Experiences with planning animal studies:

improved scientific output and animal welfare

norecopa.no/HK

Adrian Smith
adrian.smith@norecopa.no

Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of *global* 3R resources

we welcome more from you!

https://norecopa.no

Norecopa: PREPARE for better Science

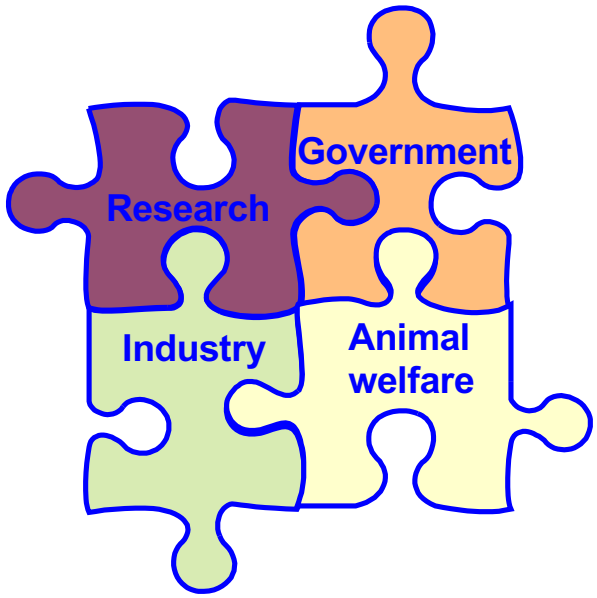
The background for the foundation of Norecopa

peta.org

fbresearch.org

European Consensus-Platform for Alternatives
ecopa.eu

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



Norecopa was established in 2007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Indian Ocean
South Pacific Ocean
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Argentina
New Zealand
ecopa (7 countries)
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Centres

- [x] Replacement
- [x] Reduction
- [x] Refinement
- [ ] ecopa

Associations

- [x] AFLAS (includes South Korea)
- [x] Culture of Care Network
- [x] EU-NETVAL
- [x] EU3Rnet
- [x] FELASA
- [x] FESSACAL
- [ ] Norecopa
- [x] Scand-LAS
- [ ] ecopa

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

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NORSK ENGLISH
Search:
About Norecopa Alternatives Databases & Guidelines Education Legislation Meetings More resources News PREPARE Species Wiki
Fish 2005 | Wildlife 2008 | Fish 2009 | Past meetings
Meetings Calendar
+ webpages for past meetings and recorded meetings
norecopa.no/meetings/meetings-calendar
Webinar and Meetings calendar
Links to past meetings can be accessed here (Many of these links will eventually die out, but they still give a useful overview of organisers and locations of relevant meetings within laboratory animal science, and it is often possible to contact the organisers for more information).
N.B. For information about courses in laboratory animal science, click here.
September 2021
Intensive Course on Experimental Design and Biostatistics, FGB online course, 3 & 17 September 2021
7th International Bio-Logging Science Symposium, Honolulu and online, 12-17 September 2021
The Three Rs and Animal Use in Science (MOOC Re-run), 13 September - 20 October 2021
2V - Personnel Security in Laboratory Biosecurity Programs, ABSA webinar (Ben Perman & Lindsay Odell), 14-16 September 2021
Experiences with Planning Animal Studies: Improved Scientific Output and Animal Welfare, webinar (Adrian Smith), 16 September 2021
Should we care about the welfare of fishes?, webinar (Lynne Sneddon), 16 September 2021
Årsmøde for Dyrevelfærdsorganerne, Valby, 16 September 2021
Compound Delivery, PK-PD, & Validation Studies in Oncology Research: Implication for refinement and reduction of animal use, webinar (Christian Schnell), 16 September 2021 (11-12 ET)

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

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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:

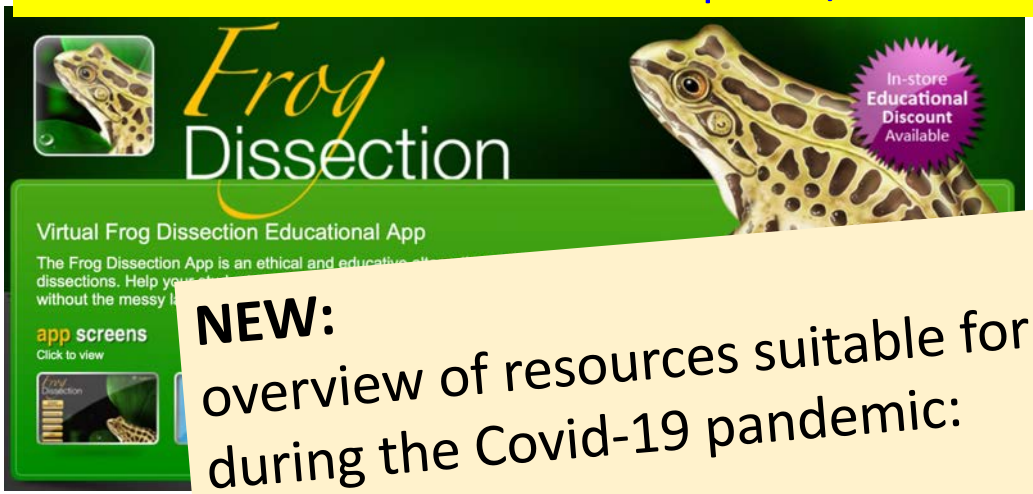
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal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

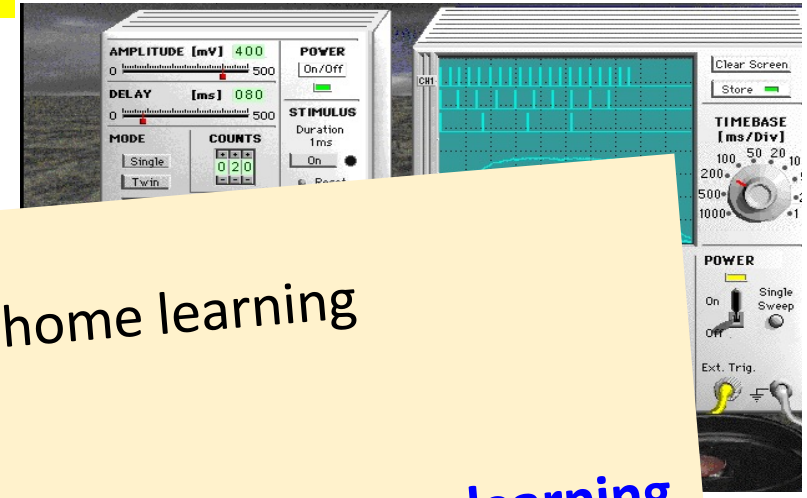
Here is an alphabetical global list of all the databases cited on the Norecopa website.

norecopa.no/databases-guidelines

links to over 70 other databases

The NORINA database: 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

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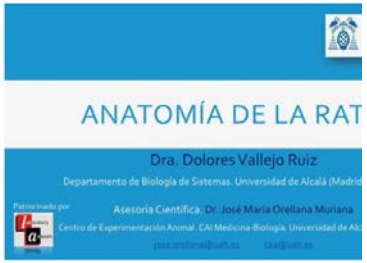
Rat s.c. injection
Norecopa | 1,380 views

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

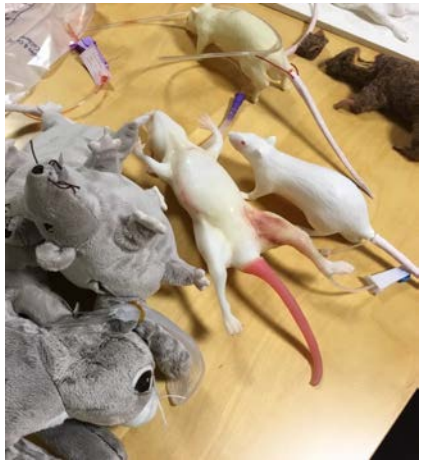
Lifting a rabbit
Norecopa | 2,420 views

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

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



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norecopa.no/NORINA

’We may need the animals, as it were, on the night;
but the machines will do very well at rehearsals’

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]

Abstract

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

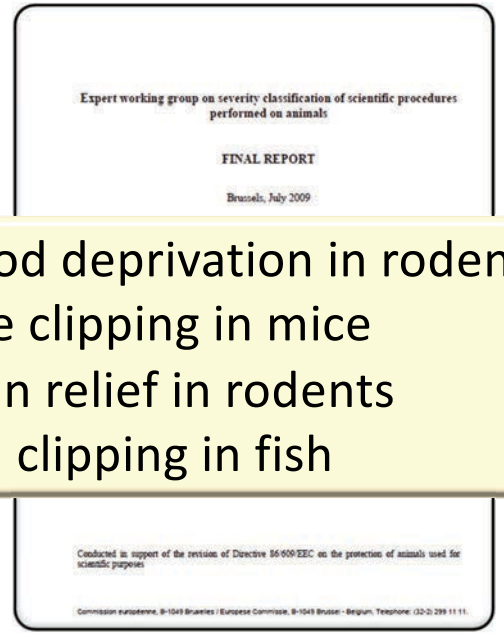
Laboratory Animals 2011; 1–6. DOI: 10.1258/la.2011.010181

Background

Copyright 2011 by the Laboratory Animals Limited

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 - België. Telephone: (32-2) 299 11 11.

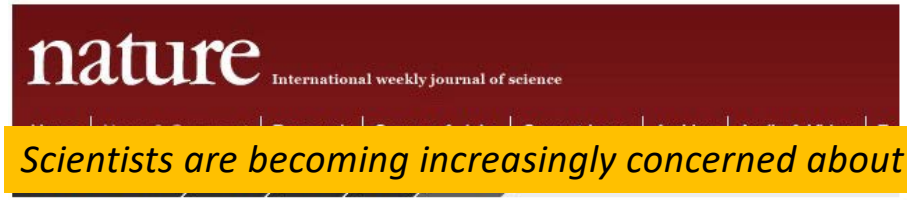
Food deprivation in rodents
Toe clipping in mice
Pain relief in rodents
Fin clipping in fish

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

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

Laboratory Animals, 45: 219-224, 2011

norecopa.no/categories



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Scientists are becoming increasingly concerned about the validity of animal experiments

NATURE | NEWS

Swiss survey highlights potential flaws in animal studies

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

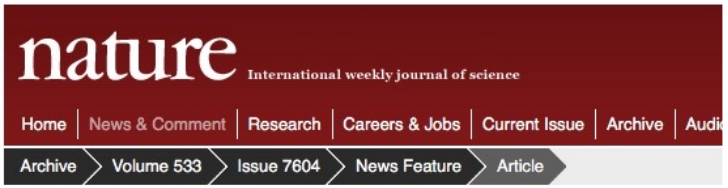
Pain management in pigs undergoing experimental surgery; a literature review (2012–4)

FREE

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

Br J Anaesth (2016) 116 (1): 37-45. **DOI:** https://doi.org/10.1093/bja/aev301
Published: 03 October 2015

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



NATURE | NEWS FEATURE

1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

25 May 2016 | Corrected: 28 July 2016

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

Frequently highlighted causes of the "reproducibility crisis":

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

norecopa.no/concerns

My/our 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?"

The burnt cake fallacy:

We can improve research by

- "better reporting"
- "courses in "Experimental Design" that leave out the animal & facility-related issues

reddit.com

reddit.com

https://www.bls.gov/ooh/images/3077.jpg

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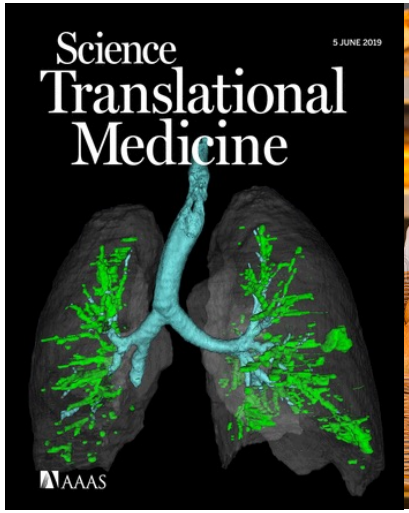
PREPARE *from day 1*

ARRIVE



https://www.dreamstime.com

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nature human behaviour

Perspective | Open Access | Published: 10 January 2017

A manifesto for reproducible science

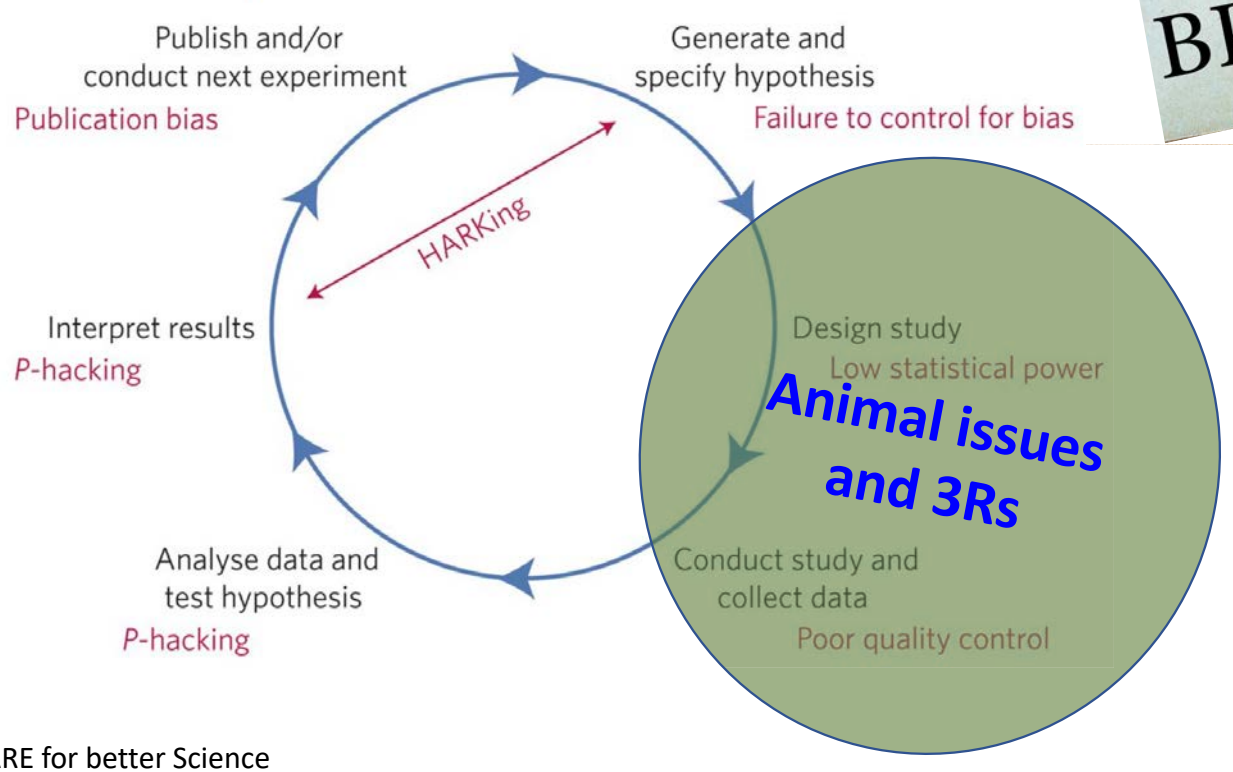
Marcus R. Munafò, Brian A. Nosek, Dorothy V. M. Bishop, Katherine S. Button, Christopher D. Chambers, Nathalie Percie du Sert, Uri Simonsohn, Eric-Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



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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? 2000 (Öbrink & Rehbinder)
- Guidelines for reporting the results of experiments on fish, 2000 (Smith & Brattelid)
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*)
- Gold 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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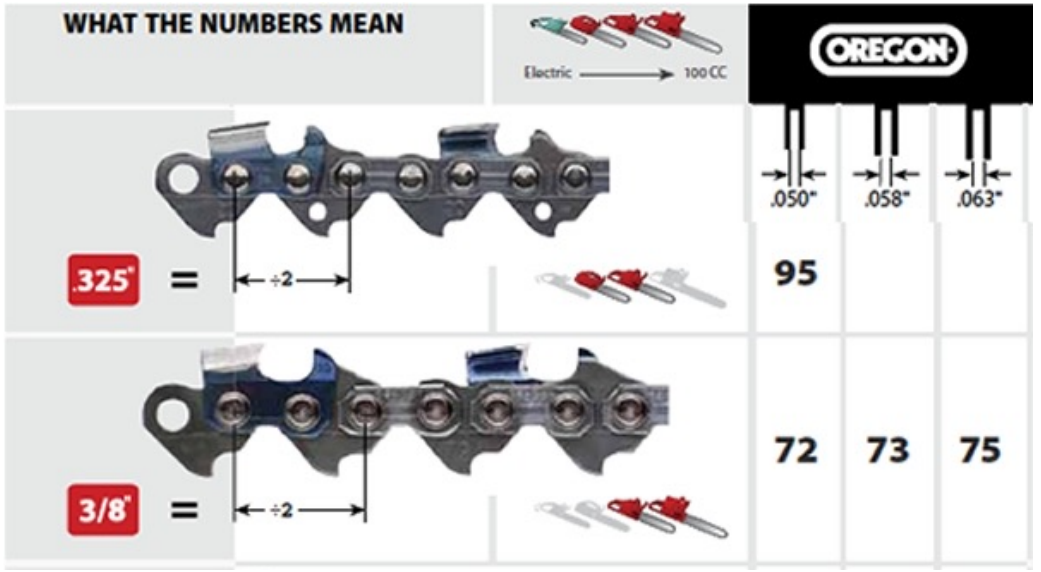
The easy parts of reporting:



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 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!

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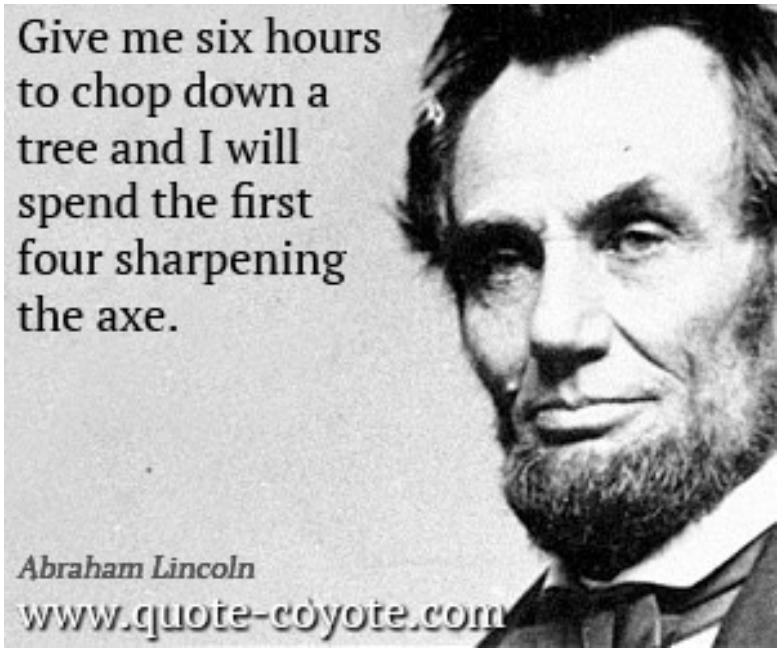
leaderonomics.com



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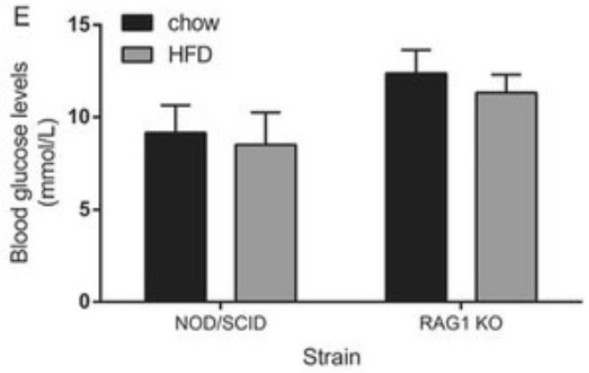
The scientist



The mouse

Breeding
New social groups
Transportation
Acclimation to research facility
Allocation to experimental group
Adaptation to new diet
Handling and immobilisation

Blood sampling

often also:
injections, gavaging, surgery
pain and distress
developing illness and death

Some of the 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

Stress caused by capture and handling

INDEPENDENT

News › Science

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

Mice picl 't act naturally

Ian Johnstor

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

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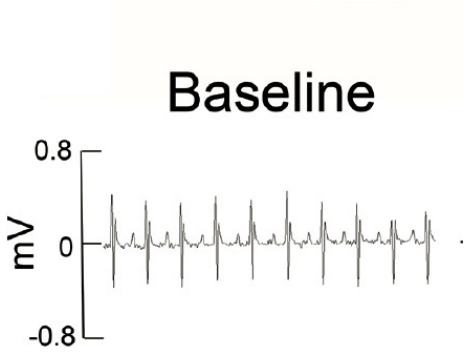
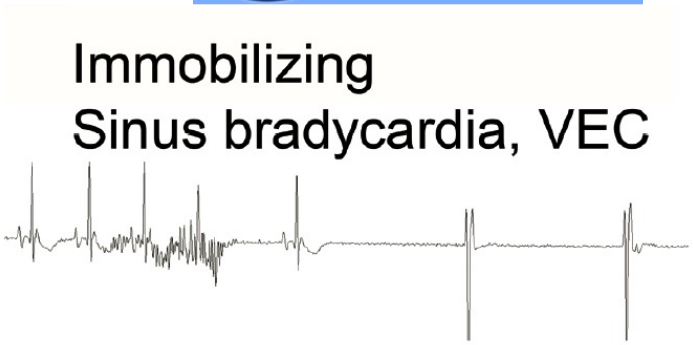
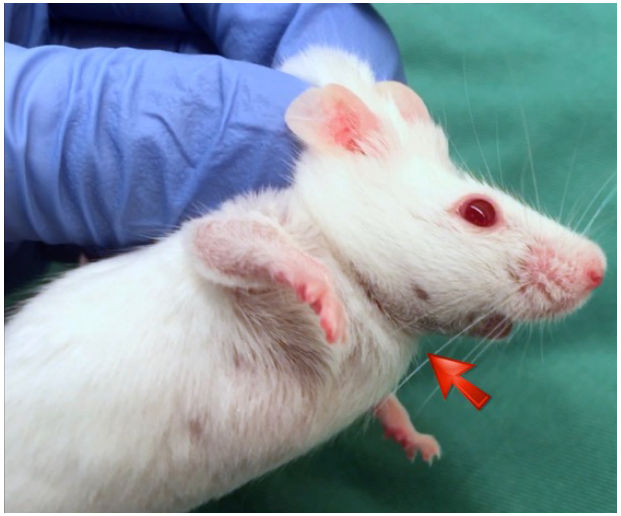




Reprinted with permission. Labitt RN, Oxford EM, Davis AK, Butler SD, Daugherity EK. 2021. A Validated Smartphone-based Electrocardiogram Reveals Severe Bradyarrhythmias during Immobilizing Restraint in Mice of Both Sexes and Four Strains. J Am Assoc Lab Anim Sci 60:201–212. DOI: 10.30802/AALAS-JAALAS-20-000069

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 simple 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!

While we are waiting for the scientific evidence...

Carol M. Newton (1925-2014)

National Library of Medicine

The three S's

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

https://norecopa.no/3S

How do others achieve reproducibility?

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

…and precision in a variable environment?

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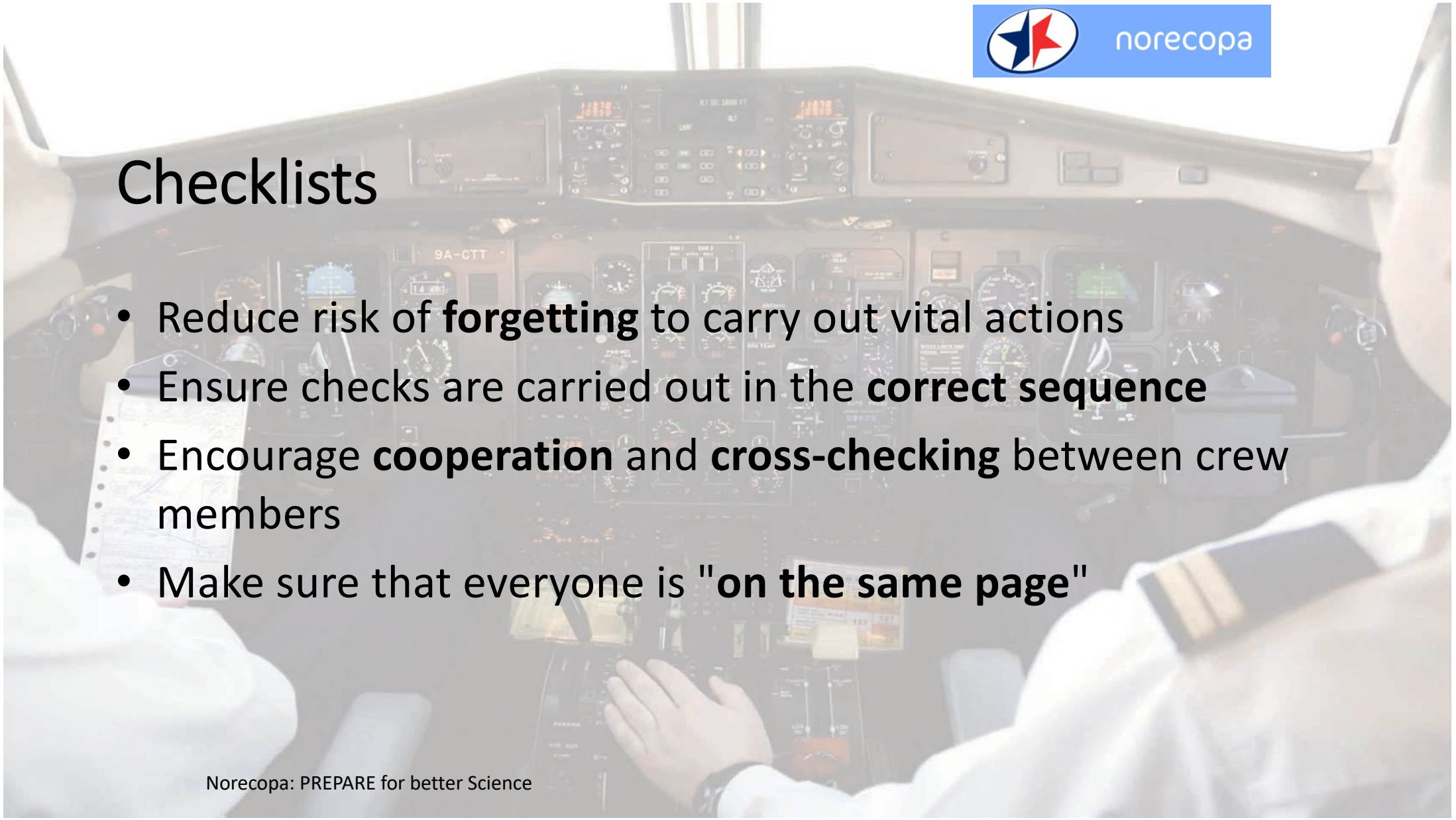
10-15 checklists even on short routine flights

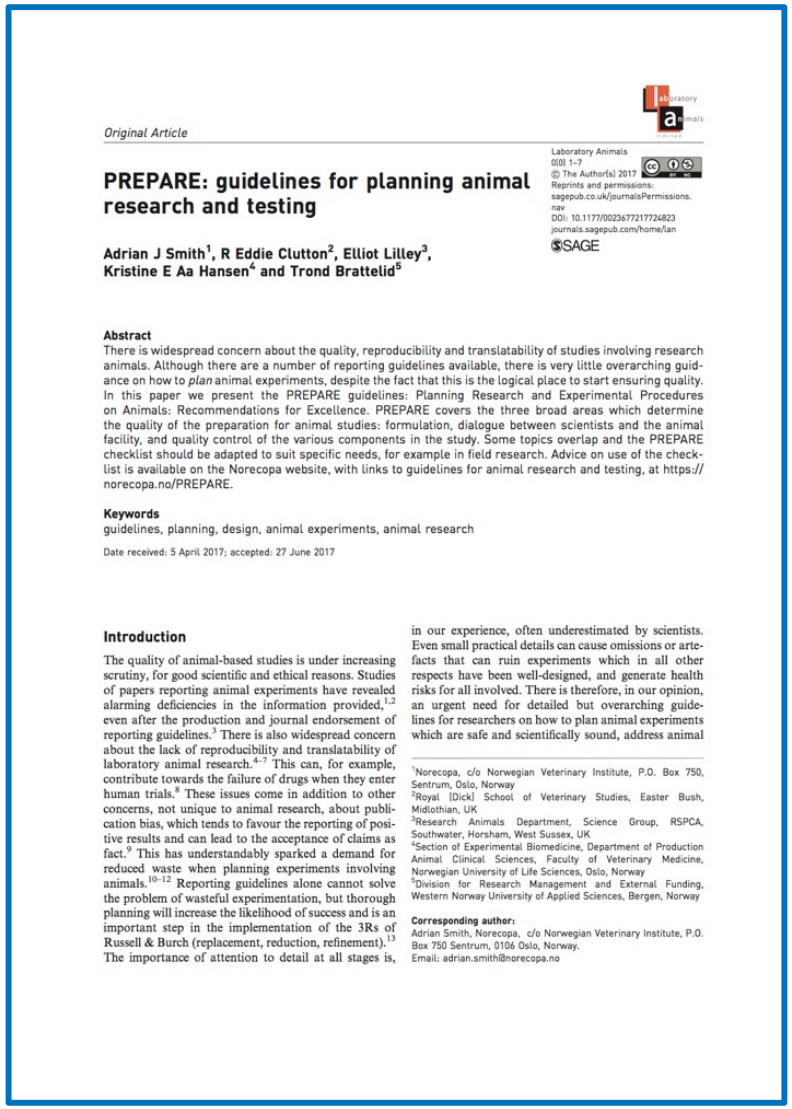


Checklists

- Reduce risk of **forgetting** to carry out vital actions
- Ensure checks are carried out in the **correct sequence**
- Encourage **cooperation** and **cross-checking** between crew members
- Make sure that everyone is "**on the same page**"

Too late to read the checklists when you have ARRIVEd!

colourbox.com



Original Article

PREPARE: guidelines for planning animal research and testing

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

Laboratory Animals
0(0) 1–7

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

Abstract

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

Keywords

guidelines, planning, design, animal experiments, animal research

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

Introduction

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

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

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Email: adrian.smith@norecopa.no

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https://doi.org/10.1177/0023677217724823

Over 20,000 views/downloads from the journal website

norecopa.no/PREPARE

PREPARE:

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

PREPARE covers 15 topics:

Formulation of the study

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

Dialogue between scientists and the animal facility

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

Methods

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

Items in pink are not typically highlighted in reporting guidelines

norecopa.no/PREPARE/prepare-checklist

PREPARE

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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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 stud

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 t facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines 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 [illegible]	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
[illegible]cation and [illegible]	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
[illegible] 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.

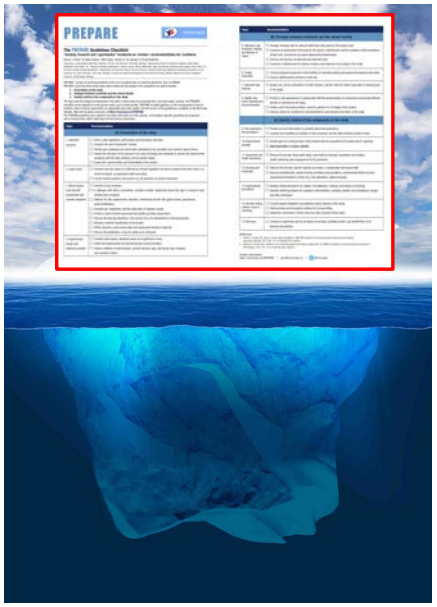
References

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

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

norecopa.no/PREPARE



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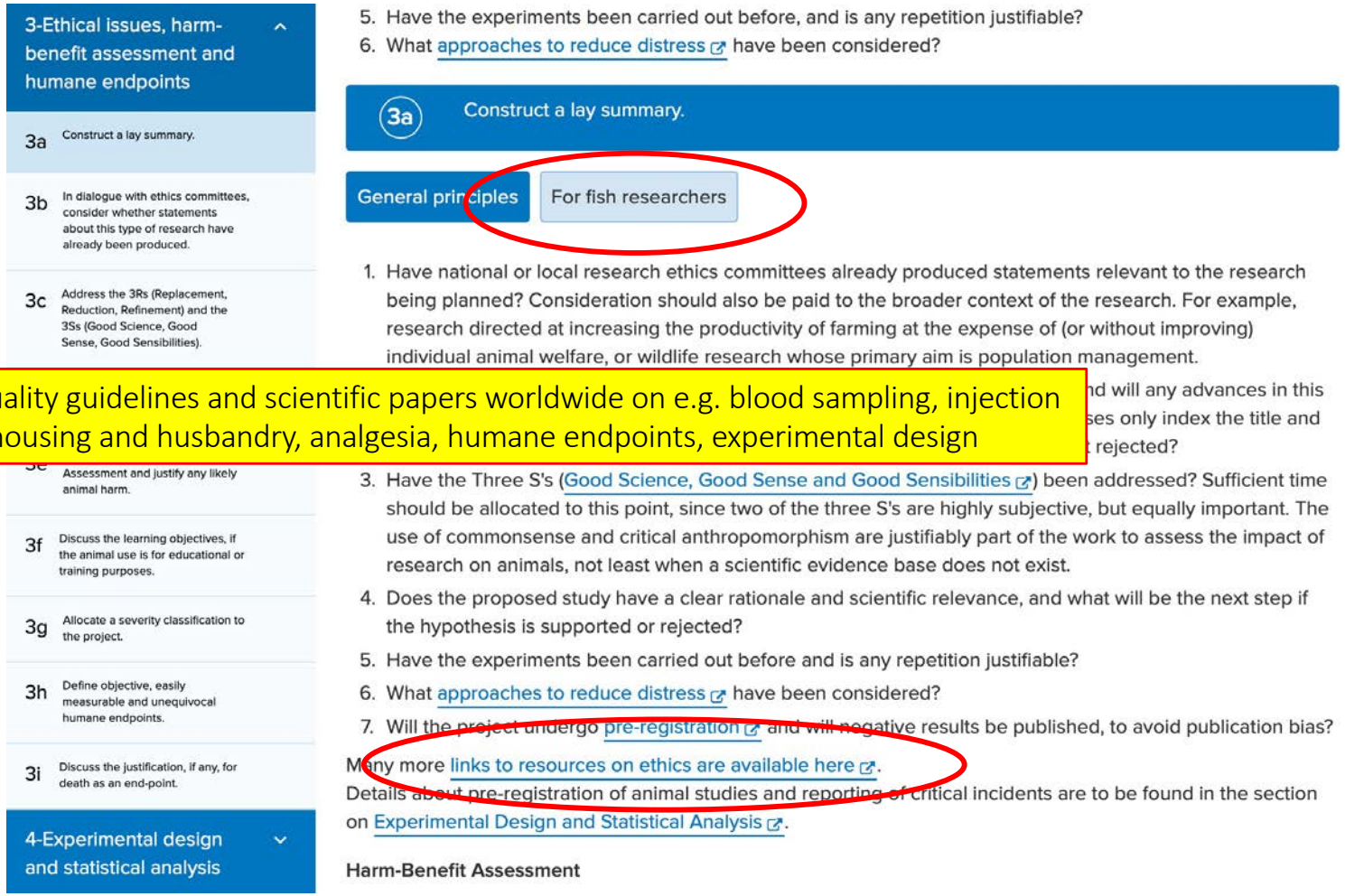
norecopa.no/PREPARE



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

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A simple but effective Master Plan

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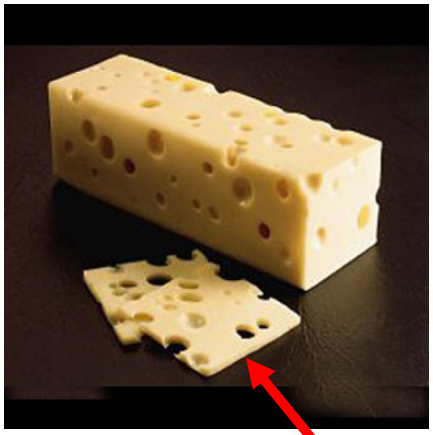
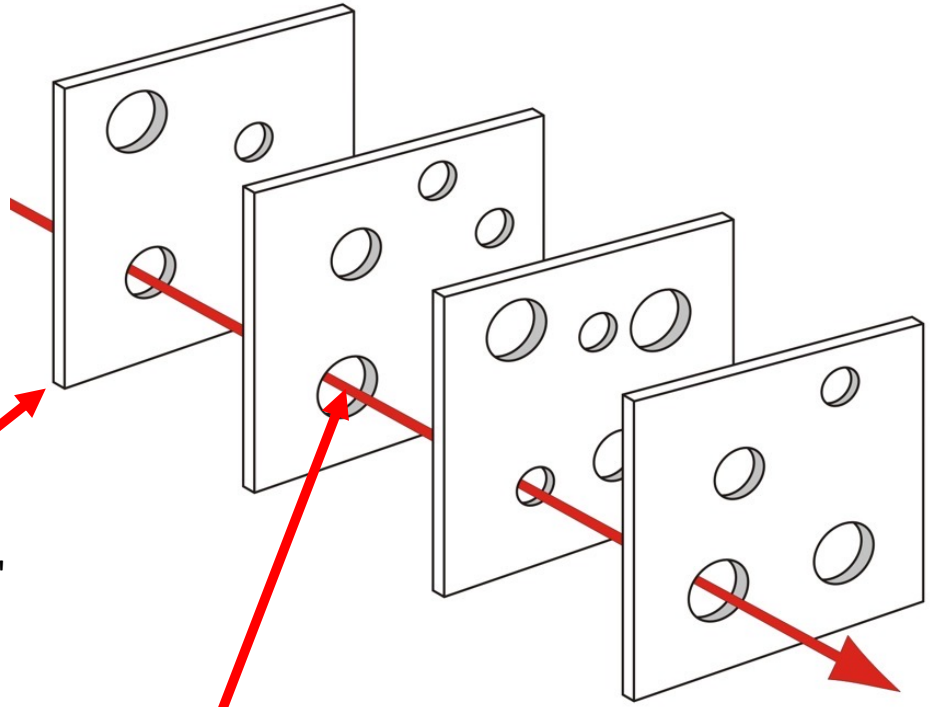
Threat and Error Management



eaugallecheese.com/Swiss-Cheese



"Layer of defence"
or redundancy

Weakness / hazard

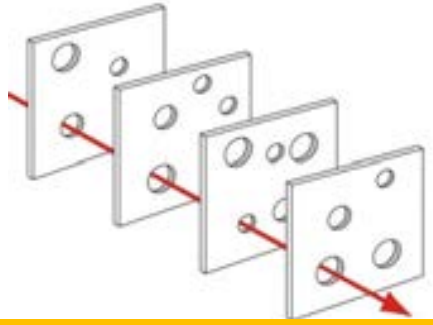
Loss

wikipedia.org/wiki/Swiss_cheese_model

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 anaphyl
  - 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

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

Fire, flooding
Water, power and ventilation failures

Health and safety issues:
Bites, kicks, scratches
Allergy
Zoonoses
Corrosives, isotopes, radiation
etc. etc.

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

reddit.com

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	required
	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
		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)
	ESTABLISHMENT LICENCE HOLDER		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
	ENGINEERS		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
		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

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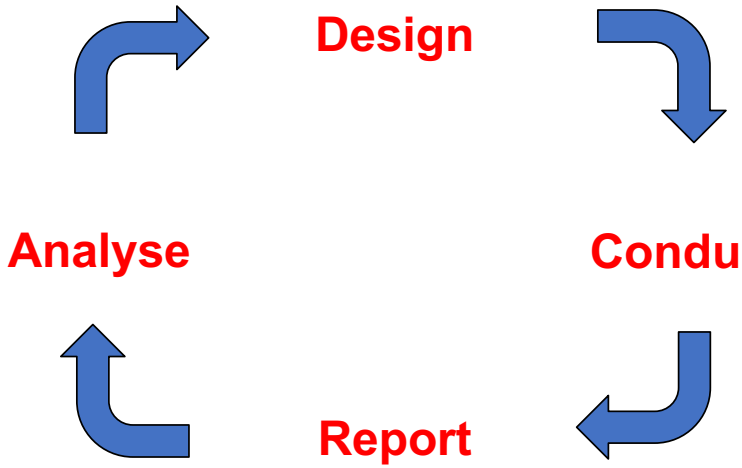


Identify and ensure the quality of (at least) the critical points in the experiment: critical for scientific validity and animal welfare

Space Shuttle, NASA

Culture of Care

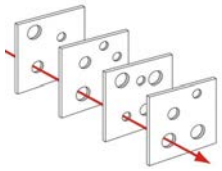
NASA

cbsnews.com

no.wikipedia.org

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

We need a Culture of Care!



Culture of Care

The International Culture of Care Network

norecopa.no/coc

A demonstrable commitment, throughout the establishment, to improving:

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

It goes beyond simply complying with the law!


Map
Satellite
Greenland
Iceland
Finland
Sweden
Norway
Russia
United Kingdom
Canada
Poland
Germany
Ukraine
Kazakhstan
Mongolia
France
Italy
Spain
Turkey
China
South Korea
Japan
North Pacific Ocean
United States
North Atlantic Ocean
Iraq
Iran
Afghanistan
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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

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

wiki.norecopa.no

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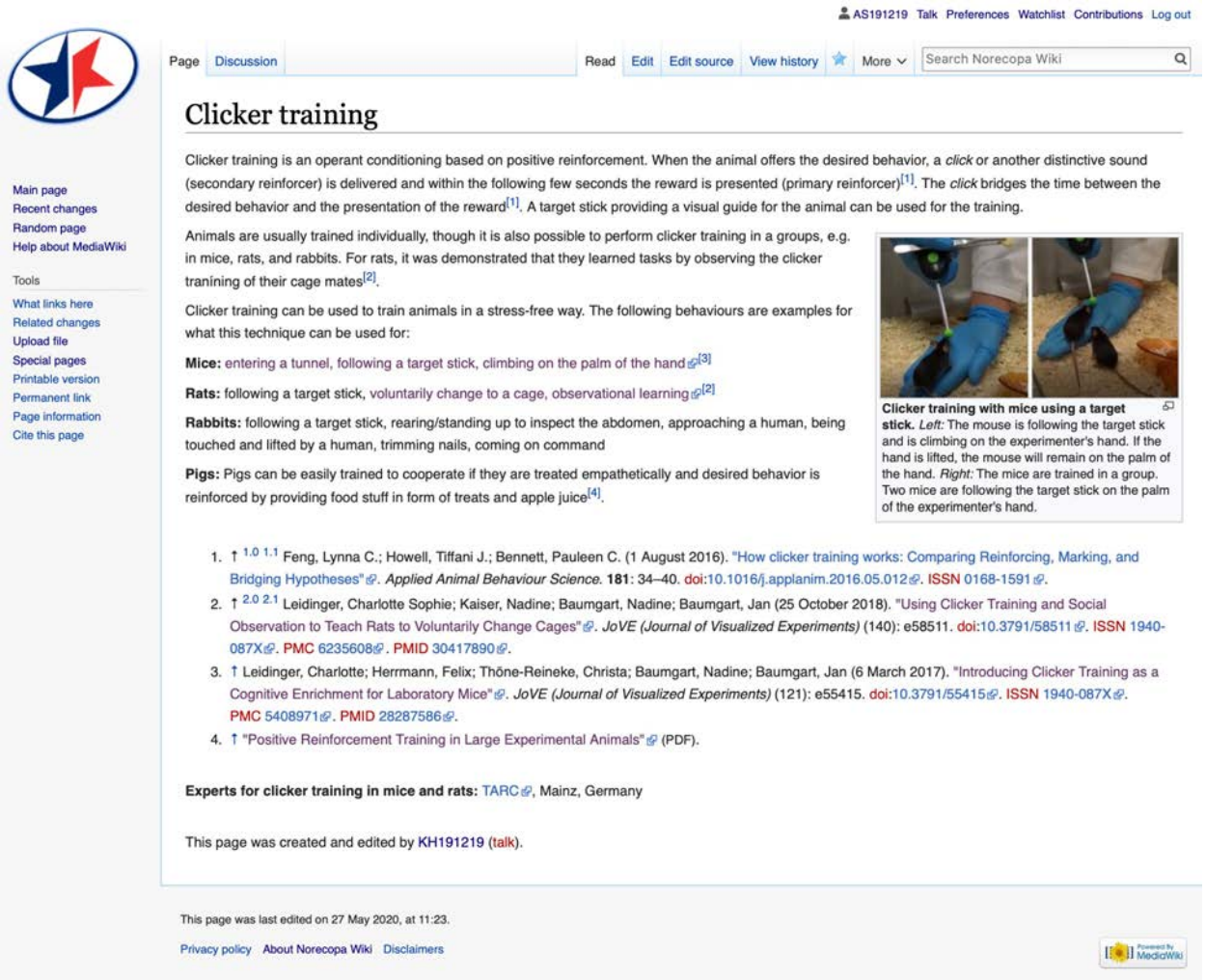

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Clicker training

Clicker training is an operant conditioning based on positive reinforcement. When the animal offers the desired behavior, a *click* or another distinctive sound (secondary reinforcer) is delivered and within the following few seconds the reward is presented (primary reinforcer)[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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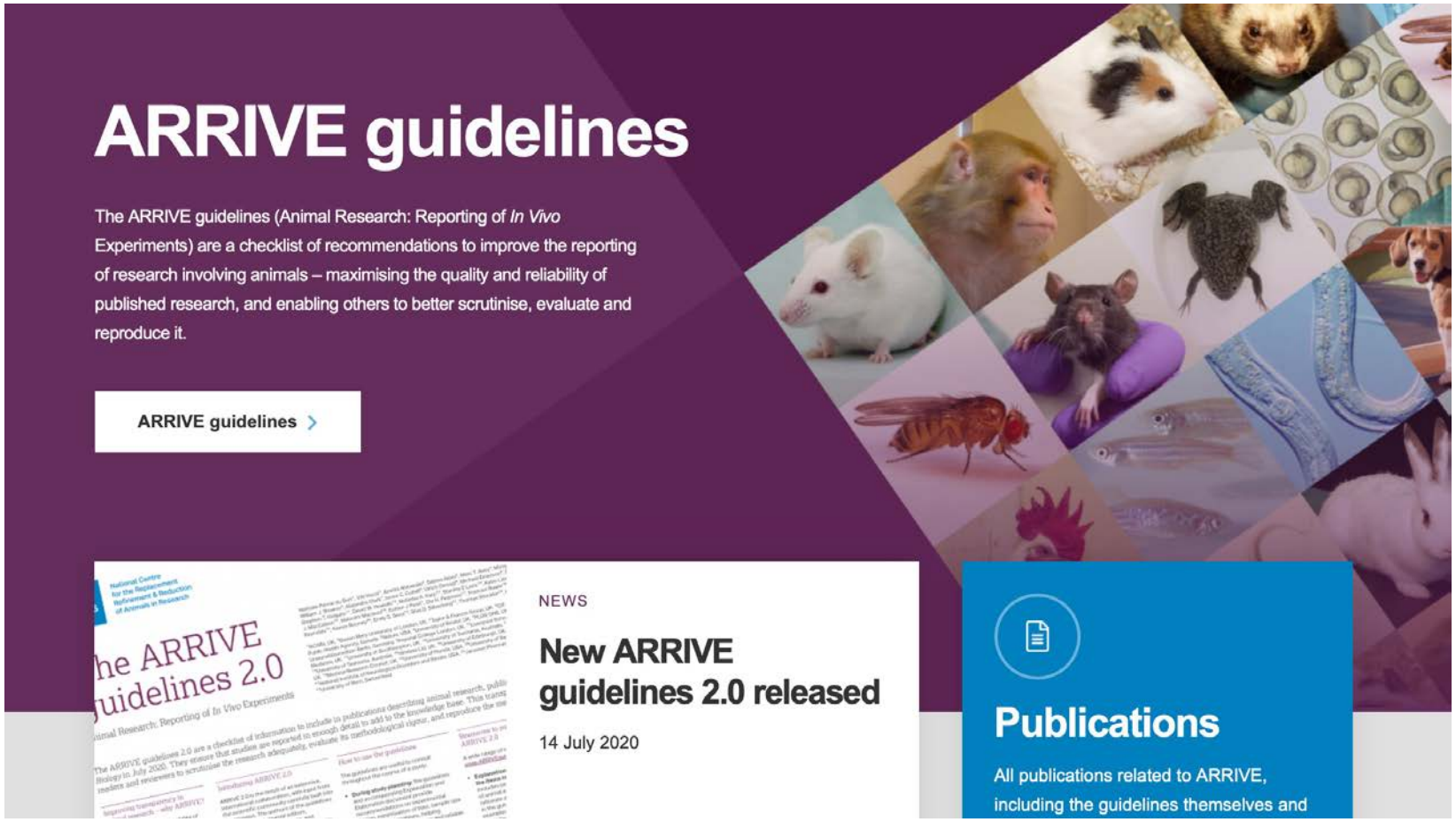
Reporting guidelines, e.g. ARRIVE



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.

Reporting guidelines
ARRIVE: "The Essential 10"

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.

biorxiv.org/content/10.1101/703181v1

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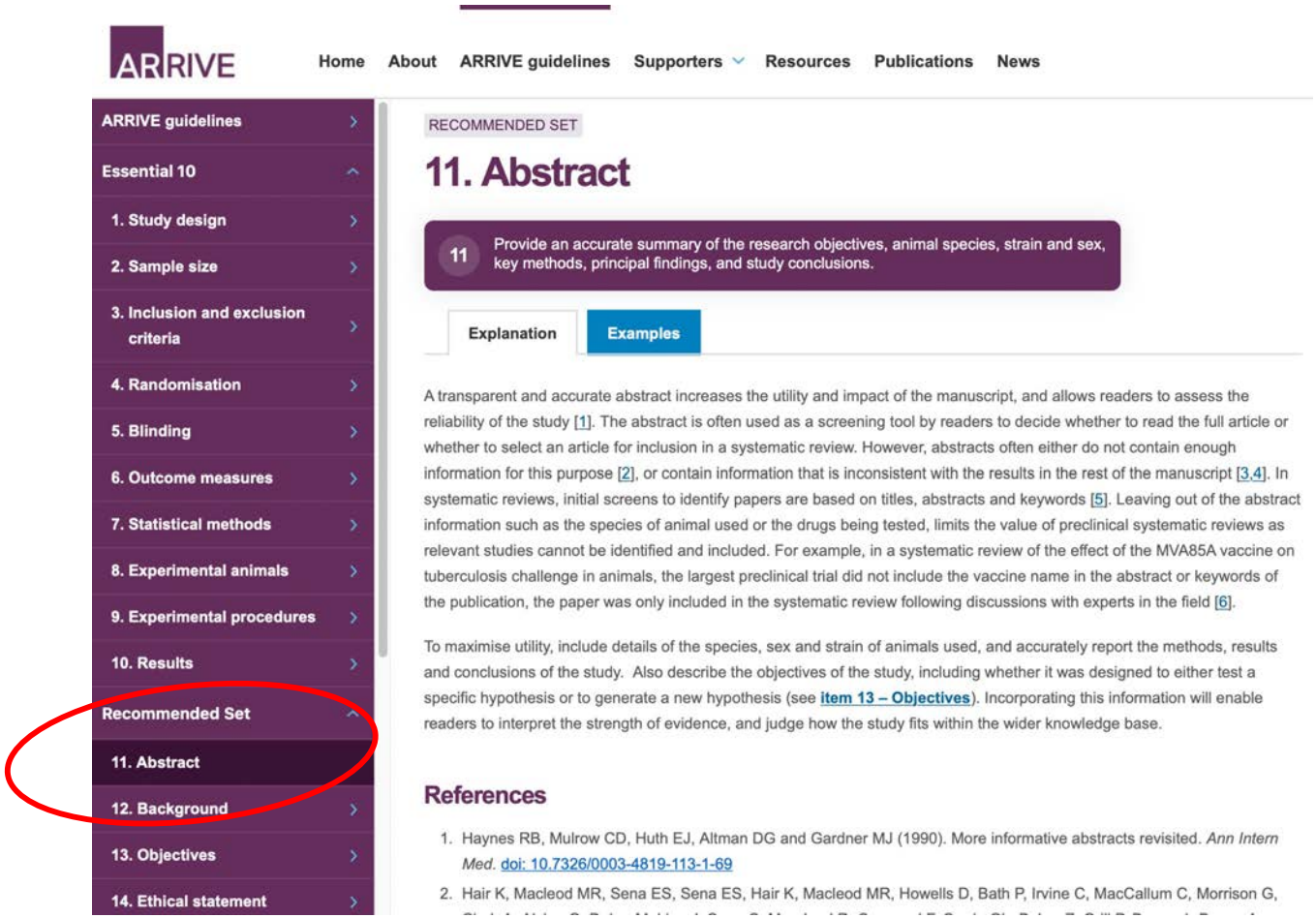

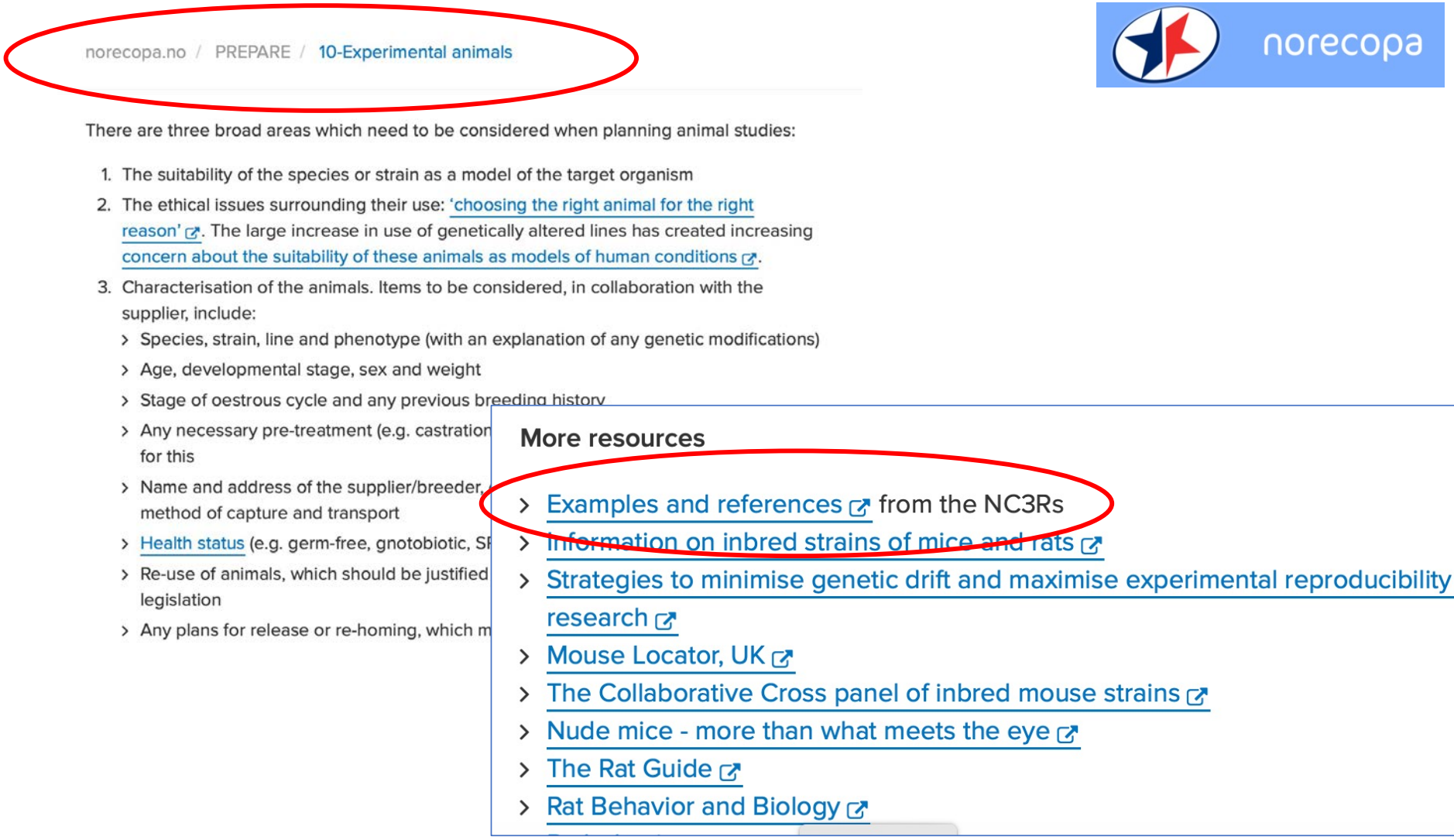

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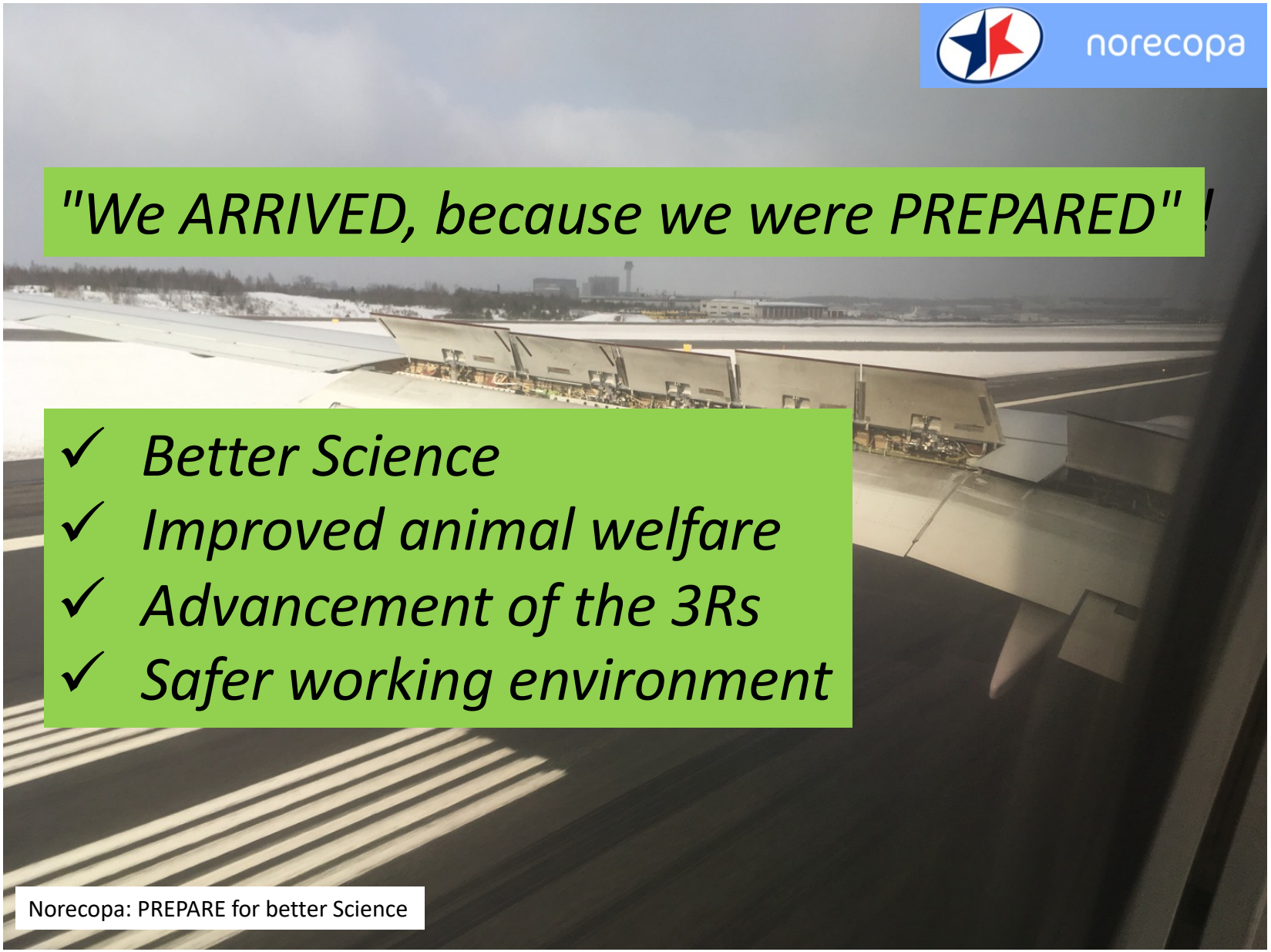
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"We ARRIVED, because we were PREPARED" !
✓ Better Science
✓ Improved animal welfare
✓ Advancement of the 3Rs
✓ Safer working environment
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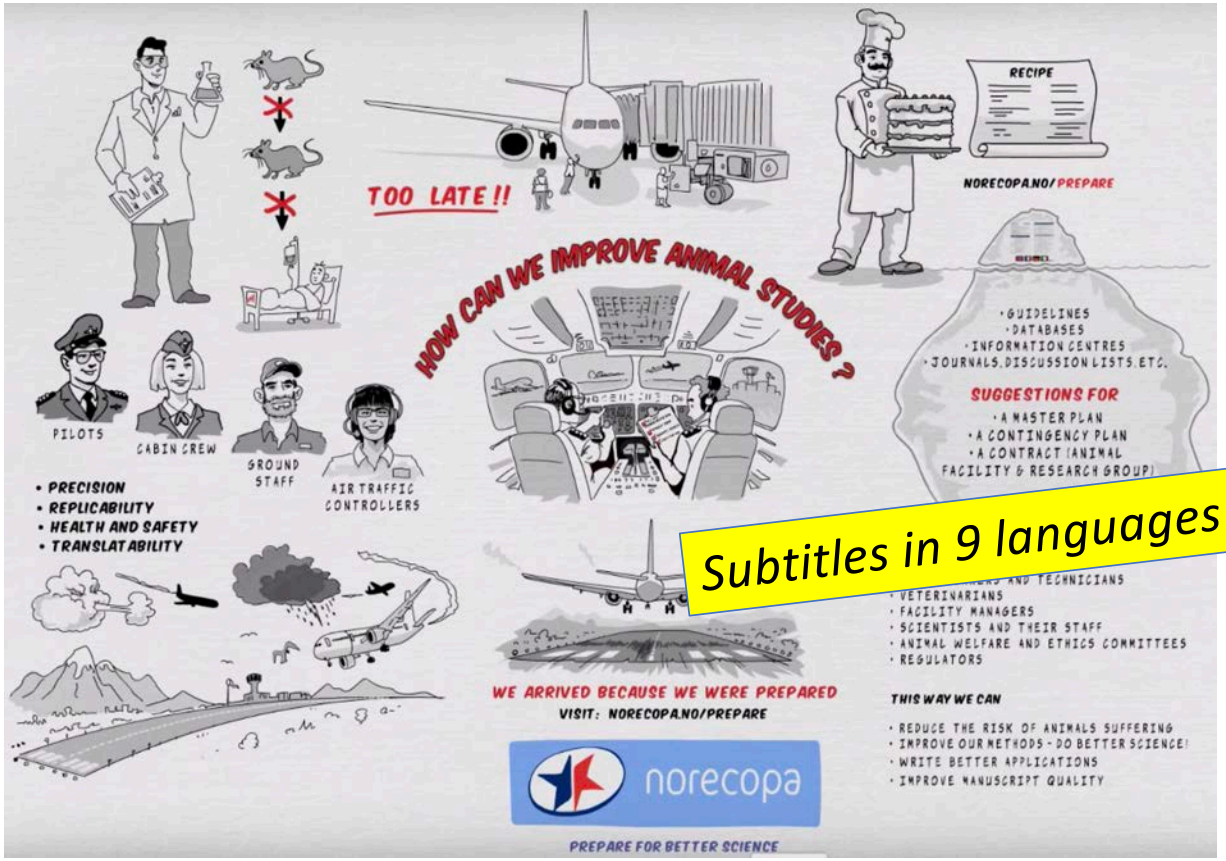
norecopa.no/PREPARE/film

a 3-minute cartoon film



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3R Flag

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]

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Not necessarily a high-impact journal

Summary

A method ... vein. This enables rapid ... the same site without a need for new ... a humane and practical alternative to cardiac and retro- ..., in species where venepuncture has traditionally been regarded as problematic.

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

PREPARING, CARING, SHARING and FLAGGING

The scientific and welfare benefits of increased collaboration and transparency

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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.

norecopa ***PREPARE for better Science***

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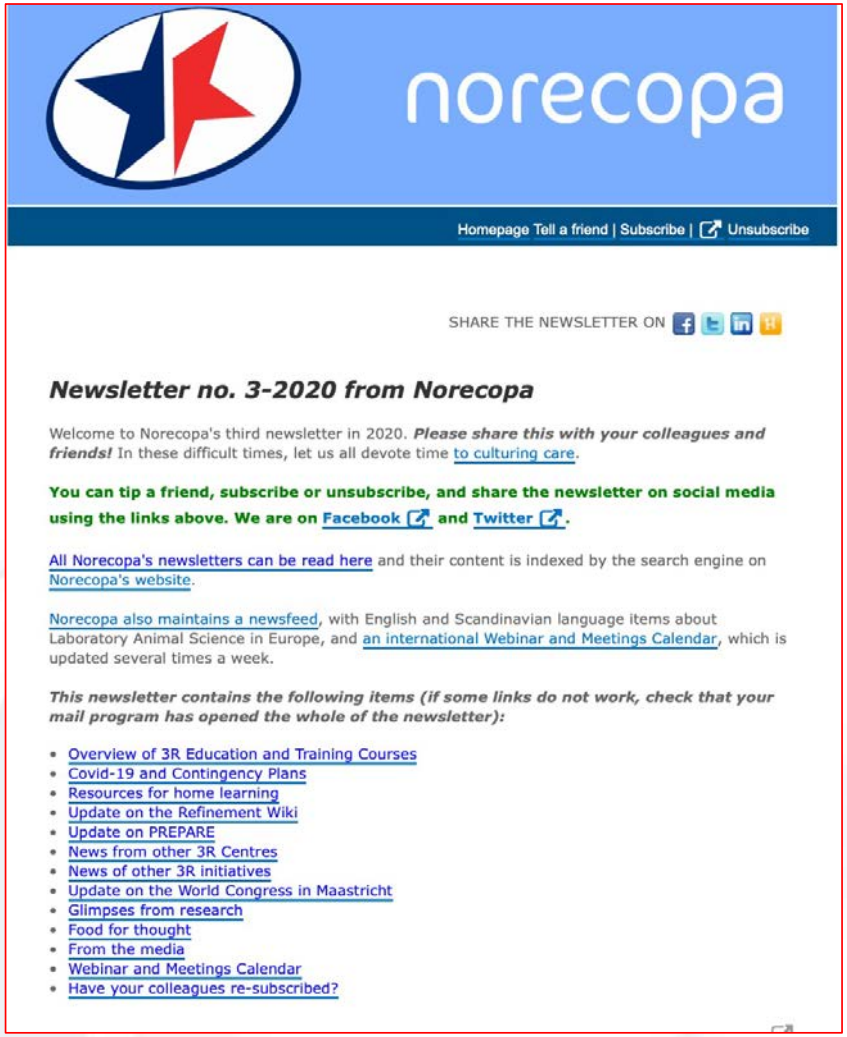
Graphics: colourbox.com



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