How to plan animal studies well

norecopa.no/Utrecht

Adrian Smith
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norecopa

https://norecopa.no

Content of this webinar

- practical tips for planning animal studies
- why reporting reporting guidelines alone are not sufficient to improve the quality of animal studies
- how checklists can facilitate planning and best practice
- about the PREPARE guidelines *(Disclosure: lead author)*
- where to go for more information

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

https://norecopa.no

Norecopa: PREPARE for better Science

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

approx. 9,000 webpages
300,000 hits annually

7-8 detailed newsletters per year

Norecopa: PREPARE for better Science

norecopa.no / Meetings / Meetings Calendar

norecopa.no/meetings/meetings-calendar

Webinar and Meetings calendar

July 2021

- Global day about openness in animal research (EARA event), 1 July 2021
- Monkey, Mouse or Zebrafish? Ethical and Scientific Considerations in Choosing Model Organisms for Animal Experiments, virtual event, 1 July 2021
- Berlin 3R seminar series: Replacement strategies, 1 July 2021
- BSTP Virtual Continuing Education Symposium: The
- Diverse and complex human skin
Walles), 8
els for heart diseases, webinar (Anna Koncz), 8
seminar series: Refinement and Reduction, 8 July 2021
- Zebrafish as experimental model for research, webinar series, 8, 9, 15 & 16 July 2021
- VetBioNet Summr School: Animal Infectious Disease Research: Good Practice Approaches, Ethics & 3Rs by Design, 12-14 July 2021
- KALAS International Symposium, Jeju Island, 14-17 July 2021
- Berlin 3R seminar series: Replacement and Refinement, 17 July 2021
- Norecopa: A National Consensus Platform working to advance the 3Rs internationally, webinar (Adrian Smith), 19 July 2021
- Animal Research: Critical, Challenging & Creative Thinking Course, 19-22 July 2021

+ webpages for past meetings and recorded meetings

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

norecopa.no/meetings/presentations

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

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:

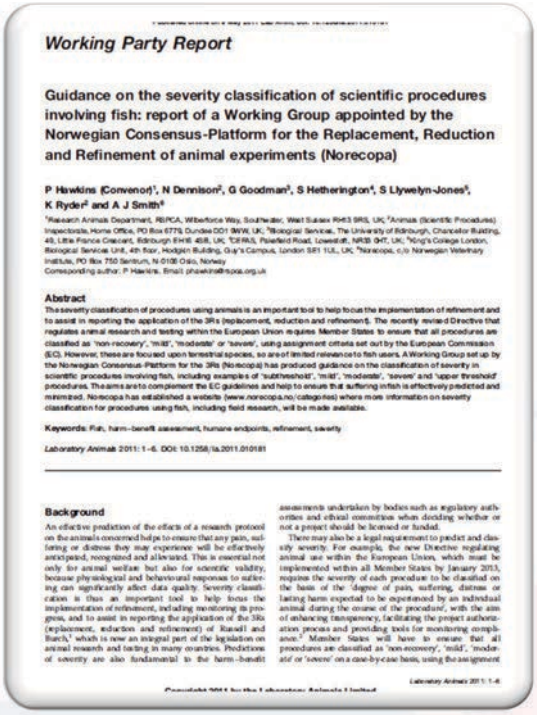
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal 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.

norecopa.no/databases-guidelines

links to over 70 other databases

From **3R-Guide** (380 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]

[1]Research Animals Department, RSPCA, Wilberforce Way, Southwater, West Sussex RH13 9RS, UK; [2]Animals (Scientific Procedures) Inspectorate, Home Office, PO Box 6779, Dundee DD1 9WW, UK; [3]Biological Services, The University of Edinburgh, Chancellor Building, 49, Little France Crescent, Edinburgh EH16 4SB, UK; [4]SFIRS, Pitsfield Road, Lowestoft, NR33 0HT, UK; [5]King's College London, Biological Services Unit, 4th floor, Hodgkin Building, Guy's Campus, London SE1 1UL, UK; [6]Norecopa, c/o Norwegian Veterinary Institute, PO Box 750 Sentrum, N-0106 Oslo, Norway
Corresponding author: P Hawkins. Email: phawkins@rspca.org.uk

Abstract

This severity classification of procedures using animals is an important tool to help focus the implementation of refinement and to assist in reporting the application of the 3Rs (replacement, reduction and refinement). The recently revised Directive that regulates animal research and testing within the European Union requires Member States to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe', using assignment criteria set out by the European Commission (EC). However, these are focused upon terrestrial species, so are of limited relevance to fish users. A Working Group set up by the Norwegian Consensus-Platform for the 3Rs (Norecopa) has produced guidance on the classification of severity in scientific procedures involving fish, including examples of 'subthreshold', 'mild', 'moderate', 'severe' and 'upper threshold' procedures. The aims are to complement the EC guidelines and help to ensure that suffering in fish is effectively predicted and minimized. Norecopa has established a website (www.norecopa.no/categories) where more information on severity classification for procedures using fish, including field research, will be made available.

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

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

Background

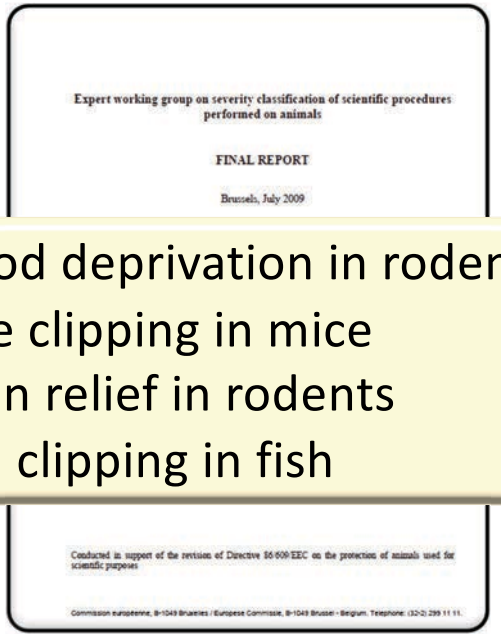
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because physiological and behavioural responses to suffering can significantly affect data quality. Severity classification is thus an important tool to help focus the implementation of refinement, including monitoring its progress, and to assist in reporting the application of the 3Rs (replacement, reduction and refinement) of Russell and Burch,[1] which is now an integral part of the legislation on animal research and testing in many countries. Predictions of severity are also fundamental to the harm–benefit assessments undertaken by bodies such as regulatory authorities and ethical committees when deciding whether or not a project should be licensed or funded.

There may also be a legal requirement to predict and classify severity. For example, the new Directive regulating animal use within the European Union, which must be implemented within all Member States by January 2013, requires the severity of each procedure to be classified on the basis of the 'degree of pain, suffering, distress or lasting harm expected to be experienced by an individual animal during the course of the procedure', with the aim of enhancing transparency, facilitating the project authorization process and providing tools for monitoring compliance.[2] Member States will have to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe' on a case-by-case basis, using the assignment

Laboratory Animals 2011; 1–6

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

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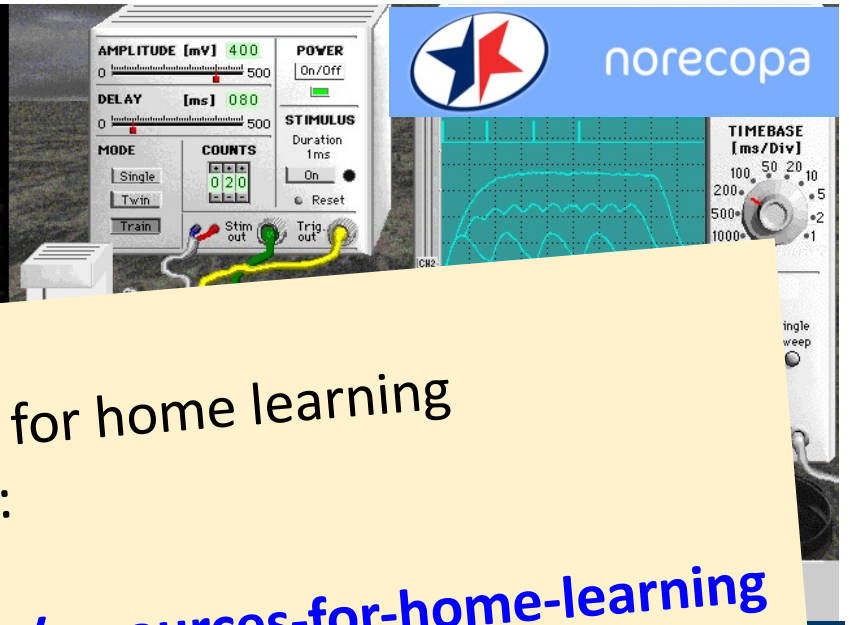
norecopa.no/categories

norecopa.no/NORINA



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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

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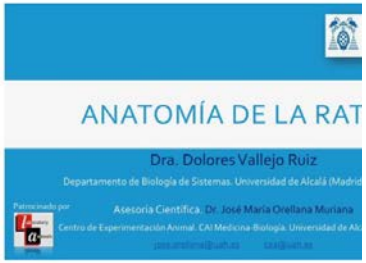
Rat s.c. injection
Norecopa | 1,380 views

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

The "reproducibility crisis"

norecopa

nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio & Video | Fo

News & Comment > News > 2017 > May > Article

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)

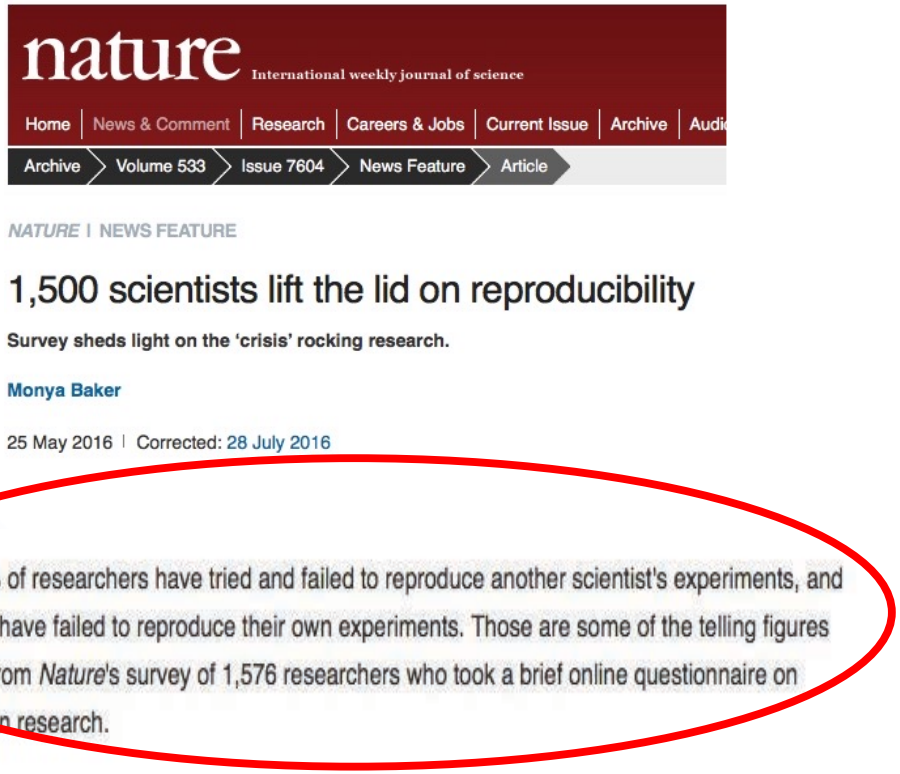
FREE

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 International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audi

Archive > Volume 533 > Issue 7604 > News Feature > Article

NATURE | NEWS FEATURE

1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

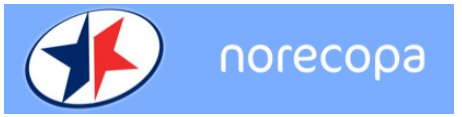
25 May 2016 | Corrected: 28 July 2016

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

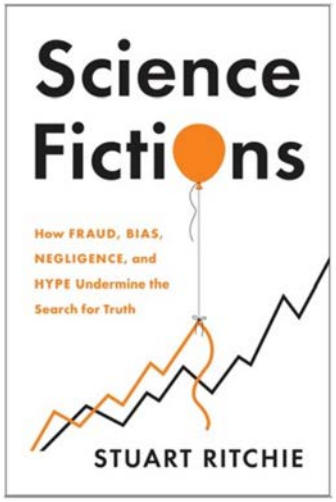


norecopa.no / TextBase / Science Fictions

Science Fictions

By Stuart Ritchie

Record number: 139853



An insider's view of science reveals why many scientific results cannot be relied upon – and how the system can be reformed.

Science is how we understand the world. Yet failures in peer review and mistakes in statistics have rendered a shocking number of scientific studies useless – or, worse, badly misleading. Such errors have distorted our knowledge in fields as wide-ranging as medicine, physics, nutrition, education, genetics, economics, and the search for extraterrestrial life. As *Science Fictions* makes clear, the current system of research funding and publication not only fails to safeguard us from blunders but actively encourages bad science – with sometimes deadly consequences.

Stuart Ritchie's own work challenging an infamous psychology experiment helped spark what is now widely known as the "replication crisis," the realization that supposed scientific truths are often just plain wrong. Now, he reveals the very human biases, misunderstandings, and

norecopa.no/textbase/science-fictions

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nature human behaviour

Perspective | Open Access | Published: 10 January 2017

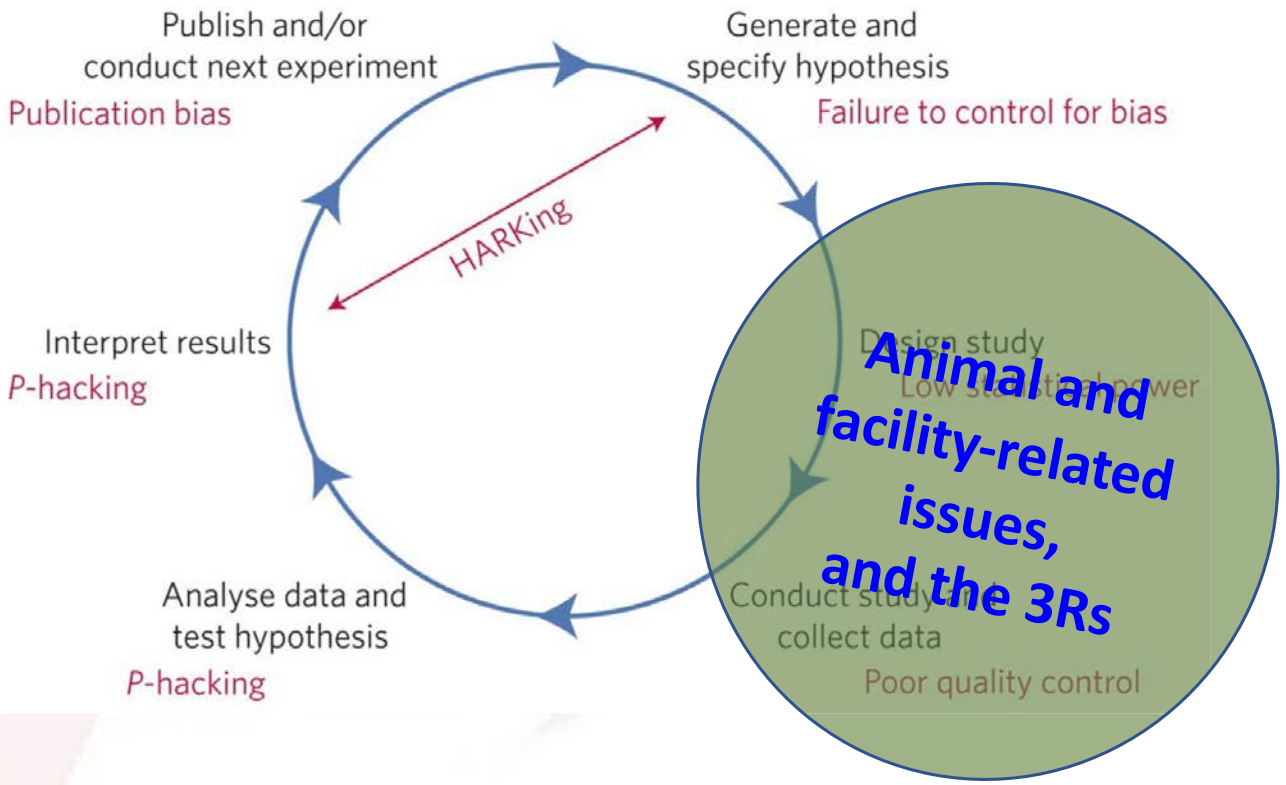
A manifesto for reproducible science

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

Nature Human Behaviour 1, Artic

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



My personal view

- One of the greatest challenges to reproducibility lies within the animals themselves and the way in which they are used
- I suspect that many scientists are unaware of the size of this challenge, or they assume that the animal facility is dealing with it

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

'achieving reproducible and reliable preclinical research results is a joint responsibility that requires a partnership between the investigative team and the animal care and use program staff.'

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

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, 1998 (Rehbinder)
- Guidelines for re… …ish, 2000 (Smith & Brattelid)
- … …emy *et al.*)
- … 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.*)

+ reporting guidelines in the journal itself

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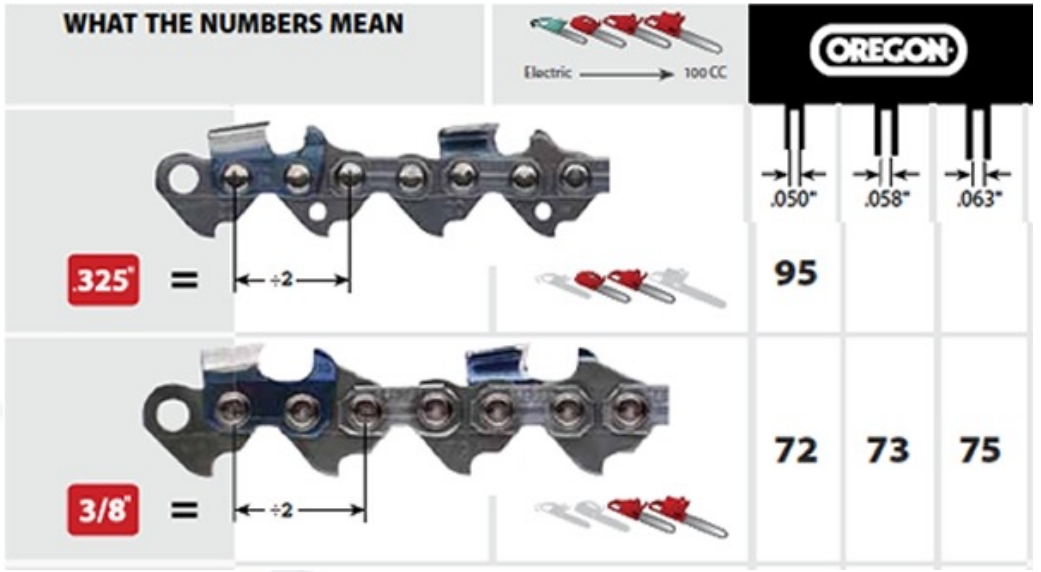
The easy parts of design and reporting:



arborist101.com

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

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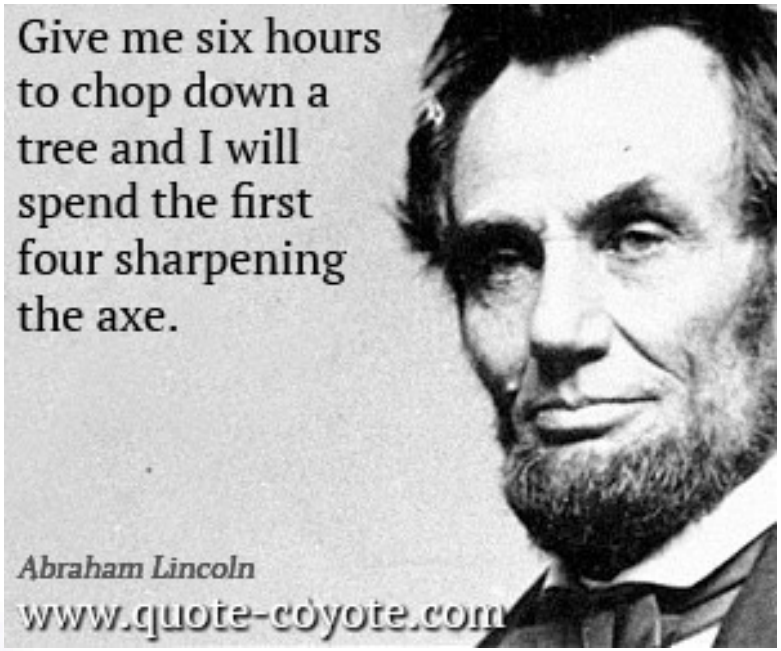
Critical issues behind the scenes that may not get reported:

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

These issues are discussed long before the actual work

leaderonomics.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

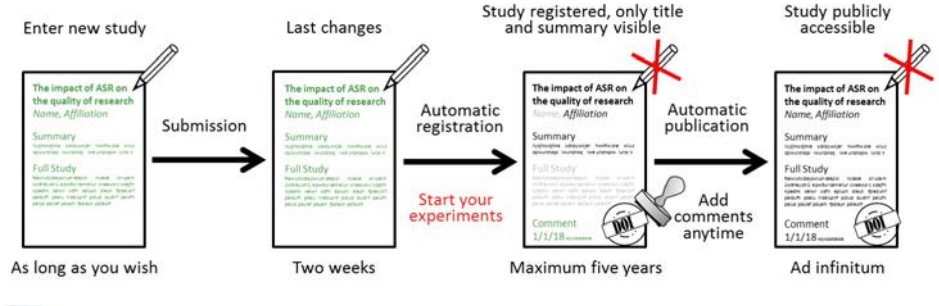
Abstract

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.

Preregistration of a study

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

PRECLINICALTRIALS.EU
International register of preclinical trial protocols



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
- The Animal Study Registry (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

How do other professionals achieve reproducibility?

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

What can we learn from the aviation industry?
Reproducibility and precision in a variable environment…

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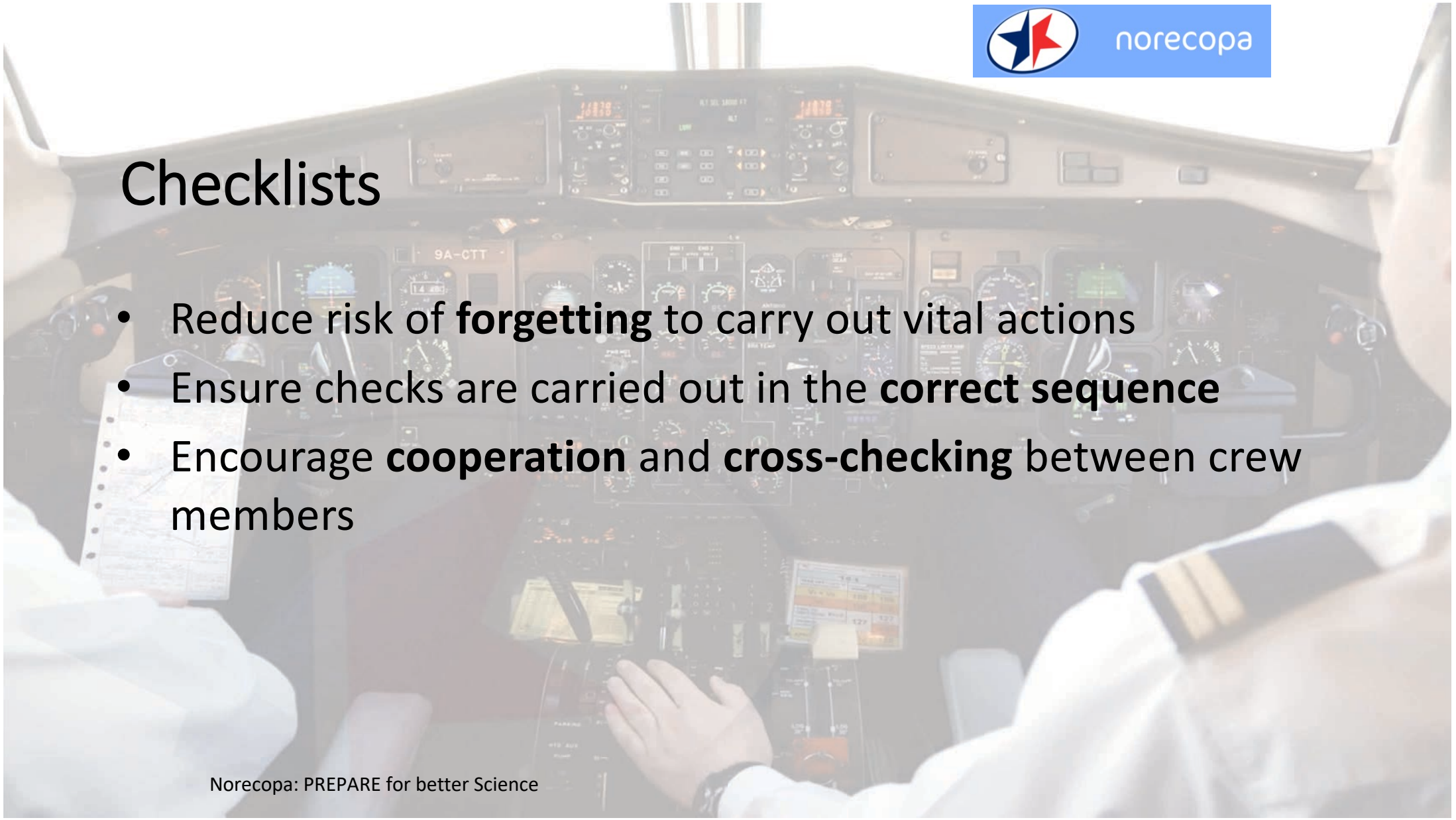
10-15 checklists even on short routine flights



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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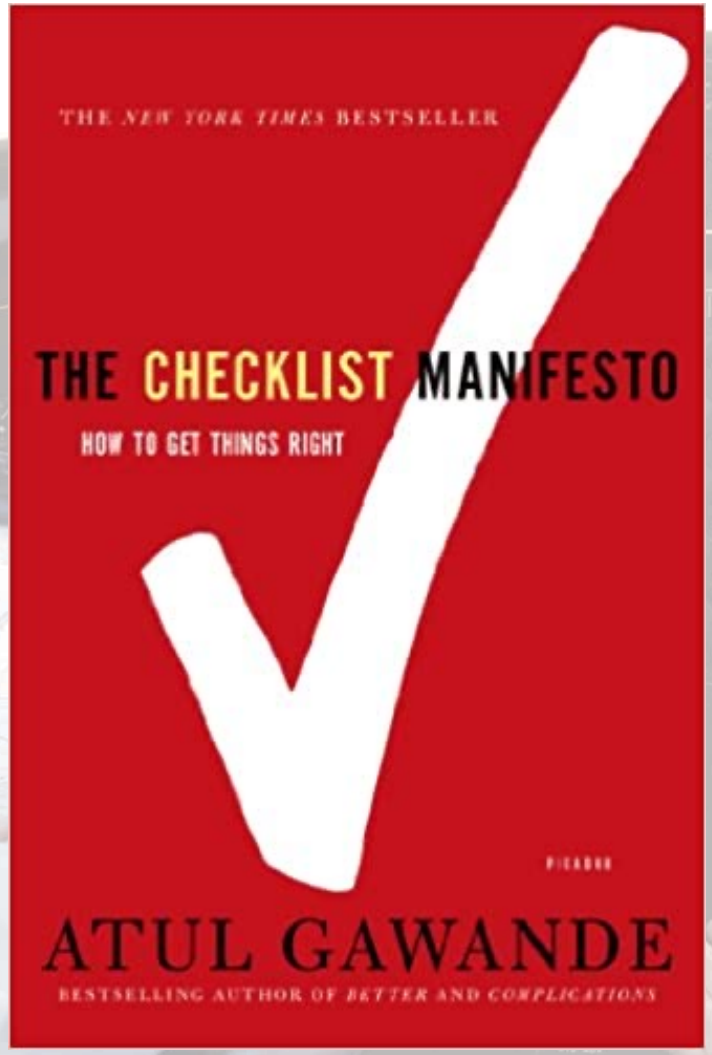

Surgical Safety Checklist

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 **Difficult airway or aspiration risk?** ☐ No ☐ Yes, and equipment/assistance available **Risk of >500ml blood loss (7ml/kg in children)?** ☐ No ☐ Yes, and two IVs/central access and fluids planned	**To Anaesthetist:** ☐ Are there any patient-specific concerns? **To Nursing Team:** ☐ Has sterility (including indicator results) been confirmed? ☐ Are there equipment issues or any concerns? **Is essential imaging displayed?** ☐ Yes ☐ Not applicable	**To Surgeon, Anaesthetist and Nurse:** ☐ What are the key concerns for recovery and management of this patient?

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

Revised 1 / 2009

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

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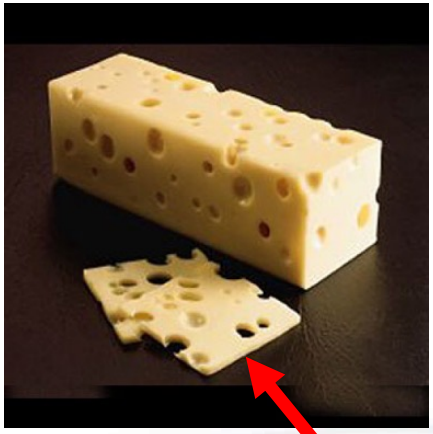
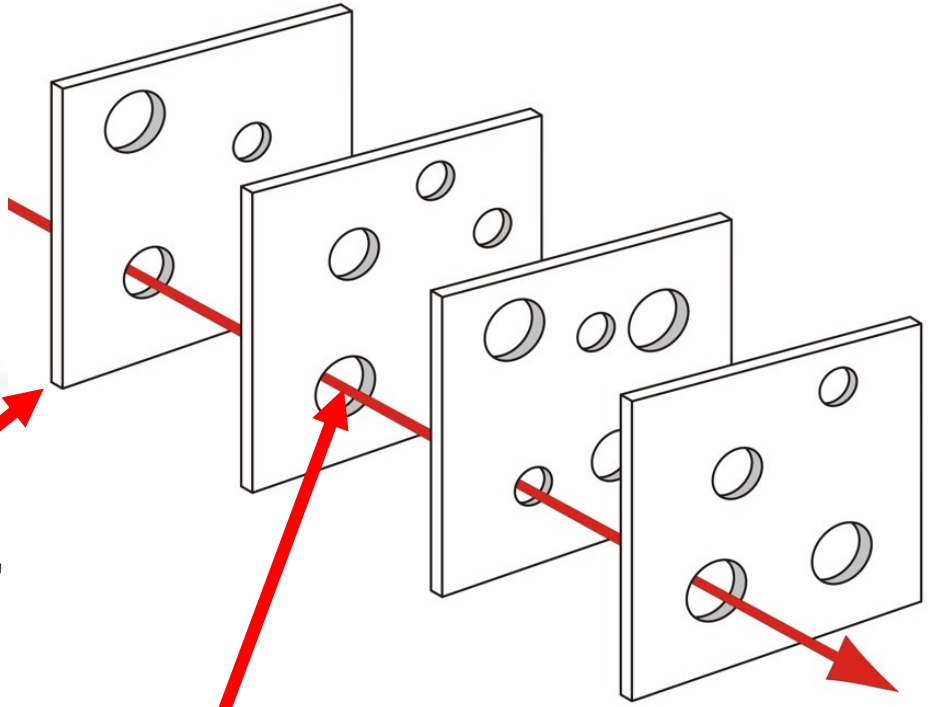
amazon.com/gp/product/0312430000

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

Program Description

A. **Animal Care and Use Program**

B. **Animal environment, Housing and Management**

C. **Veterinary Care**

D. **Physical plant**

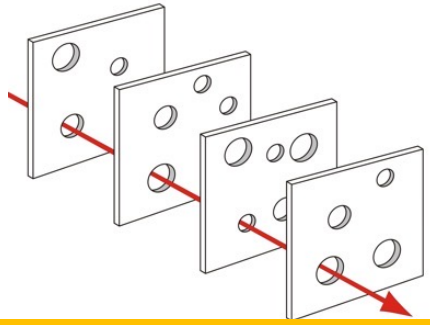
Work in the spirit of AAALAC, even if not accredited!

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 anaph
  - 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)*

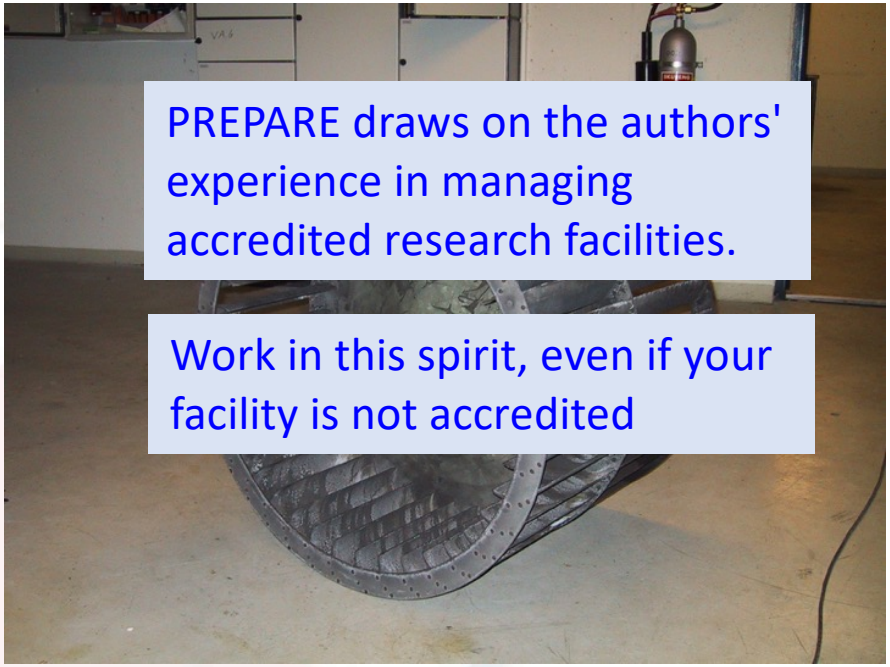


Photo: NMBU

Good advice is emerging from the Covid-19 pandemic

norecopa

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

CATEGORY		CONSIDERATIONS/SUGGESTIONS	
PERSONNEL Provide 'essential worker' letter to show authorities, include home address. Consider whether company/ photo i.d. would be helpful 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 Support mental health Consider mindfulness apps, Convert empty animal room into a relaxation/yoga room (online yoga classes).	ANIMAL TECHNICIANS	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	
		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	
		Review teams regularly – this may need to be daily in some situations	
		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	
		Limit reliance on public transport methods. Accommodate parking where possible to allow individuals to travel by car	
			Ensure all alarm systems are checked regularly and are functional. Monitor, record and act on all alarms
			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
		DELIVERIES	
		VETS	equired
	RESEARCHERS	ANIMALS / BREEDING	Ensure all non-replaceable lines are cryopreserved
			Consider stopping breeding of lines that are frozen down and have been on "tick over"
			Breed only for colony management, i.e. minimum number of breeding pairs to maintain the health of the colony
			Avoid breeding animals with phenotype – maintain animals where homozygotes may be phenotypic as wild type x heterozygote crosses to avoid generation of homozygotes
			Genotype promptly in order to identify animals required for ongoing breeding and cull animals not required ASAP
			Consider outsourcing genotyping if internal facilities are closed
	ESTABLISHMENT LICENCE HOLDER	REDUCE STOCK	Do not start new work unless absolutely essential/ internal review has been performed that confirms that the work can be properly serviced
			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
			There may be reasons for prioritising ongoing work with some species (e.g. NHPs)
			If the facilities allow, consolidate animals to one area, check light cycle, room temps & designation first
			Spread work evenly / reduce cleaning of cages – but not to extent that welfare could be compromised
			Re-assess stock levels /staff levels at least once per week
			Cull animals that are not going to be needed for colony management and cannot otherwise be used
			Avoid unnecessary movement of animals
			Prioritise the movement of animals to other facilities or establishments for contingency of valuable lines.
		ACCESS	Check your facility/ies will be open – Provide a list of names requiring access. Check with security how and when essential staff will access
			Confirm how essential supplies and waste contractors will service the facility/ies
		SUPPLIES	Stock up on diet, bedding, nesting materials, PPE, disinfectants and other essentials, aim for a minimum of 3 months
			Ensure there will there be Liquid nitrogen / dry ice for cryopreserved stocks
			Have stocks of CO_2 and sodium pentobarbitone and any other drugs as directed by the NVS
	ENGINEERS	ESTATES / ENGINEERS	Check your contractors are working and get emergency contacts. Maintain a list of mobile numbers, available to everyone
			Consider if essential equipment will require servicing or repair. Ensure that you have a plan to enable this
			Will waste be being removed from site? – prepare an area for on-site storage if necessary
		RECORDS	**Record all difficult decisions taken. What/ when /why and any related evidence**

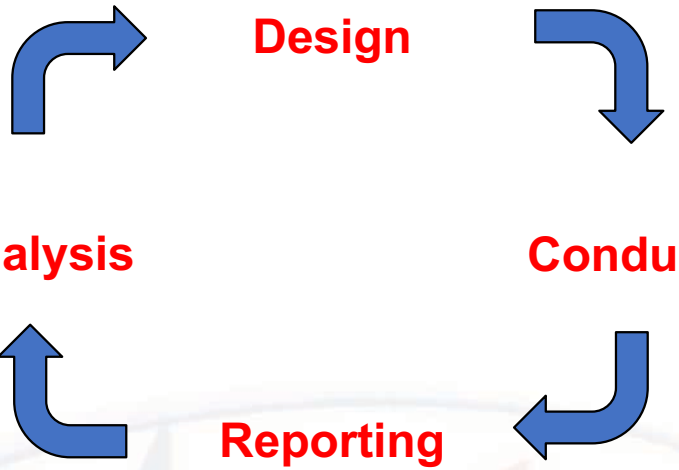
norecopa.no/be-prepared

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

Norecopa: PREPARE for better Science

A simple but effective Master Plan

Norecopa: PREPARE for better Science



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*

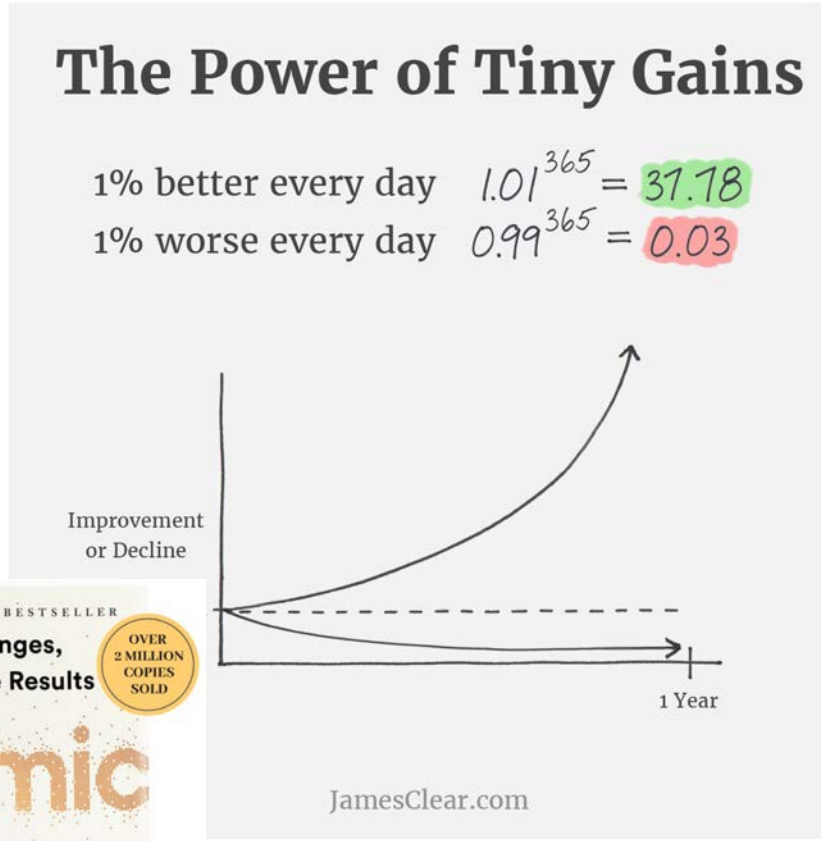
Instead of hoping for a paradigm shift (= immediate animal replacement):

Small improvements of many small components

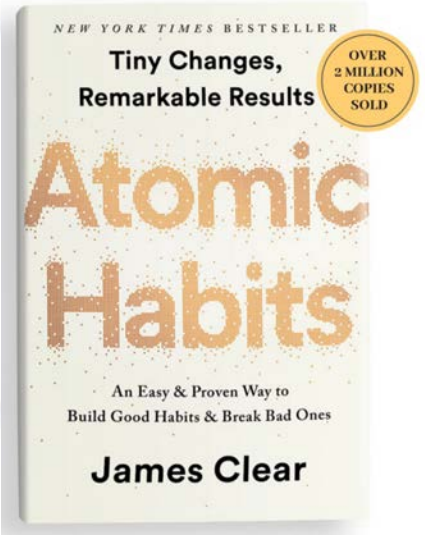
1908-2003: UK cycling team won only 1 gold medal and never won the Tour de France

2003: hired Dave Brailsford

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

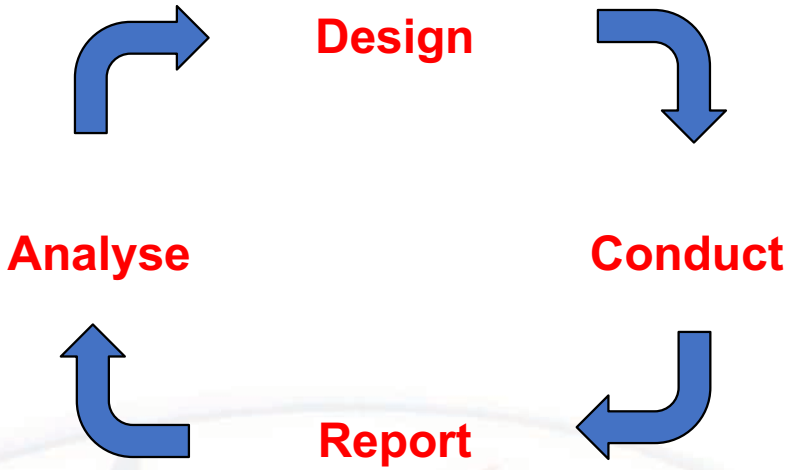


jamesclear.com/marginal-gains



Lab animal perspective:

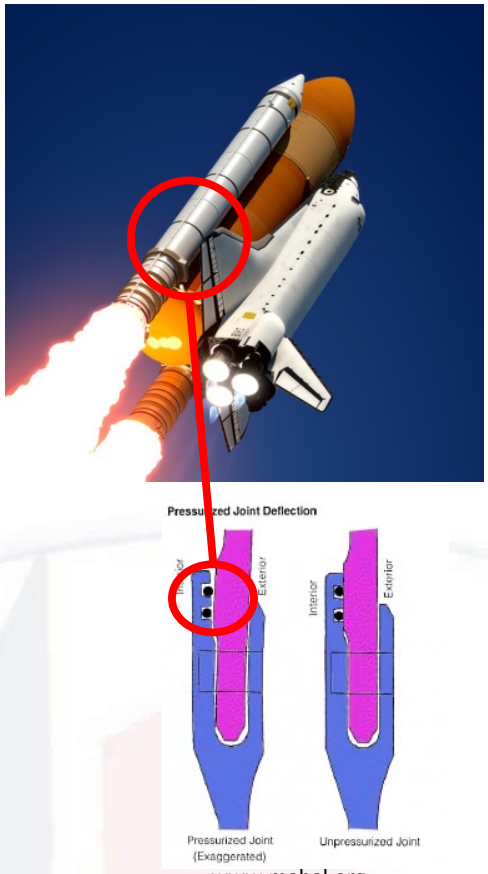
Lilley E, Jennings M. (2013) Refinement: Lessons from the 2012 Olympics. *Alternatives to Laboratory Animals (ATLA)* 41(3):P28-P29. doi:10.1177/026119291304100309
rspca.org.uk/webContent/staticImages/Downloads/2012Olympics.pdf



Space Shuttle, NASA

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

1) Challenger



www.mahal.org

Flexible rubber O-rings (seen in cross-section as black dots) prevent hot gases from escaping between the joints of the solid rocket boosters. These rings lose some of their flexibility at low temperatures.

Challenger was launched in cold weather in January 1986. The O-rings on one booster rocket malfunctioned, allowing hot gases to ignite the contents of the liquid fuel tank. The vehicle subsequently disintegrated, killing all 7 crew members.
Photo: no.wikipedia.org

2) Columbia

Photo: gettyimages.no

White insulating tiles were glued to the shuttle to prevent it from burning up on re-entry (the black areas on this photo are areas where tiles have not yet been installed).

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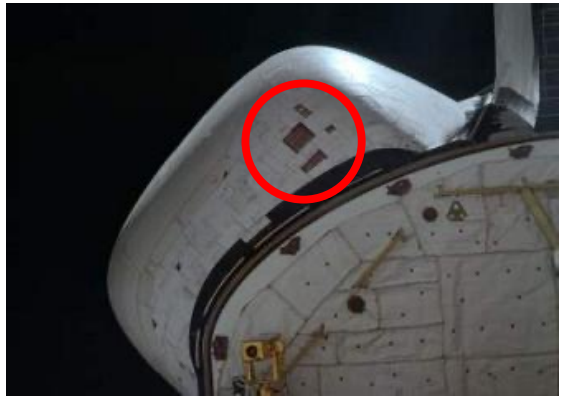


First shuttle flight, Columbia, in April 1981.
Some tiles fell off at take-off, but these were not on a critical part of the vehicle.
Photo: nasaspaceflight.com

Columbia burnt up in 2003, killing all 7 crew members, because tiles on a critical area (the leading edge of the wing) fell off.
Photo: cbsnews.com

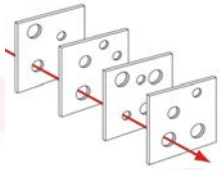
NASA

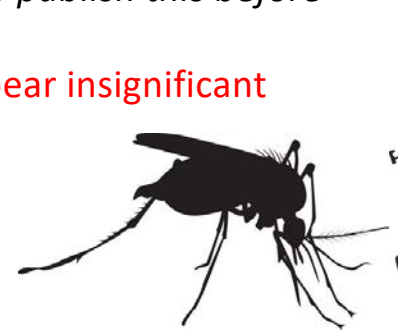
cbsnews.com

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!





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!

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"

CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

Refine
Reduce
Replace

Operating principles

Recent incidents

Injury of the mesentery by vertebral kyphoplasty

Mouse neonates exposed to CO2

Animal escapes during transportation

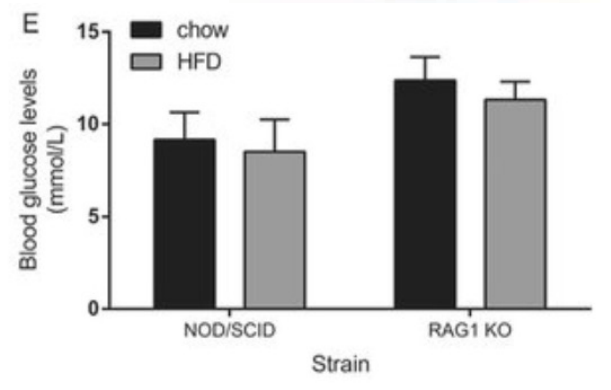
Kidney damage in mouse after surgery on heating mat

Soft tissue implant in rabbit

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

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

Neglected Factors in Pharmacology and Neuroscience Research: Biopharmaceutics, Animal Characteristics, Maintenance, Testing Conditions

By Claassen, Volkert

Record number: 13335 (legacy id: 6153)

The objective of this book is to indicate those variables which in general may need a better control. Examples, gathered from the literature, are presented to illustrate the impact that those neglected variables may have on various characteristics. The book presents a series of representatives studies from a broad field of interest so that insight can be obtained about the potential effects of these parameters in experimental outcomes. In this way, an impetus should be given to the critical consideration of test design and limitations of conclusions from experimental results. In part, the book is written as a reaction to frustrations endured during pharmacological research of many years' standing, and therefore the choice of examples from the literature is largely related to this discipline. As pharmacological research is to a large extent based on the other life sciences, this volume may be of interest to a much broader audience. This may certainly be the case for pharmacokineticists and toxicologists for whom drugs are the main object of study. This book may also help to improve test designs for biochemists and physiologists, not only when using drugs as tools in their experiments, but also to improve generally the control of animal characteristics and test conditions. This book is Volume 12 in a series entitled *Techniques in the Behavioral and Neural Sciences*.

Comments & References: First Edition. 496 pages. Paperback. A review is available in Laboratory Animals, April 1996, Volume 30 (2).

Review:

'This book is essential reading for anybody that wishes to take the problem of experimental variability seriously. There are no magic cures offered for experimental problems, but there are many explanations offered within this book. A worthwhile addition to any library.'

norecopa.no/textbase/neglected-factors-in-pharmacology-and-neuroscience-research-biopharmaceutics-animal-characteristics-maintenance-testing-conditions

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

Some of the common animal-related issues…

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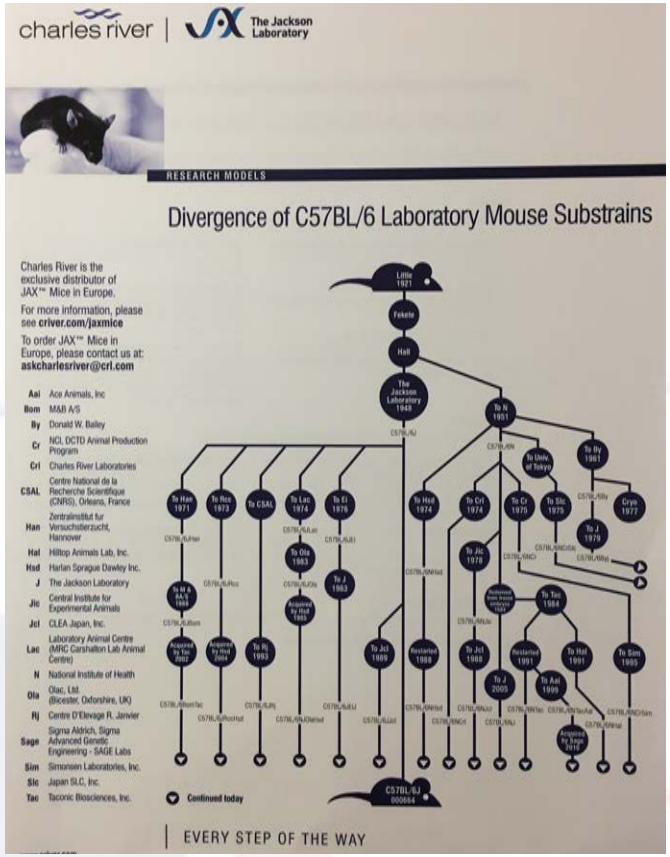
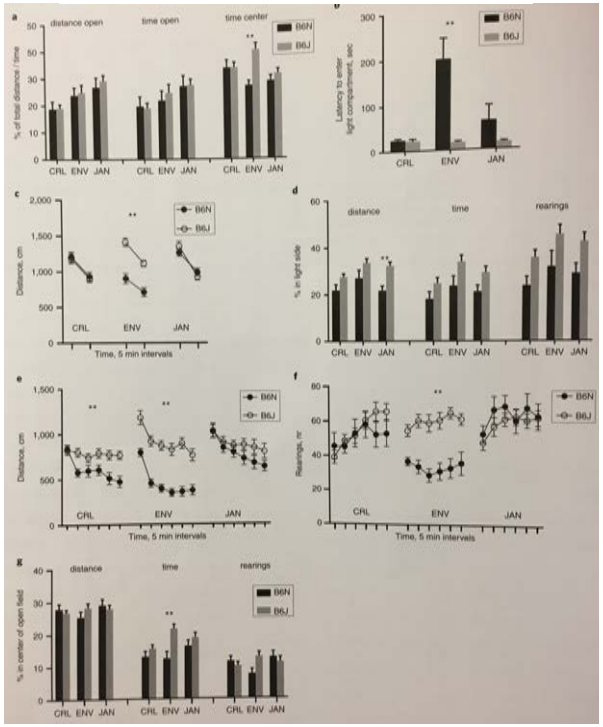
The C57BL/6 mouse



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

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

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

Norecopa: PREPARE for better Science

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

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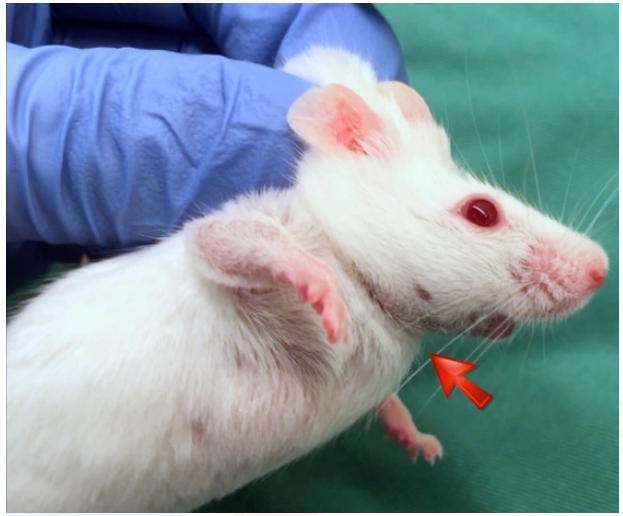
Baseline

Immobilizing
Sinus bradycardia, VEC

Reprinted with permission. 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 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

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.

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

© 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

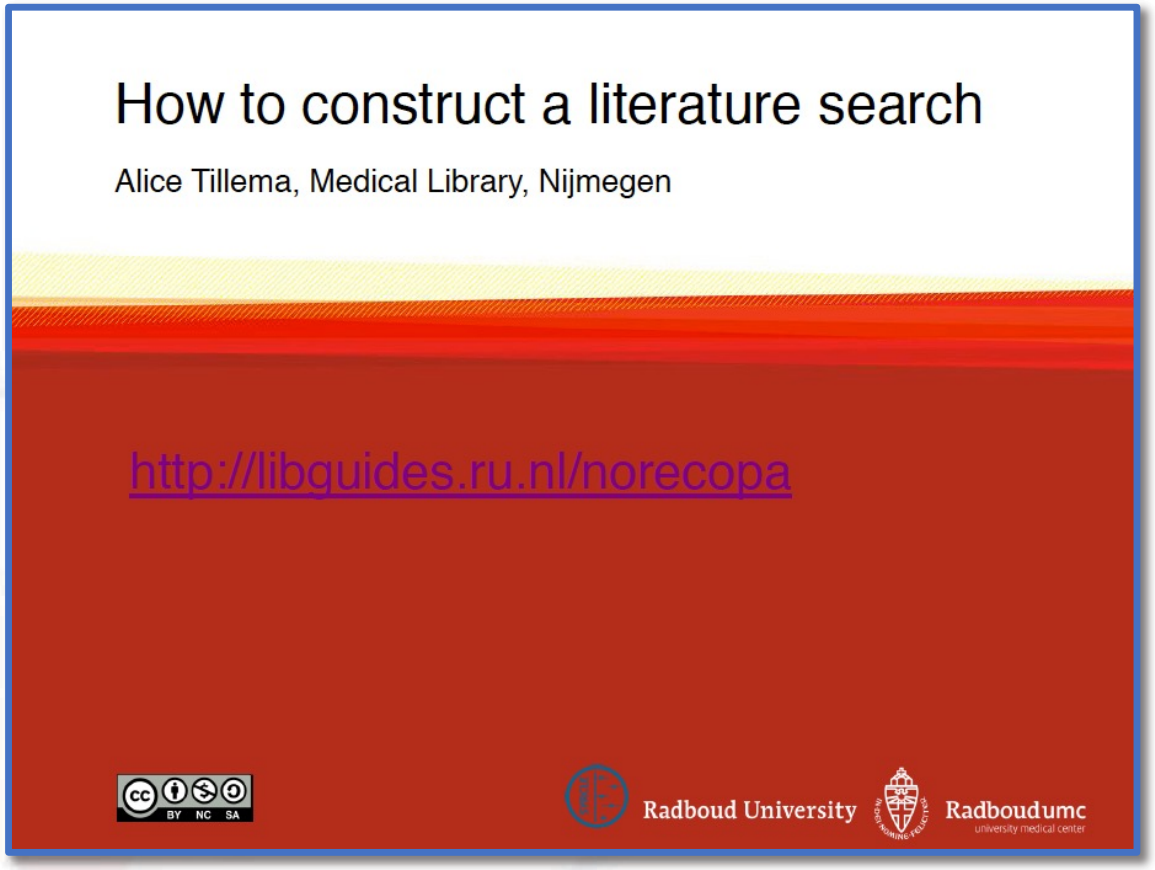
Not necessarily a high-impact journal

norecopa

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



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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

wiki.norecopa.no

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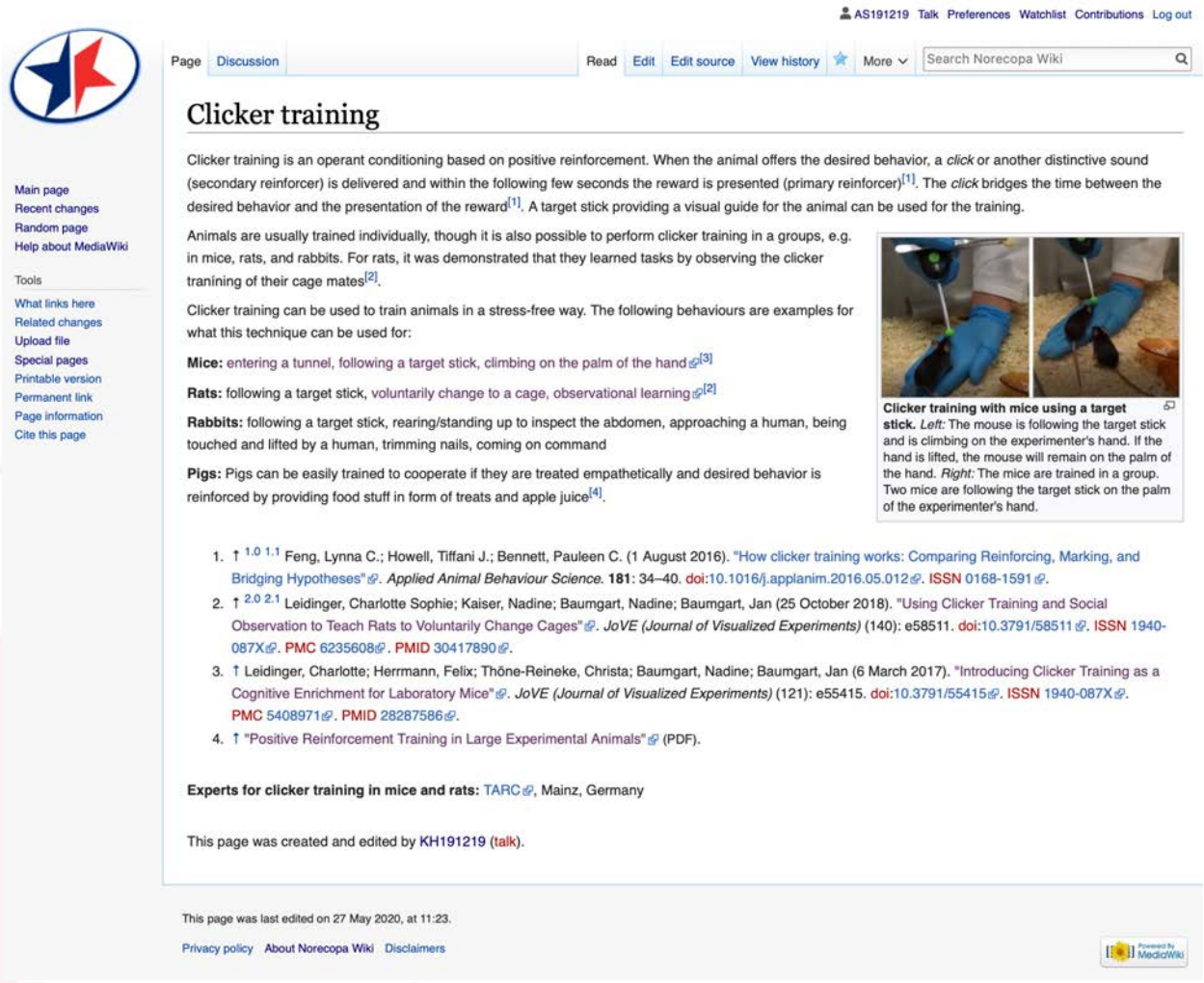

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Clicker training

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Cite this page

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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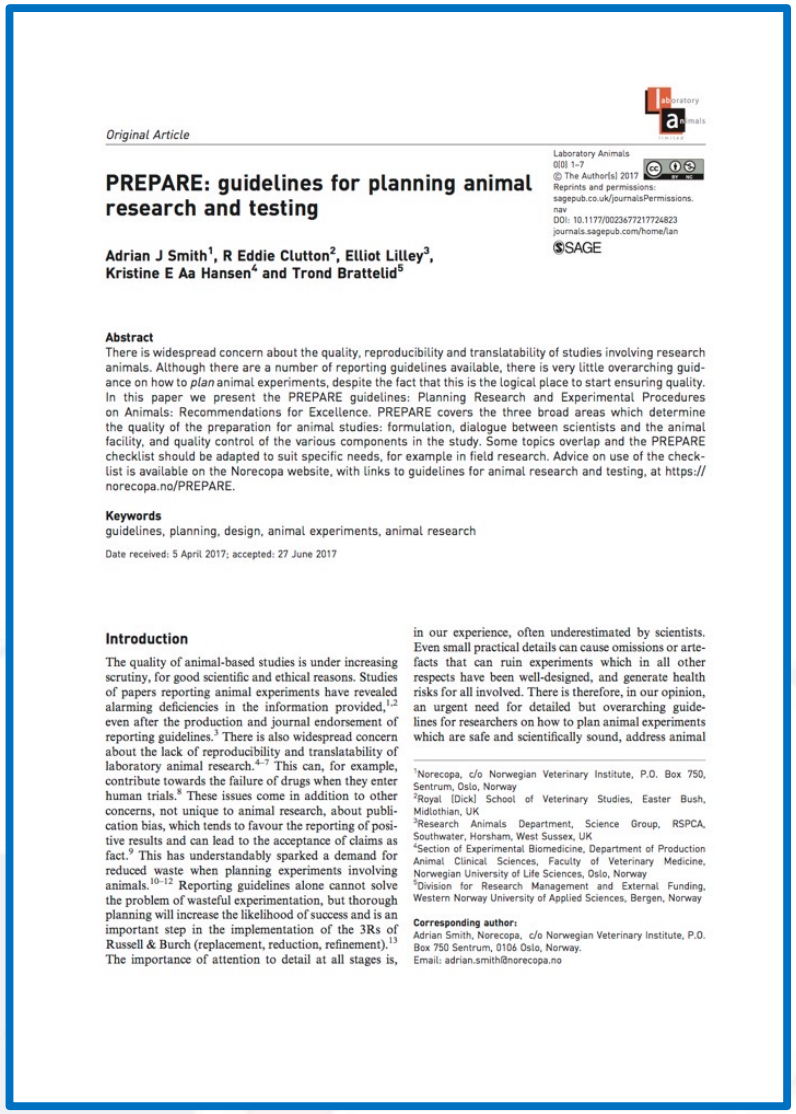
Pages created as of today

- Acclimatisation
- Adrian Smith
- Anaesthesia in neonates
- Analgesia
- Blood sampling of hamsters
- Blood sampling of rainbow trout
- Clicker training
- Contingency plans
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- General discusson on use of analgesics
- Hot Bead Sterilisers
- Housing research fish
- Humane endpoints
- Intraperitoneal injection
- Ketamine and alpha-2 agonist combinations
- Lumpfish
- Main Page
- Metabolic cages
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Rotarod Test
- TTEAM and TTouch
- Tail vein injection
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality



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

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Norecopa: PREPARE for better Science

Pre-published under Open Access on 3 August 2017 in *Laboratory Animals*, sponsored by the Universities Federation for Animal Welfare (UFAW), UK

https://doi.org/10.1177/0023677217724823

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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

Maybe the study shouldn't go ahead

Systematic review of published research?

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Items in pink are not typically highlighted in reporting guidelines

norecopa.no/PREPARE/prepare-checklist

PREPARE

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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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 st

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 topi
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://norecopa.no/PREPARE**.
The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	☐ 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. ☐ Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	☐ Construct a lay summary. ☐ In dialogue with ethics committees, consider whether statements about this type of research have already been produced. ☐ Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities). ☐ Consider pre-registration and the publication of negative results. ☐ Perform a harm-benefit assessment and justify any likely animal harm. ☐ Discuss the learning objectives, if the animal use is for educational or training purposes. ☐ Allocate a severity classification to the project. ☐ Define objective, easily measurable and unequivocal humane endpoints. ☐ Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	☐ Consider pilot studies, statistical power and significance levels. ☐ Define the experimental unit and decide upon animal numbers. ☐ Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.

Three Rs!

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

Further information
https://norecopa.no/PREPARE / *post@norecopa.no* / @norecopa

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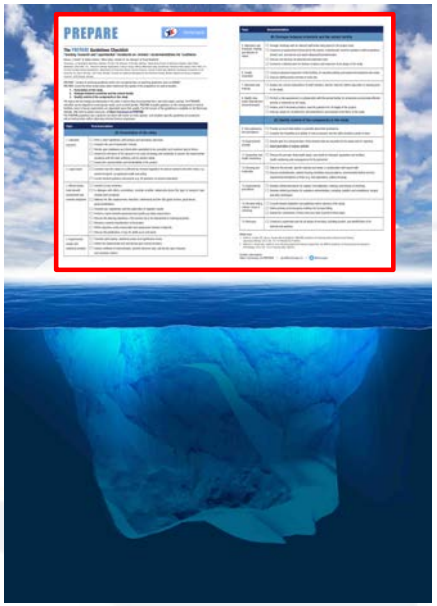
In addition to the checklist, much more information is available on:

norecopa.no/PREPARE



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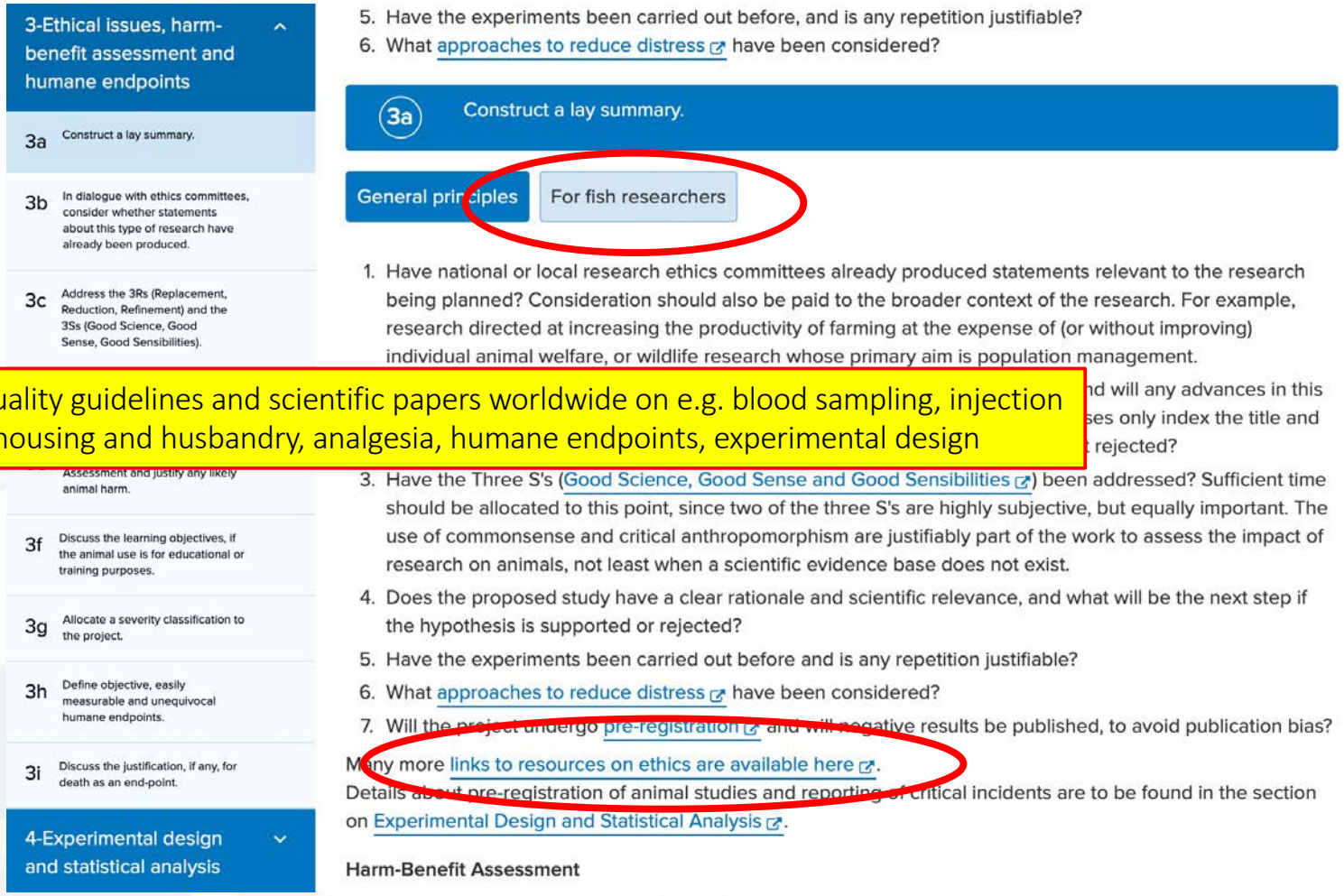

Links to quality guidelines and scientific papers worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design

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A simple but effective Master Plan

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A contract between the animal facility and the research group

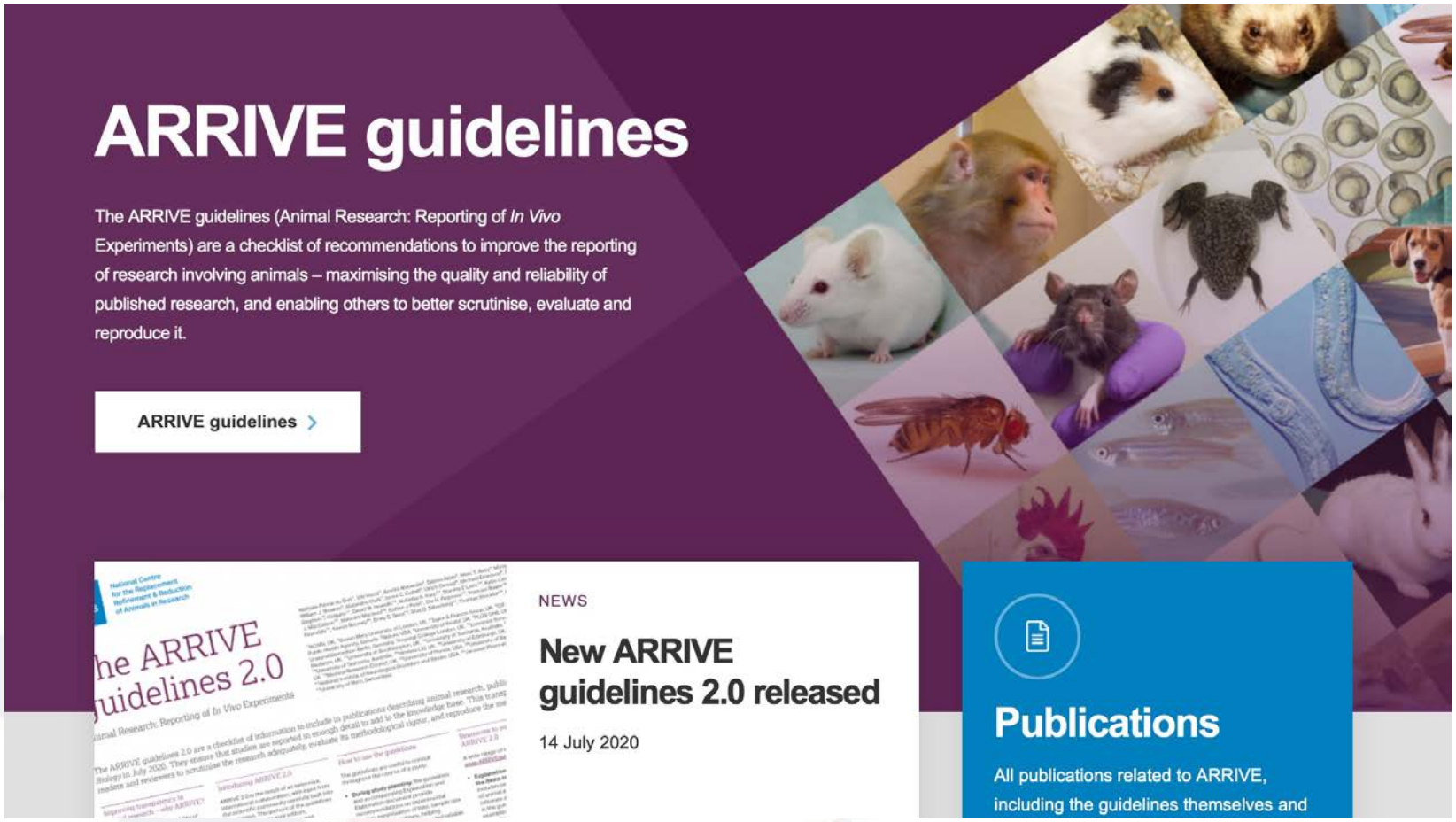
The division of labour and responsibilities

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			

Reporting guidelines, e.g. ARRIVE



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

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

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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The ARRIVE guidelines 2019: updated guidelines for reporting animal research

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.

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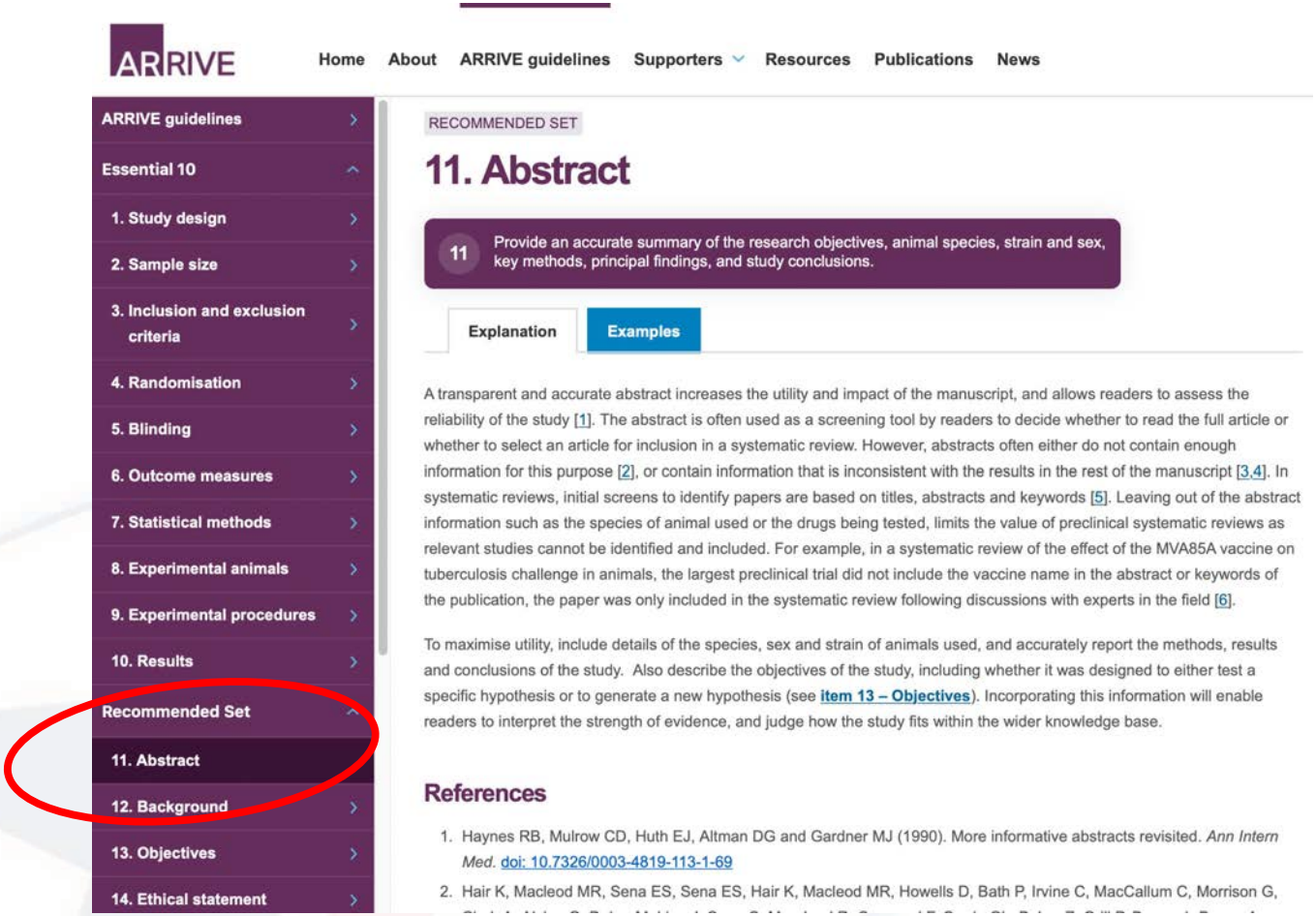

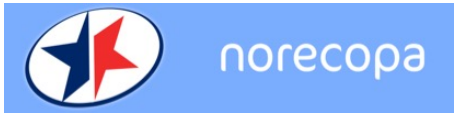

norecopa.no / PREPARE / 10-Experimental animals

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 breed
   - Any necessary pre-treatment (e.g. castration or
     for this
   - Name and address of the supplier/breeder, or, if
     method of capture and transport
   - Health status (e.g. germ-free, gnotobiotic, SPF, c
   - Re-use of animals, which should be justified and
     legislation
   - Any plans for release or re-homing, which may b

More resources

- Examples and references from ARRIVE 2.0
- 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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DEPART guidelines for osteoarthritis research

'Most of the current instruments/checklists are designed for use after study completion during publication or in subsequent systematic review of Risk of Bias and quality-of-evidence.'

Osteoarthritis and Cartilage

OARSI OSTEOARTHRITIS RESEARCH SOCIETY INTERNATIONAL

Considerations for the design and execution of protocols for animal research and treatment to improve reproducibility and standardization: "DEPART well-prepared and ARRIVE safely"

M.M. Smith †, E.C. Clarke ‡, C.B. Little † *

norecopa.no/3r-guide/depart-guidelines-for-osteoarthritis-research


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"We ARRIVED, because we were PREPARED"
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✓ Advancement of the 3Rs
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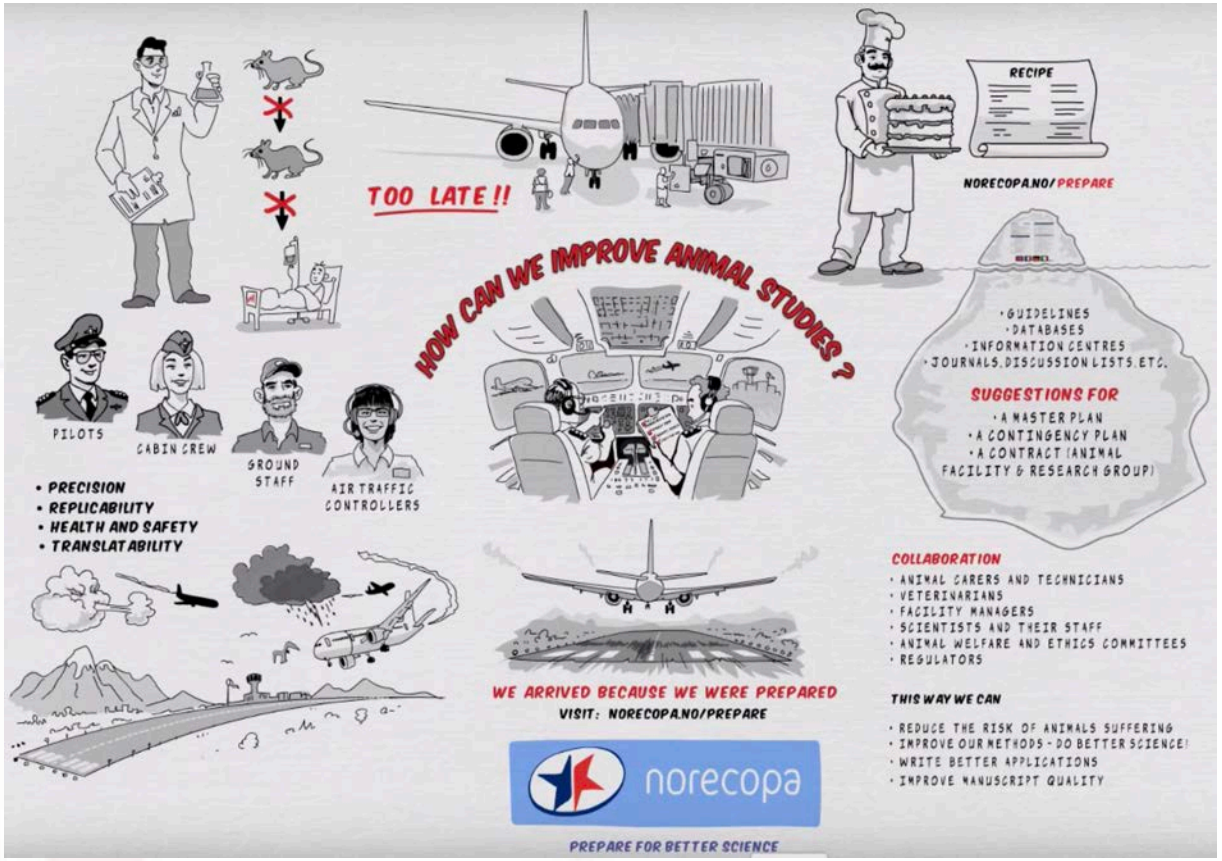
a 3-minute cartoon film



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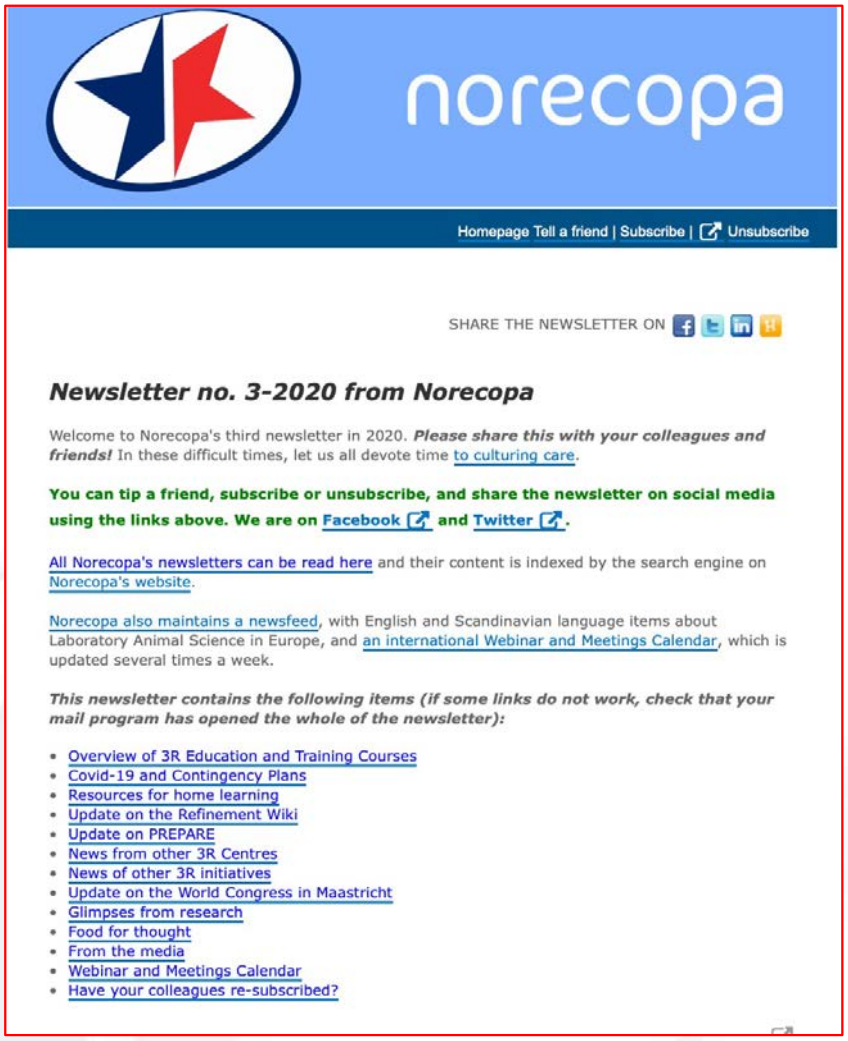

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Newsletter no. 3-2020 from Norecopa

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.

All Norecopa's newsletters can be read here and their content is indexed by the search engine on Norecopa's website.

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
- News from other 3R Centres
- News of other 3R initiatives
- Update on the World Congress in Maastricht
- Glimpses from research
- Food for thought
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- Have your colleagues re-subscribed?

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900 international subscribers

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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