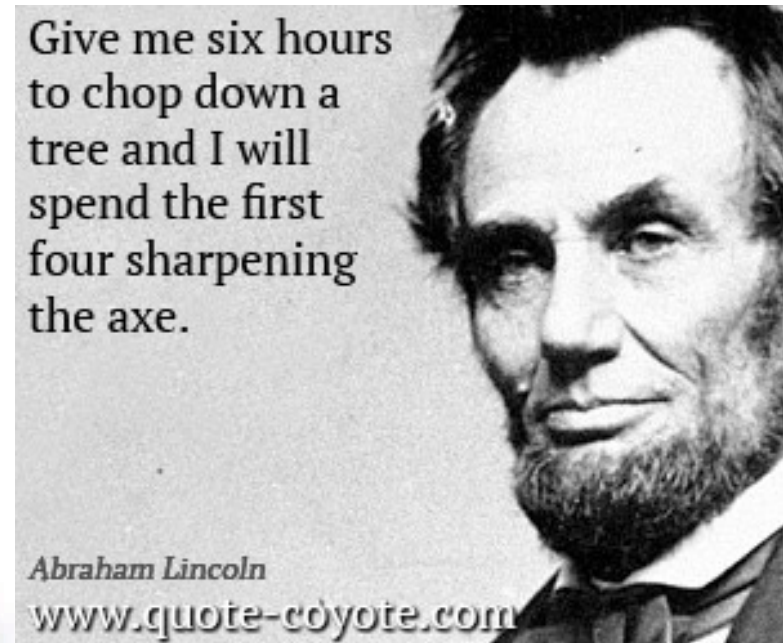
stihl.no

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Critical issues behind the scenes that may not get reported:

- Experience of the workers
- Inspection for signs of damage
- Decision about direction of felling
- Additional equipment (winch, chains, straps, wedges)
- Equipment and routines for maintenance
- Clearing-up and transport of logs
- **Health and safety precautions – clothing, onlookers**
- **Division of labour and costs**

These issues are discussed long before the actual work



leadereconomics.com

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editorial | Published: February 2010

Measure twice, think three times, cut once

[L. Noyez](#) 

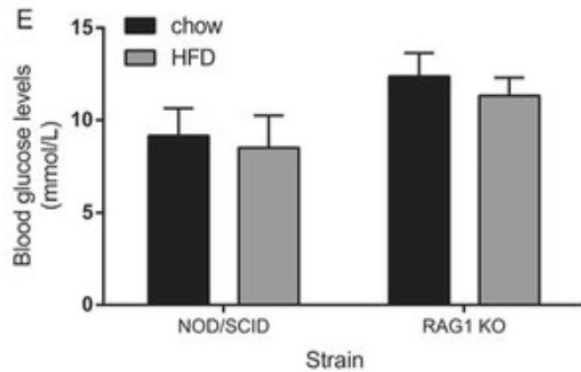
[Netherlands Heart Journal](#) **18**, 60(2010) | [Cite this article](#)

doi.org/10.1007/BF03091738

Abstract

When I was a child, my father taught me how to fix a punctured tyre. He stressed the importance of checking the whole tyre, even if I had already found a puncture, because there could always be more. In addition, he made me check the outer tyre for sharp pieces that could again damage the inside tyre.

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, immobilisation, sampling

Blood

often also:

injections, gavaging, surgery

pain and distress

developing illness and death

Some of the common animal-related issues...



Contingent suffering



animalcaresystems.com

(not just the direct suffering caused by the procedure)

Fear, boredom, discomfort and pain

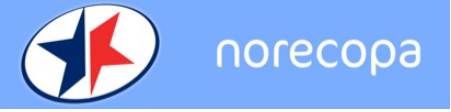
Caused by, for example:

Transport, changes in environmental conditions, husbandry, social groups, age-related or infectious disease

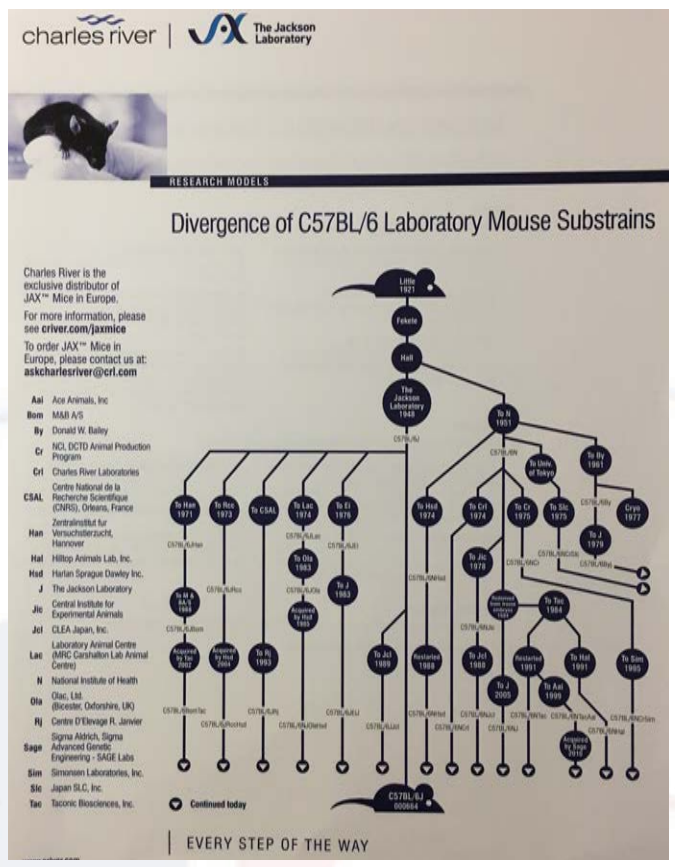
Single-housed male mice show symptoms of what in humans would be characterised as depression

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



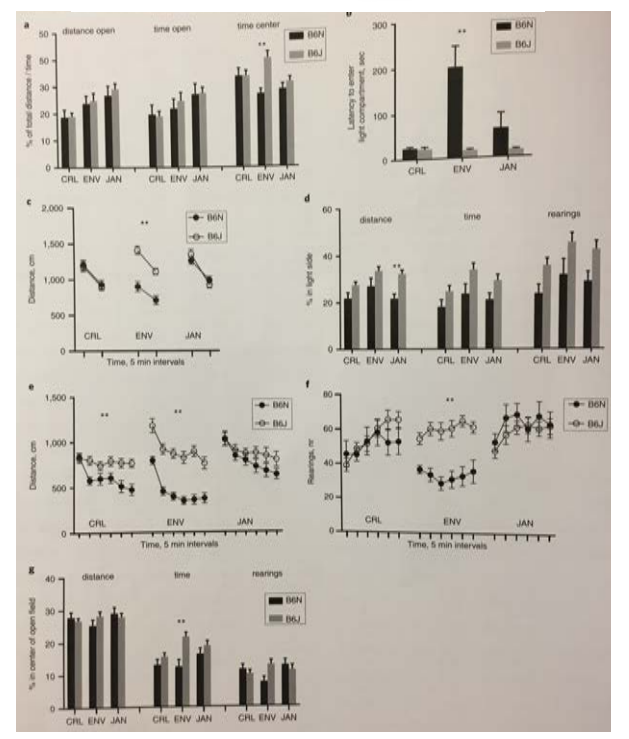


The C57BL/6 mouse



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...



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

We need more guidance on nutrition (a FELASA working group has been convened)

norecopa.no/prepare/12-housing-and-husbandry/12a/general-principles

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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.

Stress caused by capture and handling



News > Science

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

Mice pick naturally

Ian Johnstone



't act

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

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Baseline

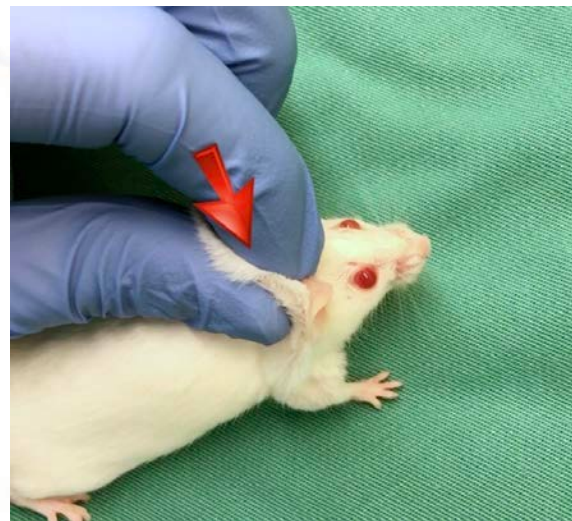
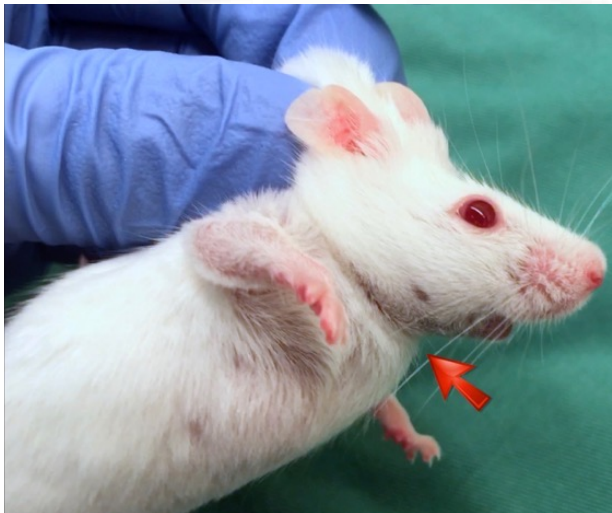


Immobilizing Sinus bradycardia, VEC



Reprinted with permission. 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* 60:201–212. DOI: 10.30802/AALAS-JAALAS-20-000069

norecopa.no/scruff



Three fingers better than two

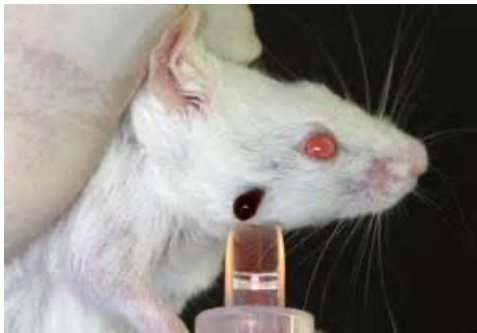
Artefacts caused by poor administration techniques



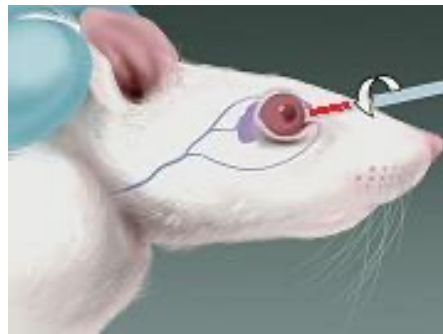
Photo: NMBU

- *Do injections always end up in the same place?*
- *Are the injections painful?*
- *Are they realistic? (intramuscular injections in small animals)*

"All I need is a blood sample..."



medipoint.com/html/for_use_on_mice.html



theodora.com/rodent_laboratory/blood_collection.html



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 shock, metabolic changes due to differing storage times before centrifugation, etc.
- ✓ agree that they are feasible in the time available!

What if we can't find evidence of best practice in the scientific literature?

Carol M. Newton (1925-2014)



National Library of Medicine

The three S's

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

norecopa.no/3S

*How do other professionals achieve reproducibility?
What can we learn from the aviation industry?*



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



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Reproducibility and precision in a variable environment...



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10-15 checklists even on short routine flights



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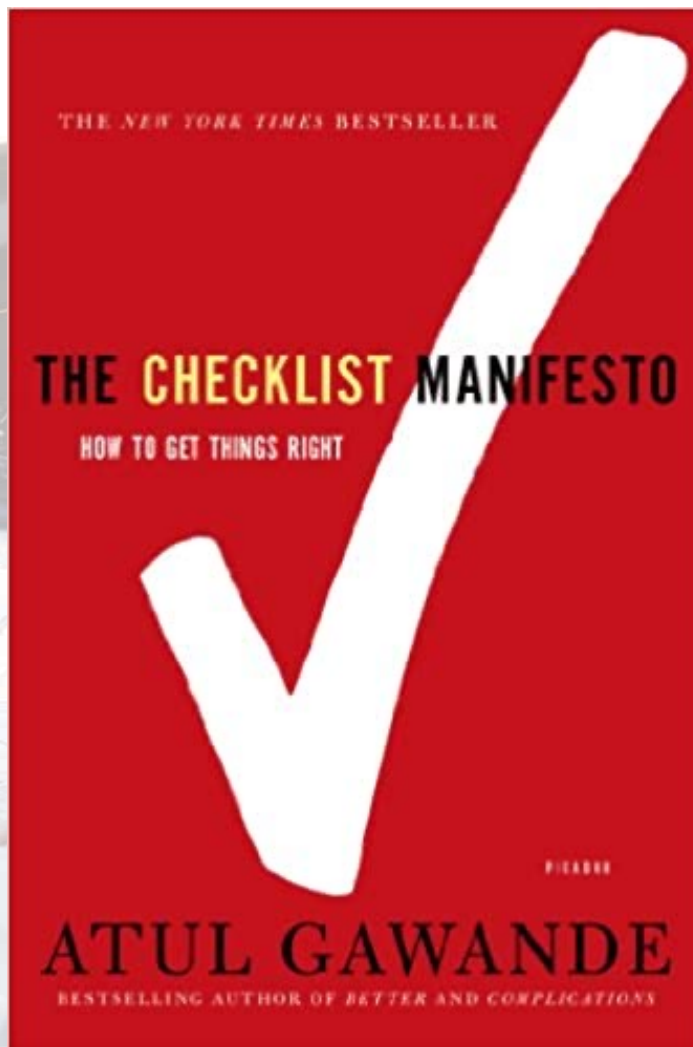
Checklists

- Reduce risk of **forgetting** to carry out vital actions
- Ensure checks are carried out in the **correct sequence**
- Encourage **cooperation** and **cross-checking** between crew members

Too late to read the checklists when you have ARRIVED!



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amazon.com/gp/product/0312430000



Surgical Safety Checklist



Before induction of anaesthesia

 →

Before skin incision

 →

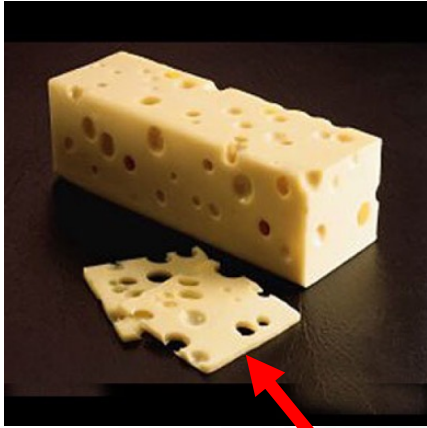
Before patient leaves operating room

<p><i>(with at least nurse and anaesthetist)</i></p> <p>Has the patient confirmed his/her identity, site, procedure, and consent? <input type="checkbox"/> Yes</p> <p>Is the site marked? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable</p> <p>Is the anaesthesia machine and medication check complete? <input type="checkbox"/> Yes</p> <p>Is the pulse oximeter on the patient and functioning? <input type="checkbox"/> Yes</p> <p>Does the patient have a:</p> <p>Known allergy? <input type="checkbox"/> No <input type="checkbox"/> Yes</p> <p>Difficult airway or aspiration risk? <input type="checkbox"/> No <input type="checkbox"/> Yes, and equipment/assistance available</p> <p>Risk of >500ml blood loss (7ml/kg in children)? <input type="checkbox"/> No <input type="checkbox"/> Yes, and two IVs/central access and fluids planned</p>	<p><i>(with nurse, anaesthetist and surgeon)</i></p> <p><input type="checkbox"/> Confirm all team members have introduced themselves by name and role.</p> <p><input type="checkbox"/> Confirm the patient's name, procedure, and where the incision will be made.</p> <p>Has antibiotic prophylaxis been given within the last 60 minutes? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable</p> <p>Anticipated Critical Events</p> <p>To Surgeon: <input type="checkbox"/> What are the critical or non-routine steps? <input type="checkbox"/> How long will the case take? <input type="checkbox"/> What is the anticipated blood loss?</p> <p>To Anaesthetist: <input type="checkbox"/> Are there any patient-specific concerns?</p> <p>To Nursing Team: <input type="checkbox"/> Has sterility (including indicator results) been confirmed? <input type="checkbox"/> Are there equipment issues or any concerns?</p> <p>Is essential imaging displayed? <input type="checkbox"/> Yes <input type="checkbox"/> Not applicable</p>	<p><i>(with nurse, anaesthetist and surgeon)</i></p> <p>Nurse Verbally Confirms:</p> <p><input type="checkbox"/> The name of the procedure</p> <p><input type="checkbox"/> Completion of instrument, sponge and needle counts</p> <p><input type="checkbox"/> Specimen labelling (read specimen labels aloud, including patient name)</p> <p><input type="checkbox"/> Whether there are any equipment problems to be addressed</p> <p>To Surgeon, Anaesthetist and Nurse:</p> <p><input type="checkbox"/> What are the key concerns for recovery and management of this patient?</p>
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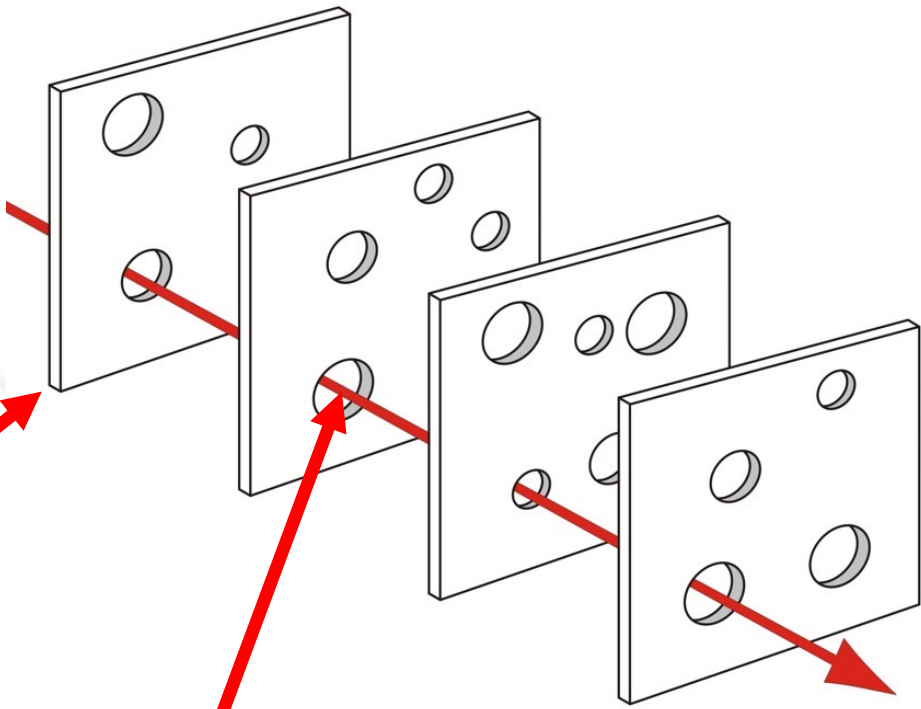
This checklist is not intended to be comprehensive. Additions and modifications to fit local practice are encouraged. Revised 1 / 2009 © WHO, 2009

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

Threat and Error Management



eaugallecheese.com/Swiss-cheese



"Layer of defence"
or redundancy

Weakness / hazard

Loss

wikipedia.org/wiki/Swiss_cheese_model

Those who plan animal studies should ask relevant questions about quality assurance of the animal facility itself

The AAALAC Program Description Template is a good checklist for the facility as a whole

<https://www.aaalac.org/program-description>



Disclosure:

I have prepared for and managed an animal facility with AAALAC accreditation for 10 years

No other connection to AAALAC International



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

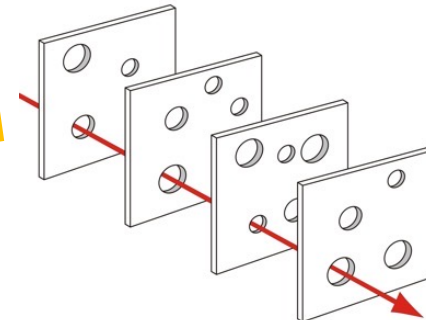
III. Veterinary Care.....	29
A. Animal Procurement and Transportation	29
1. Animal Procurement.....	29
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1. Animal Biosecurity.....	29
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4. Diagnostic Resources	32
5. Drug Storage and Control	32
D. Surgery.....	32
1. Pre-Surgical Planning.....	32
2. Surgical Facilities	33
3. Surgical Procedures	33
4. Aseptic Technique.....	33
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63 pages

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 and anaphylactic reactions
 - bites
 - 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

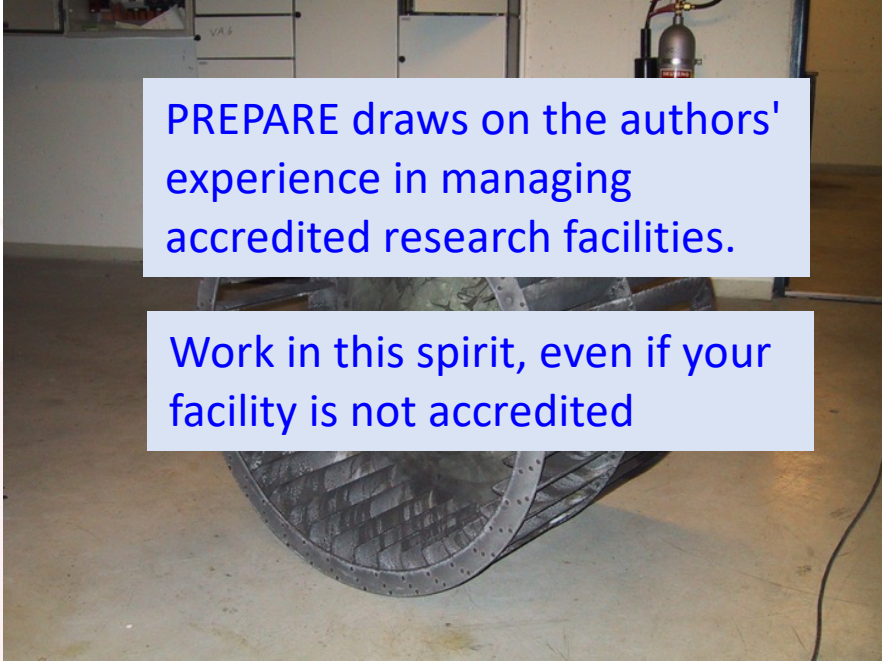


Temporary staff at weekends and holidays

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

Contingency and redundancy

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

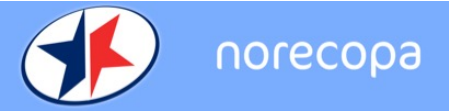


PREPARE draws on the authors' experience in managing accredited research facilities.

Work in this spirit, even if your facility is not accredited

Photo: NMBU

Good advice is emerging from the Covid-19 pandemic



Suggested considerations for establishment working under ASPA during the COVID19 lock-down

CATEGORY		CONSIDERATIONS/SUGGESTIONS	
<p>PERSONNEL</p> <p>Provide 'essential worker' letter to show authorities, include home address. Consider whether company/photo I.d. would be helpful</p> <p>All personnel must prioritise their health and the health of others by wearing suitable PPE and by observing social distancing as advised by the government</p> <p>Support mental health Consider mindfulness apps, Convert empty animal room into a relaxation/yoga room (online yoga classes).</p>	<p>ANIMAL TECHNICIANS</p>	<p>Run 2 or more teams if possible to lower the risk of transmission(each team is treated as 'household') to the wider team. Examples of how onsite teams might be run include alternate days, 2days on 2days off and utilising an early shift / a late shift to reduce contact and total staff in an area at any one time. If people are in isolation or have caring responsibilities they may (if well enough) be able to work offsite as part of a "virtual office" team</p> <p>Where teams can't be separated use full PPE/ RPE and have staggered entry/break/exit times or other means of avoiding people not in PPE. Physically segregate in unit if possible</p> <p>Review teams regularly – this may need to be daily in some situations</p> <p>Introduce regular and frequent routines for surface decontamination, paying particular attention to door handle/ door plates, taps and work surfaces. Clean with detergent / 70% isopropyl alcohol or similar</p> <p>Limit reliance on public transport methods. Accommodate parking where possible to allow individuals to travel by car</p>	
	<p>RESEARCHERS</p>	<p>DELIVERIES</p>	<p>Ensure all alarm systems are checked regularly and are functional. Monitor, record and act on all alarms</p> <p>Review contingencies for critical system failure (e.g. HVAC) and have an action plan. Make sure all backup systems are fully functional and that sufficient spare parts are available and accessible</p>
		<p>VETS</p>	<p>norecopa.no/be-prepared required</p>
		<p>ANIMALS</p>	<p>BREEDING</p> <p>Ensure all non-replaceable lines are cryopreserved</p> <p>Consider stopping breeding of lines that are frozen down and have been on "tick over"</p> <p>Breed only for colony management, i.e. minimum number of breeding pairs to maintain the health of the colony</p> <p>Avoid breeding animals with phenotype – maintain animals where homozygotes may be phenotypic as wild type x heterozygote crosses to avoid generation of homozygotes</p> <p>Genotype promptly in order to identify animals required for ongoing breeding and cull animals not required ASAP</p> <p>Consider outsourcing genotyping if internal facilities are closed</p> <p>REDUCE STOCK</p> <p>Do not start new work unless absolutely essential/ internal review has been performed that confirms that the work can be properly serviced</p> <p>Essential research work may continue if staffing levels allow it. A local decision making process which records decision making as to which projects may remain ongoing should be in place. Examples of what may be reasonable are COVID-19 work, aged animal work and work to complete studies</p> <p>There may be reasons for prioritising ongoing work with some species (e.g. NHPs)</p> <p>If the facilities allow, consolidate animals to one area, check light cycle, room temps & designation first</p> <p>Spread work evenly / reduce cleaning of cages – but not to extent that welfare could be compromised</p> <p>Re-assess stock levels /staff levels at least once per week</p> <p>Cull animals that are not going to be needed for colony management and cannot otherwise be used</p> <p>Avoid unnecessary movement of animals</p> <p>Prioritise the movement of animals to other facilities or establishments for contingency of valuable lines.</p>
	<p>ESTABLISHMENT LICENCE HOLDER</p>	<p>ACCESS</p>	<p>Check your facility/ies will be open – Provide a list of names requiring access. Check with security how and when essential staff will access</p>
		<p>ENGINEERS</p>	<p>Confirm how essential supplies and waste contractors will service the facility/ies</p> <p>Stock up on diet, bedding, nesting materials, PPE, disinfectants and other essentials, aim for a minimum of 3 months</p> <p>Ensure there will be Liquid nitrogen / dry ice for cryopreserved stocks</p> <p>Have stocks of CO₂ and sodium pentobarbitone and any other drugs as directed by the NVS</p>
		<p>ESTATES / ENGINEERS</p>	<p>Check your contractors are working and get emergency contacts. Maintain a list of mobile numbers, available to everyone</p> <p>Consider if essential equipment will require servicing or repair. Ensure that you have a plan to enable this</p> <p>Will waste be being removed from site? – prepare an area for on-site storage if necessary</p>
		<p>RECORDS</p>	<p>Record all difficult decisions taken. What/ when /why and any related evidence</p>

Norecopa: PREPARE for better Science

lava.uk.net/viewtopic.php?f=3&p=80



Original Article

PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Litley³, Kristine E Aa Hansen⁴ and Trond Bratteli⁵

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

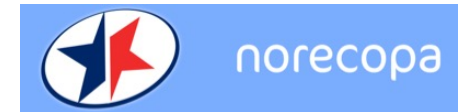
Date received: 5 April 2017; accepted: 27 June 2017

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

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laboratory animals



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

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norecopa.no/PREPARE

Norecopa: PREPARE for better Science

PREPARE:

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

PREPARE covers 15 topics:

Formulation of the study

1. Literature searches
2. Legal issues
3. Ethical issues, harm-benefit assessment and humane endpoints
4. Experimental design and statistical analysis

Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

Methods

9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Maybe the study
should not go ahead

Systematic review of
published research?

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
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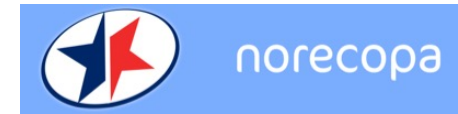
Dialogue between scientists and the animal facility

5. Objectives and timescale, funding and division of labour
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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

Adrian J. Smith¹, R. Eddie Clutton², Elliot Lilley¹,
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 Midtøien, EK25 98G, U.K.; ²Research Animals Depart-
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 Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; ²Division for Research Management and External Training, Western Norway University of Applied
 Sciences, 5020 Bergen, Norway.

PREPARE¹ consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE².
 PREPARE covers the three broad areas which determine the quality of the preparation for animal studies.

1. Formulation of the study
2. Dialogue between scientists and the animal facility
3. Quality control of the components in the study

The topics will not always be addressed in the order in which they are presented here, and some topics
 checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on
 facilities, since in-house experiments are dependent upon their quality. The full version of the guideline
 website, with links to global resources, at <https://norecopia.no/PREPARE>.
 The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced,
 and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	<input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes. <input type="checkbox"/> Consider the use of systematic reviews. <input type="checkbox"/> <i>Decide upon databases and information specialists to be consulted, and construct search terms.</i> <input type="checkbox"/> <i>Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering and to welfare needs.</i> <input type="checkbox"/> Assess the reproducibility and translatability of the project.
2. Legal issues	<input type="checkbox"/> Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. <input type="checkbox"/> Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	<input type="checkbox"/> Construct a lay summary. <input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced. <input type="checkbox"/> <i>Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities).</i> <input type="checkbox"/> <i>Consider pre-registration and the publication of negative results.</i> <input type="checkbox"/> <i>Perform a harm-benefit assessment and justify any likely animal harm.</i> <input type="checkbox"/> <i>Discuss the learning objectives, if the animal use is for educational or training purposes.</i> <input type="checkbox"/> <i>Allocate a severity classification to the project.</i> <input type="checkbox"/> <i>Define objective, easily measurable and unequivocal humane endpoints.</i> <input type="checkbox"/> <i>Discuss the justification, if any, for death as an end-point.</i>
4. Experimental design and statistical analysis	<input type="checkbox"/> <i>Consider pre-studies, statistical power and significance levels.</i> <input type="checkbox"/> <i>Define the experimental unit and decide upon animal numbers.</i> <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.

Many thanks to Dr. Siavash Noorbakhsh

Three Rs!

Topic	Recommendation
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding	<input type="checkbox"/> Arrange meetings with all relevant staff when early plans for the project exist. <input type="checkbox"/> Construct an approximate timescale for the project, indicating the need for assistance with preparation, all stages of the study.
6. Facility	<input type="checkbox"/> Conduct a physical inspection of the facilities, to evaluate training and equipment standards and needs. <input type="checkbox"/> Discuss staffing levels at times of extra risk.
7. Education and training	<input type="checkbox"/> <i>Assess the current competence of staff members and the need for further education or training prior to the study.</i>
8. Risks	<input type="checkbox"/> <i>Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study.</i> <input type="checkbox"/> Assess, and if necessary produce, specific guidance for all stages of the project. <input type="checkbox"/> Discuss means for containment, decontamination, and disposal of all items in the study.
9. Waste disposal and decontamination	<input type="checkbox"/> <i>Assess, and if necessary produce, specific guidance for all stages of the project.</i> <input type="checkbox"/> Discuss means for containment, decontamination, and disposal of all items in the study.
(C) Quality control of the components in the study	
9. Test substances and procedures	<input type="checkbox"/> Provide as much information as possible about test substances. <input type="checkbox"/> Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	<input type="checkbox"/> <i>Decide upon the characteristics of the animals that are essential for the study and for reporting.</i> <input type="checkbox"/> Avoid generation of surplus animals.
11. Quarantine and health monitoring	<input type="checkbox"/> Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	<input type="checkbox"/> <i>Attend to the animals' specific instincts and needs, in collaboration with expert staff.</i> <input type="checkbox"/> <i>Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).</i>
13. Experimental procedures	<input type="checkbox"/> <i>Develop refined procedures for capture, immobilisation, marking, and release or rehoming.</i> <input type="checkbox"/> <i>Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.</i>
14. Humane killing, release, reuse or rehoming	<input type="checkbox"/> Consult relevant legislation and guidelines well in advance of the study. <input type="checkbox"/> Define primary and emergency methods for humane killing. <input type="checkbox"/> <i>Assess the competence of those who may have to perform these tasks.</i>
15. Necropsy	<input type="checkbox"/> Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

References

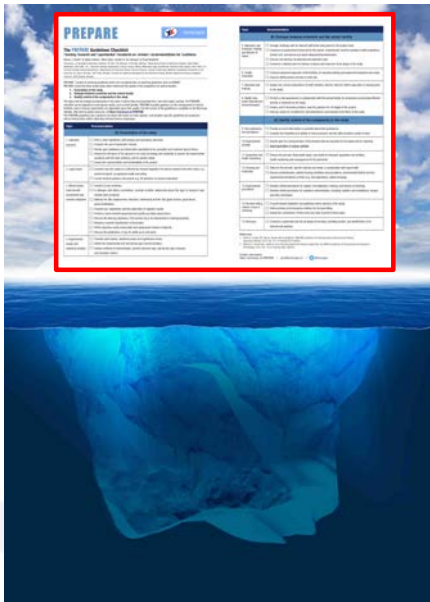
1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Bratteild T. PREPARE Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
2. Kilenny C, Browne WJ, Cuthill IC et al. Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting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

Further information

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

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

norecopa.no/PREPARE



PREPARE
PREPARE checklist
Comparison with ARRIVE
Endorsements
Film
1-Literature searches
2-Legal issues
3-Ethical issues,

PREPARE

The PREPARE Guidelines, and this section of the Norecopa website, have been developed with the involvement and support of the [RSPCA](#).



As part of ongoing efforts to reduce waste, promote animal alternatives (all [the three Rs](#)), and increase the reproducibility of research and testing, a group of experts from the UK and Norway, led by Norecopa, has produced a set of guidelines for **planning** experiments:

PREPARE (*Planning Research and Experimental Procedures on Animals: Recommendations for Excellence*)

Norecopa: PREPARE for better Science

- 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, to avoid publication bias? 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?
- 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

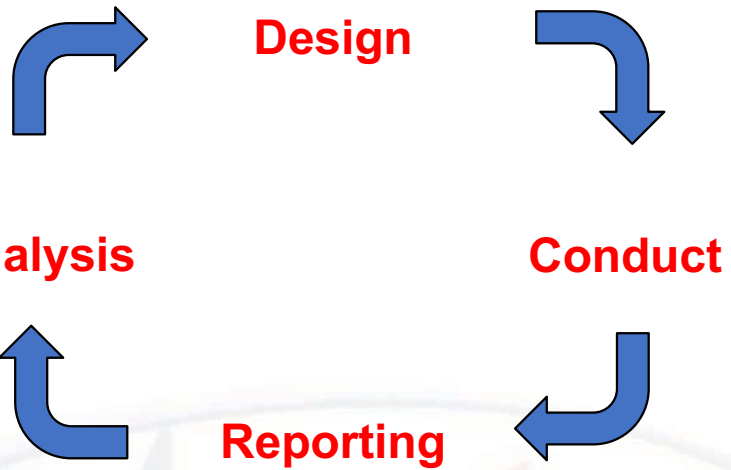
A contract between the animal facility and the research group

The division of labour and responsibilities

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			



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



Aggregation of marginal gains – *not rocket science*

Instead of hoping for a paradigm shift (= immediate animal replacement):

Small improvements of many small components

1908-2003: UK cycling team won only 1 gold medal and never won the Tour de France

2003: hired Dave Brailsford

2007-2017: 178 world championships, 66 Olympic or Paralympic Gold Medals and 5 Tour de France victories

Lab animal perspective:

Lilley E, Jennings M. (2013) Refinement: Lessons from the 2012 Olympics. *Alternatives to Laboratory Animals (ATLA)* 41(3):P28-P29.

doi:10.1177/026119291304100309

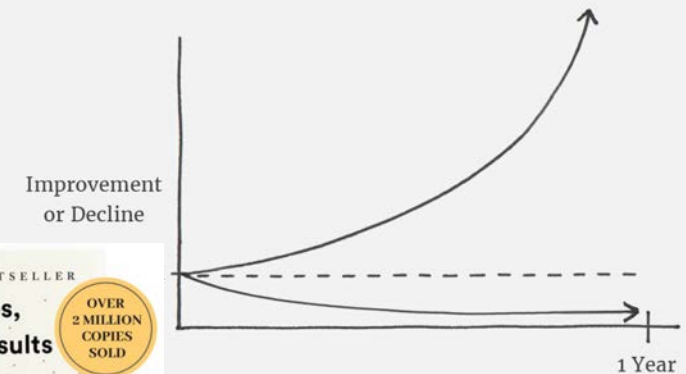
rspca.org.uk/webContent/staticImages/Downloads/2012Olympics.pdf

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The Power of Tiny Gains

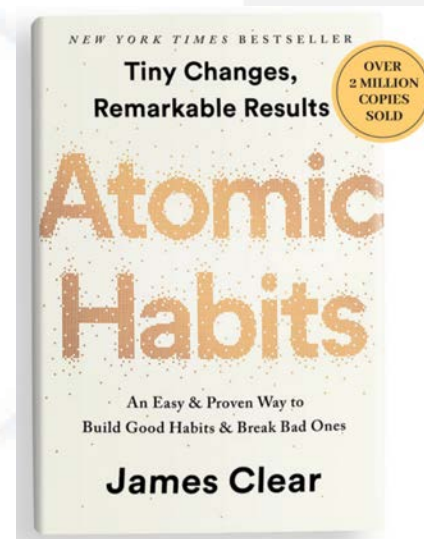
$$1\% \text{ better every day } 1.01^{365} = 37.78$$

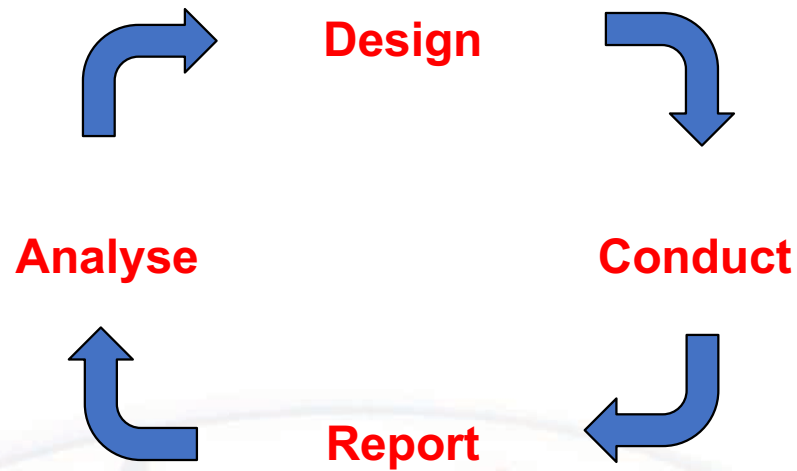
$$1\% \text{ worse every day } 0.99^{365} = 0.03$$



JamesClear.com

jamesclear.com/marginal-gains





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



Space Shuttle, NASA



NASA



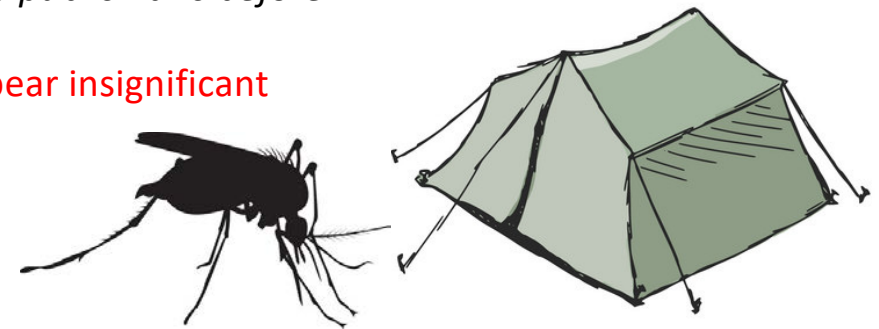
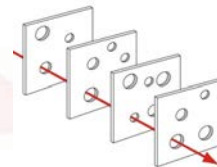
cbsnews.com



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

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/updates

Special events

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



+ Quick Start Guide

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

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.



"as often as necessary"

"because we've always done it that way"

Encourage scientists to collaborate with animal carers and technicians from Day 1

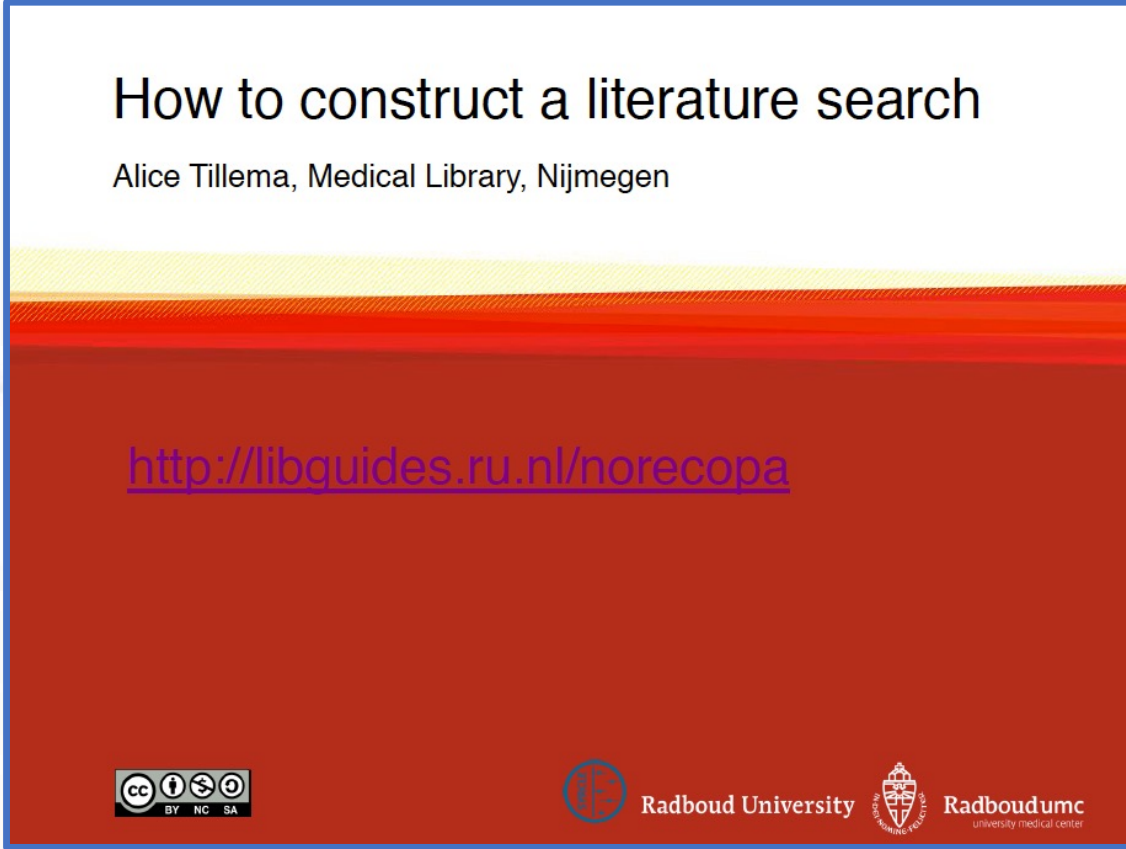
- they have a right to know and will be more motivated
- they know the possibilities (and limitations) in the animal facility
- they possess a large range of practical skills and are good at lateral thinking
- they know the animals best
- the animals know them best
- lack of involvement creates anxiety,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



Why is 3R literature hard to find?

- We need to search in several databases (poor overlapping between them)
- Too few scientists are aware of the specialist 3R-databases
- Scientists rarely use "3R" words when they write titles/abstracts/keywords for their papers
- We have no single "Journal of Alternatives"




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

wiki.norecopa.no

The Refinement Wiki

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



Designed to be

- a portal for rapid publication and dissemination of these ideas
- a place to identify experts on specific refinement techniques
- an aid to finding collaborators for multi-lab studies on refinement

Refinement Wiki



- Main page
- Recent changes
- Random page
- Help about MediaWiki
- Tools
- What links here
- Related changes
- Upload file
- Special pages
- Printable version
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Clicker training

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

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

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

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

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

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

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



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

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

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

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

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

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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.

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

Annelise Hem¹, Adrian J. Smith² & Per Solberg¹

¹Laboratory Animal Unit, National Institute of Public Health, PO Box 4404 Torshov, N-0403 Oslo and
²Laboratory Animal Unit, Norwegian School of Veterinary Science, PO Box 8146 Dep., N-0033 Oslo, Norway

© Laboratory Animals Ltd. *Laboratory Animals* (2011) 41, 1–4

Summary

A method is described for saphenous vein puncture. This enables rapid blood sampling from the same site without a need for new puncture sites. It 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

Not necessarily a high-impact journal

Reporting guidelines, e.g. ARRIVE

ARRIVE guidelines

The ARRIVE guidelines (Animal Research: Reporting of *In Vivo* Experiments) are a checklist of recommendations to improve the reporting of research involving animals – maximising the quality and reliability of published research, and enabling others to better scrutinise, evaluate and reproduce it.

[ARRIVE guidelines >](#)



NEWS

New ARRIVE guidelines 2.0 released

14 July 2020



Publications

All publications related to ARRIVE, including the guidelines themselves and

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The ARRIVE guidelines 2019: updated guidelines for reporting animal research

Nathalie Percie du Sert¹, Viki Hurst¹, Amrita Ahluwalia², Sabina Alam³, Marc T. Avey⁴, Monya Baker⁵, William J. Browne⁶, Alejandra Clark⁷, Innes C. Cuthill⁶, Ulrich Dirnagl⁸, Michael Emerson⁹, Paul Garner¹⁰, Stephen T. Holgate¹¹, David W. Howells¹², Natasha A. Karp¹³, Katie Lidster¹, Catriona J. MacCallum¹⁴, Malcolm Macleod¹⁵, Ole Petersen¹⁶, Frances Rawle¹⁷, Penny Reynolds¹⁸, Kieron Rooney¹⁹, Emily S. Sena¹⁵, Shai D. Silberberg²⁰, Thomas Steckler²¹, Hanno Würbel²²

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

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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The ARRIVE guidelines 2019: updated guidelines for reporting animal research

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

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

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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.

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



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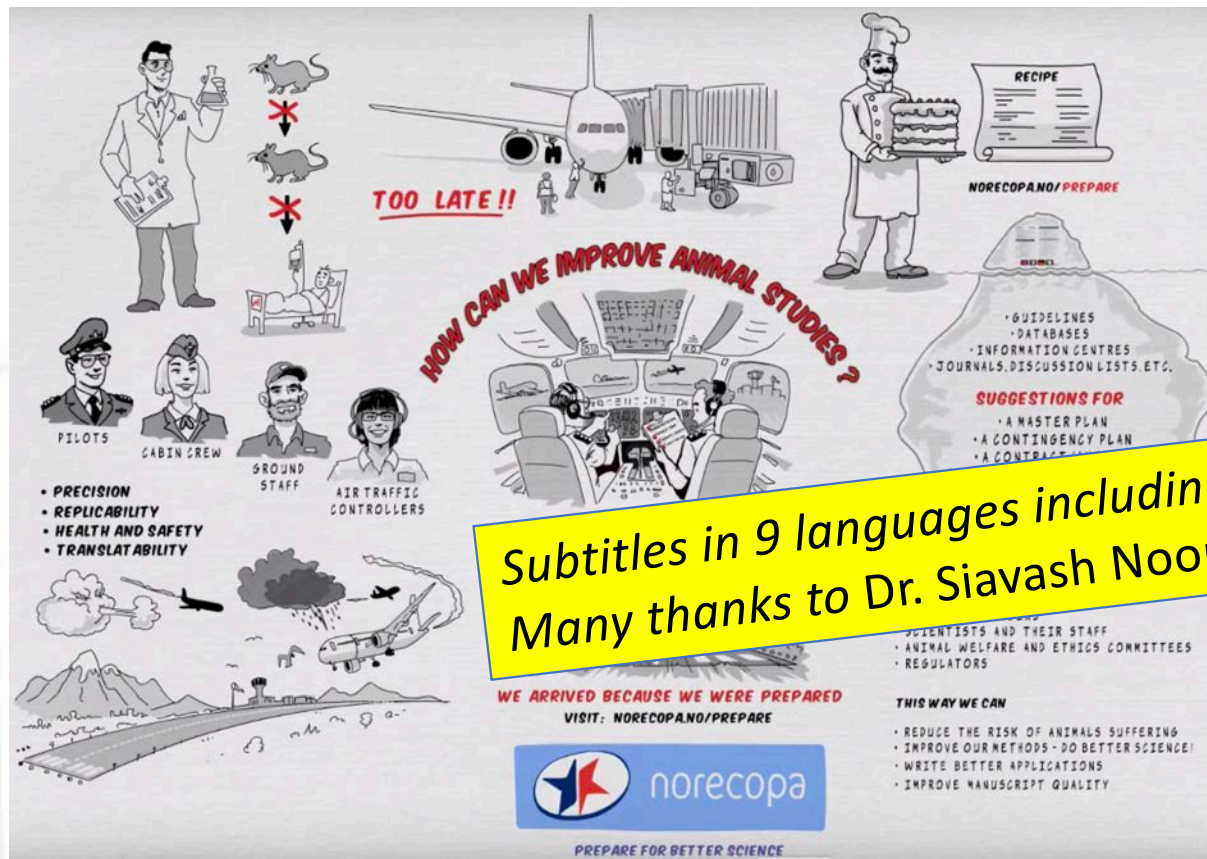
"We ARRIVED, because we were PREPARED"

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

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norecopa.no/PREPARE/film

a 3-minute cartoon film



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Many thanks to Dr. Siavash Noorbakhsh

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Newsletter no. 3-2020 from Norecopa

Welcome to Norecopa's third newsletter in 2020. *Please share this with your colleagues and friends!* In these difficult times, let us all devote time [to culturing care](#).

You can tip a friend, subscribe or unsubscribe, and share the newsletter on social media using the links above. We are on [Facebook](#) and [Twitter](#).

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Norecopa also maintains a [newsfeed](#), with English and Scandinavian language items about Laboratory Animal Science in Europe, and [an international Webinar and Meetings Calendar](#), which is updated several times a week.

This newsletter contains the following items (if some links do not work, check that your mail program has opened the whole of the newsletter):

- [Overview of 3R Education and Training Courses](#)
- [Covid-19 and Contingency Plans](#)
- [Resources for home learning](#)
- [Update on the Refinement Wiki](#)
- [Update on PREPARE](#)
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PREPARING, CARING, SHARING and FLAGGING

The scientific and welfare benefits of increased collaboration and transparency

Adrian Smith, Norecopa, Norway (adrian.smith@norecopa.no)

This poster presents a set of four icons which were made by Norecopa (the Norwegian platform for Replacement, Reduction & Refinement of animal experiments) to illustrate the 4 essential steps of good preclinical science.



Ensure that scientists and animal care staff collaborate closely from day one, to ensure all aspects of a study that potentially uses animals have been addressed

norecopa.no/PREPARE



Promote examples of improvements in the care and use of animals, for example by using the Refinement Wiki

norecopa.no/wiki



Encourage a strong Culture of Care around animal research, promoting mutual respect, animal and human wellbeing, and safety

norecopa.no/coc



Highlight advances made within the 3Rs in scientific papers, if necessary in a separate methodology paper

norecopa.no/3R

These icons can be downloaded as jpg and mp4 files from norecopa.no/PREPARE-CARE-SHARE-FLAG and used freely.

Thanks to Per Trystad for the artwork.



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