PREPARE: New perspectives on refinement

norecopa.no/Fincopa

Adrian Smith
adrian.smith@norecopa.no

https://norecopa.no

Norecopa

Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of global 3R resources

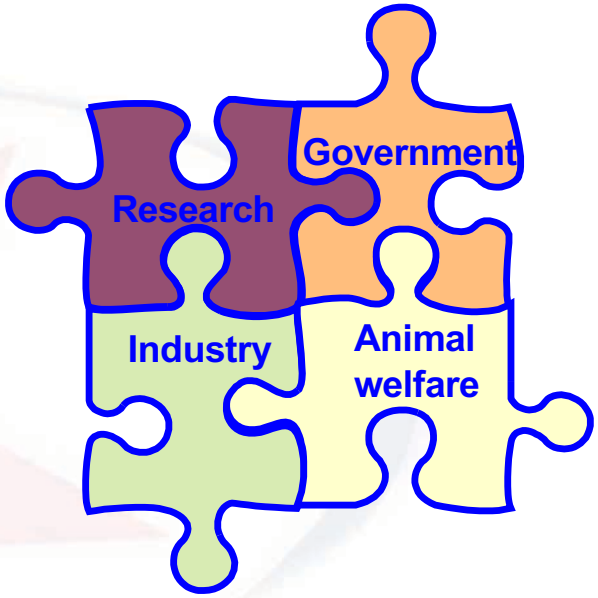
https://norecopa.no

Norecopa: PREPARE for better Science

European Consensus-Platform for Alternatives

ecopa.eu

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



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
NORSK ENGLISH
Search:
About Norecopa Alternatives Databases & Guidelines Education Legislation Meetings More resources News PREPARE Species Wiki
Fish 2005 | Wildlife 2008 | Fish 2009 | Agricultural animals 2012 | Field research 2017 | Past meetings |
Meetings Calendar | An informal guide to arranging a scientific meeting | Presentations
norecopa.no / Meetings / Meetings Calendar
norecopa.no/meetings/meetings-calendar
Webinar and Meetings calendar
May 2021
SETAC Europe 31st Annual Meeting, online, 3-6 May 2021
Laboratory Animal Science course, Porto, 3-14 May 2021
Kick-off meeting, 3R Centre Network in Baden-Würrtemberg (online meeting in German)
2021
Avoid Allergies and Infections when Working with
2021
Nordic 3R
Welfare Act, webinar, 6 May 2021
Hamburg, 6-7 May 2021
Swedish 3R Center Workshop: Replace strategy and networking activities, 10 May 2021
Animal Research: Critical, Challenging & Creative Thinking Course, 10-13 May 2021
Dirty or clean mice - What is better for research? Webinar (André Bleich), 11 May 2021
Poultry in biomedical research, 6th Meeting of LASA Large Animal Research Network (LARN),
11 May 2021
3rd Pan-American Conference for Alternative Methods, Windsor, 12-14 May 2021
+ webpages for past meetings and recorded meetings

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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norecopa.no/3r-guide/fincopa

Fincopa

Record number: c73d9 (legacy id: 15307)
Category: 3R Center
Type:

Fincopa, the Finnish National Consensus Platform for Alternatives, was established in 2003 and is a member of ecopa.

Fincopa, the Finnish National Consensus Platform for Alternatives, was established in 2003. Fincopa brings together the four stakeholder groups involved in animal research: regulators, industry, academia and animal welfare organisations.

Fincopa arranges its own meetings as well as participating in other initiatives to implement the 3Rs in Finland, particularly within the area of regulatory toxicology. Fincopa is a Full Member of *ecopa* (European Consensus Platform on Alternatives).

Here is an overview of European 3R Centres.

This page was updated on 12 January 2021

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:

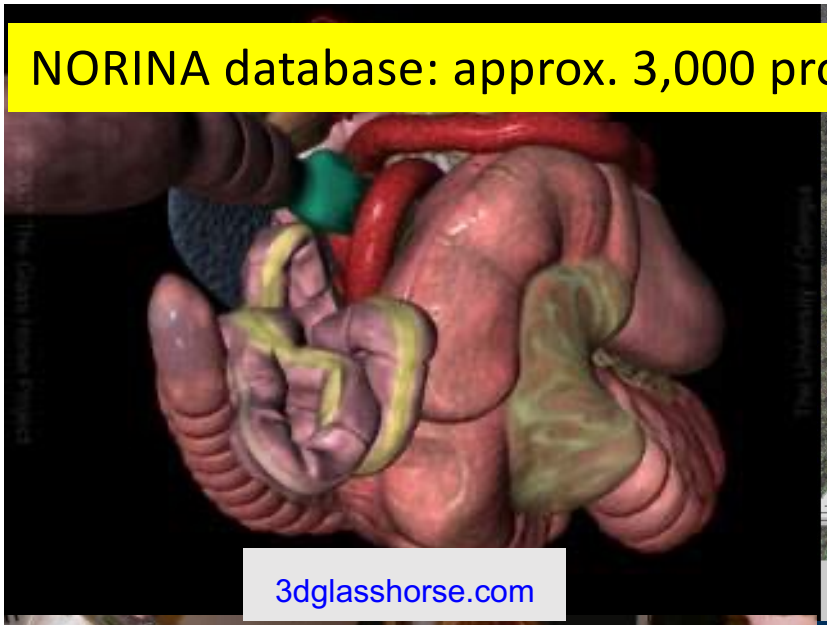
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal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

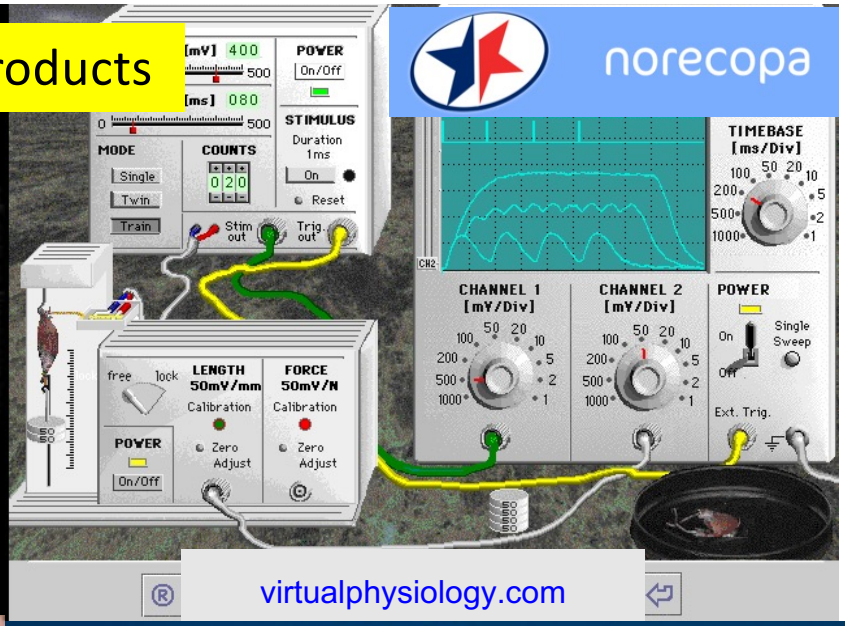
norecopa.no/databases-guidelines

links to over 70 other databases

NORINA database: approx. 3,000 products

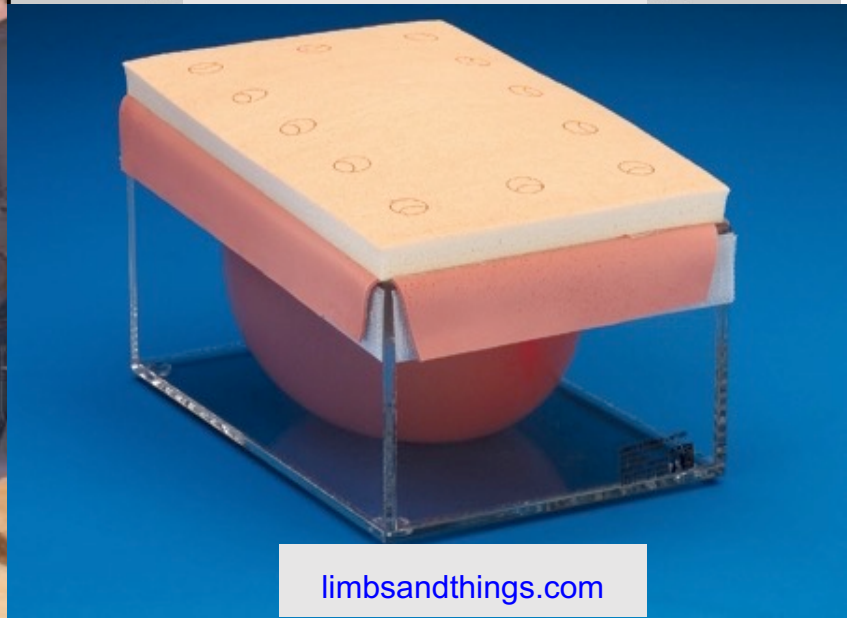


3dglasshorse.com



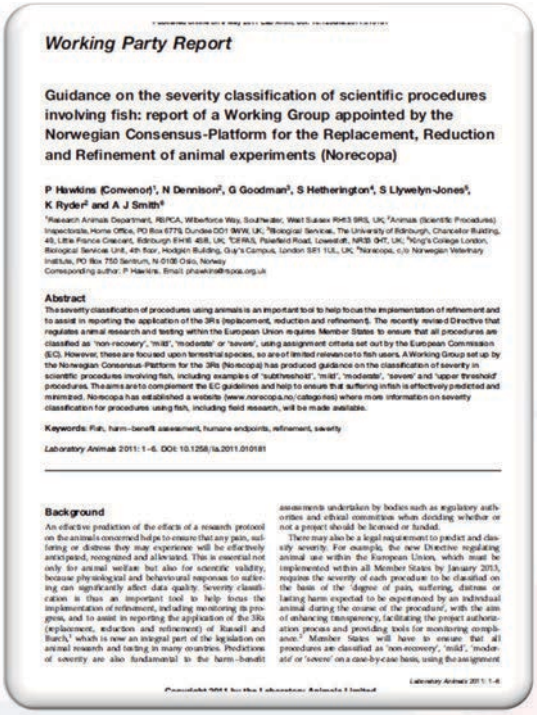
virtualphysiology.com

rescuecritters.com



limbsandthings.com

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

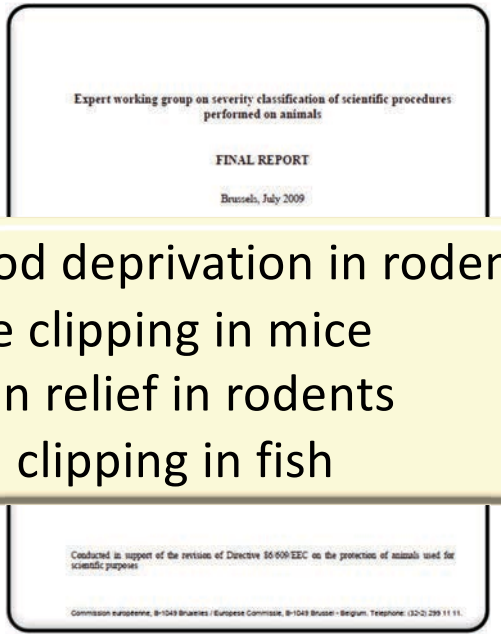
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because 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

norecopa.no/categories

Animals used in research in 2020

[A1] Mice (Mus musculus)	50 222
[A2] Rats (Rattus norvegicus)	3 355
[A3] Guinea-Pigs (Cavia porcellus)	296
[A7] Other Rodents (other Rodentia)	568
[A8] Rabbits (Oryctolagus cuniculus)	8
[A10] Dogs (Canis familiaris)	201
[A12] Other carnivores (other Carnivora)	125
[A13] Horses, donkeys & cross-breeds (Equidae)	59
[A14] Pigs (Sus scrofa domesticus)	696
[A16] Sheep (Ovis aries)	736
[A17] Cattle (Bos primigenius)	14
[A27] Other Mammals (other Mammalia)	541
[A28] Domestic fowl (Gallus gallus domesticus)	1 298
[A29] Other birds (other Aves)	11 435
[A30] Reptiles (Reptilia)	27
[A32] Xenopus (Xenopus laevis and Xenopus tropicalis)	13
[A34] Zebra fish (Danio rerio)	38 867
[A35] Other Fish (other Pisces)	2 174 234
SUM	2 282 710

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nature International weekly journal of science

norecopa

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 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.

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Frequently highlighted causes of the "reproducibility crisis"

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

norecopa.no/concerns

nature human behaviour

Perspective | Open Access | Published: 10 January 2017

A manifesto for reproducible science

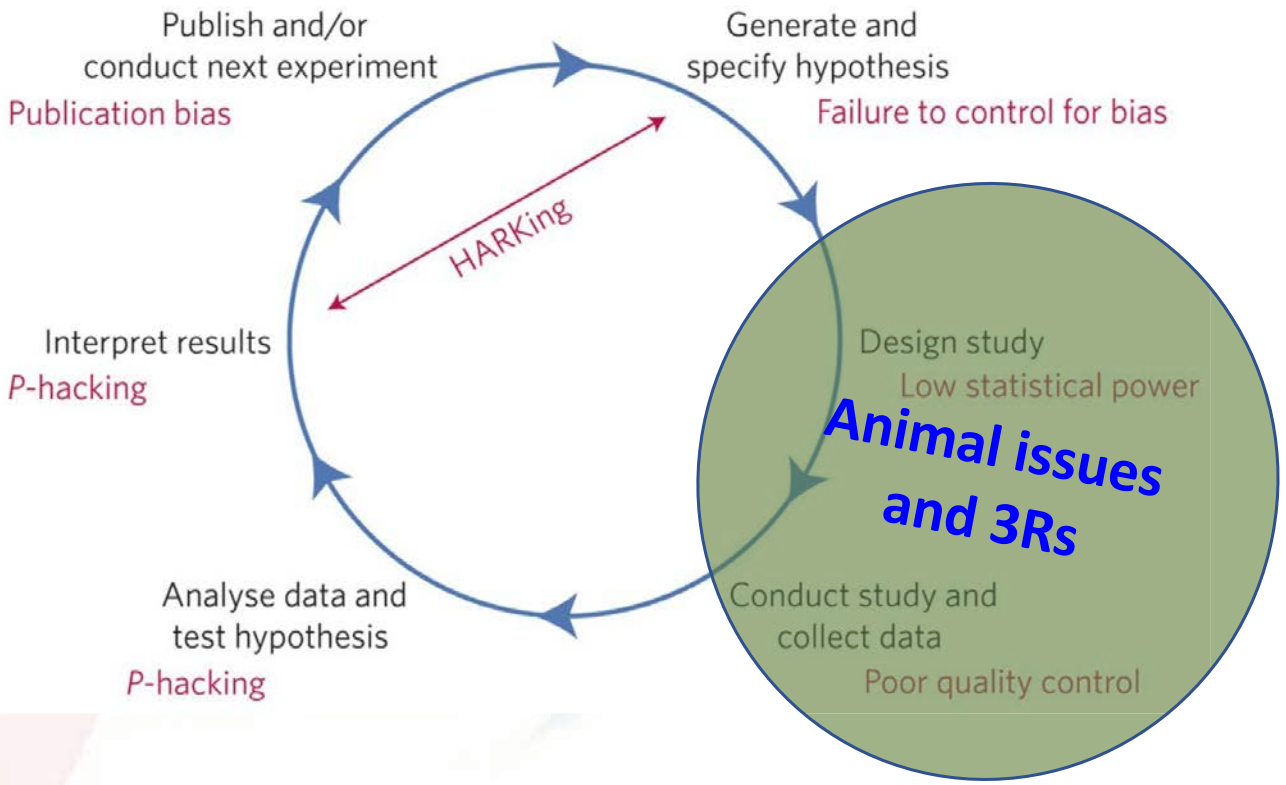
Marcus R. Munafò, Brian A. No
Button, Christopher D. Chambers,
Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



Two frustrations:

'We can solve the reproducibility crisis by'

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

- **better reporting**

reddit.com

Refinement **Reduction** **Replacement**

Lab animal community -//- Statisticians -//- *In vitro* experts

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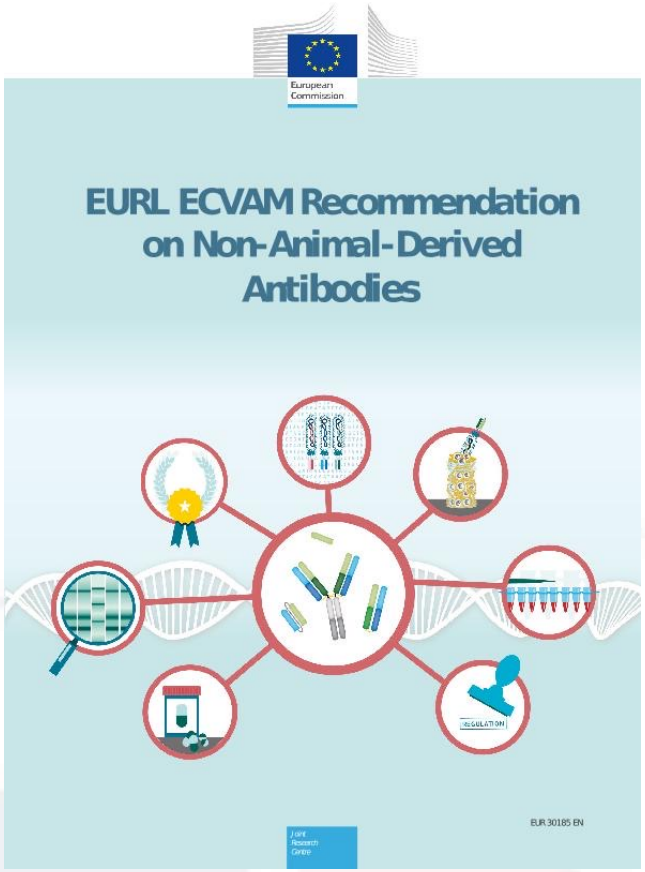
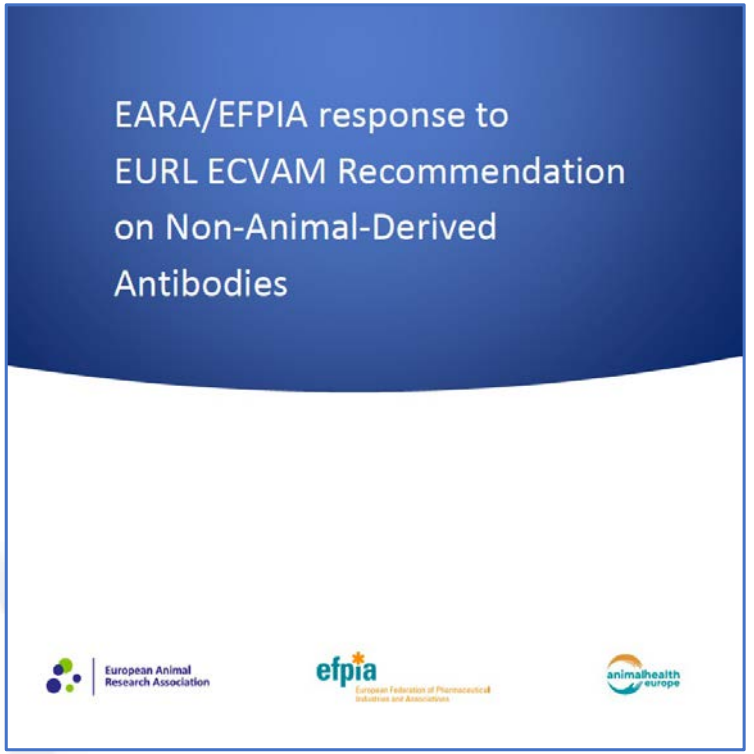
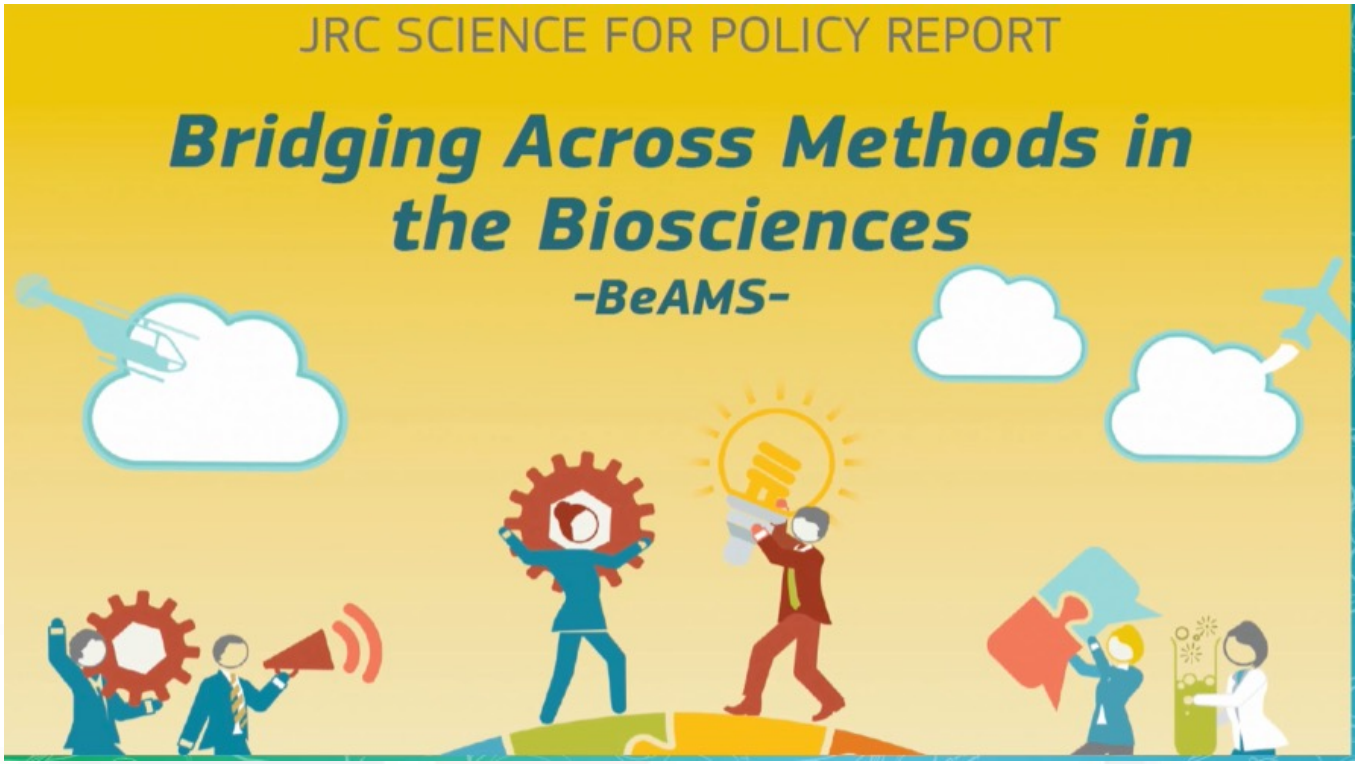


https://publications.jrc.ec.europa.eu/repository/handle/JRC120199



https://www.eara.eu/post/eara-efpia-response-to-antibody-recommendation



ec.europa.eu/jrc/en/news/bridging-silos-biosciences

This may be a challenge for scientists used to humanising animal models in basic research

Collaboration on the road to better preclinical research

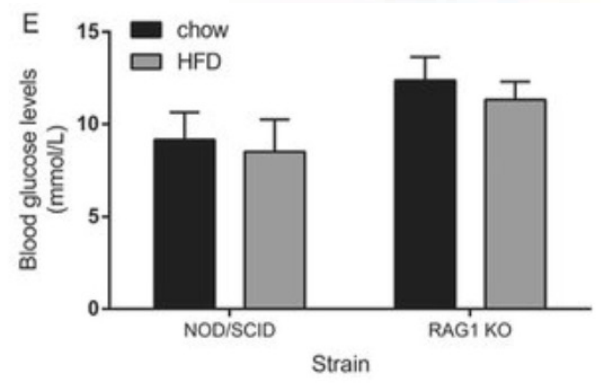
October 6, 2020 / PLoS ONE Guest Blogger / Guest Post

https://everyone.plos.org/2020/10/06/prepare

Reporting: scientific output and animal welfare

Planning

The scientist



The mouse

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

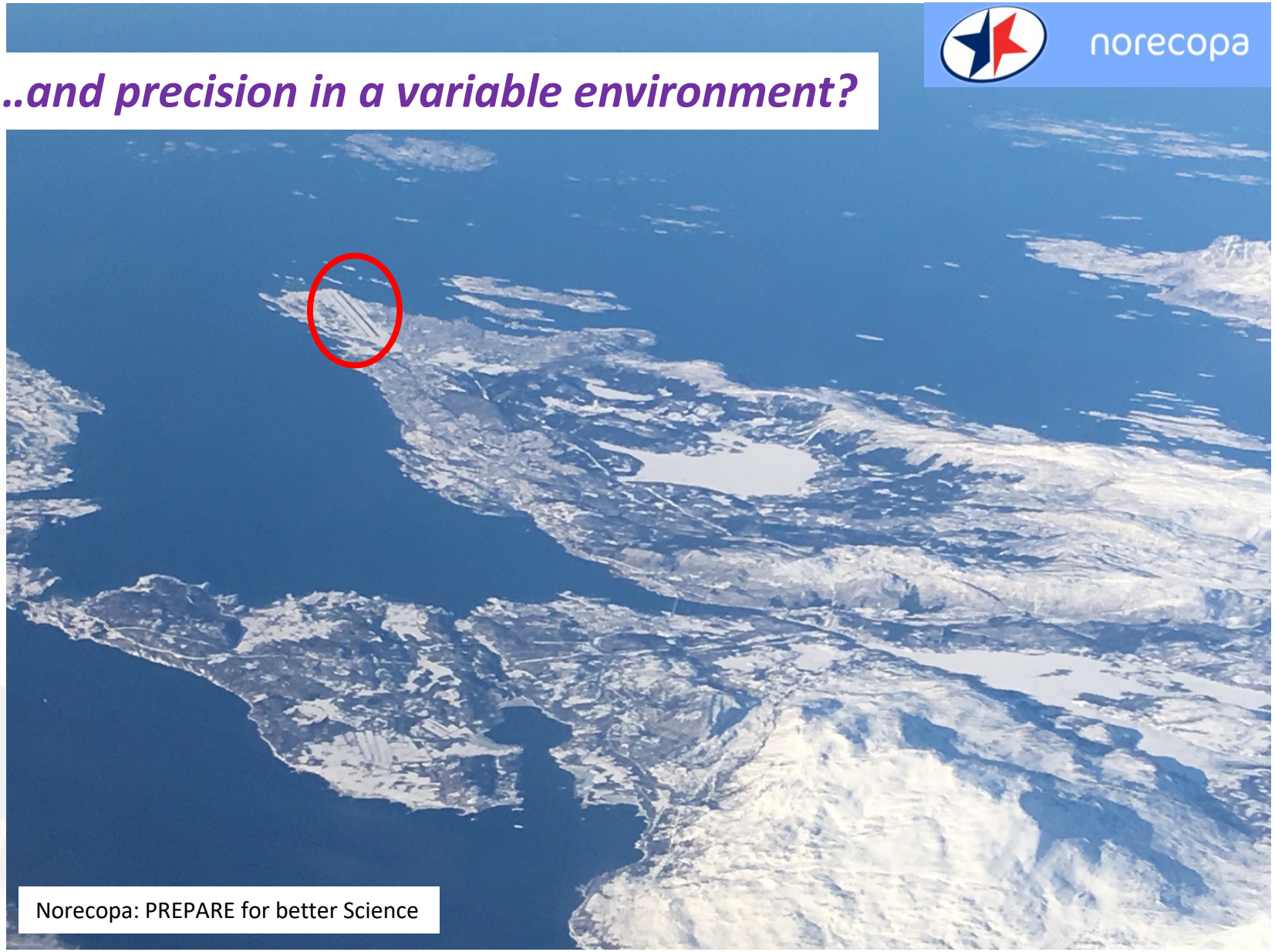
Blood sampling

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

How do others achieve reproducibility?

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

…and precision in a variable environment?



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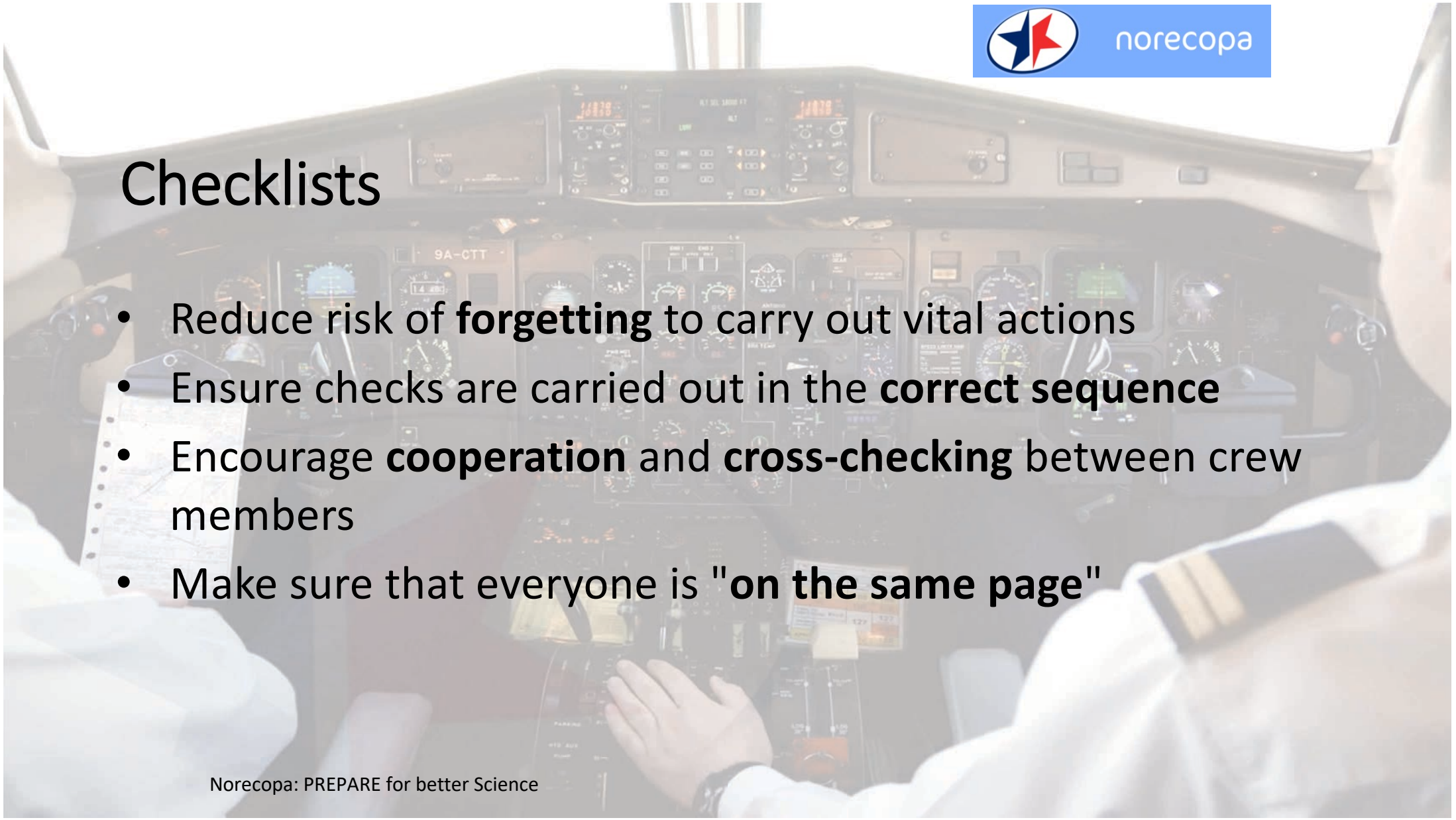
10-15 checklists even on short routine flights



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

Contingent suffering

animalcaresystems.com

(not just the direct suffering caused by the procedure)

Fear, boredom and discomfort

Caused by, for example:

Transport, or changes in housing, husbandry and social groups

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

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

photo: colourbox.com

Stress caused by capture and handling

INDEPENDENT

News › Science

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

Mice picl
naturally

't act

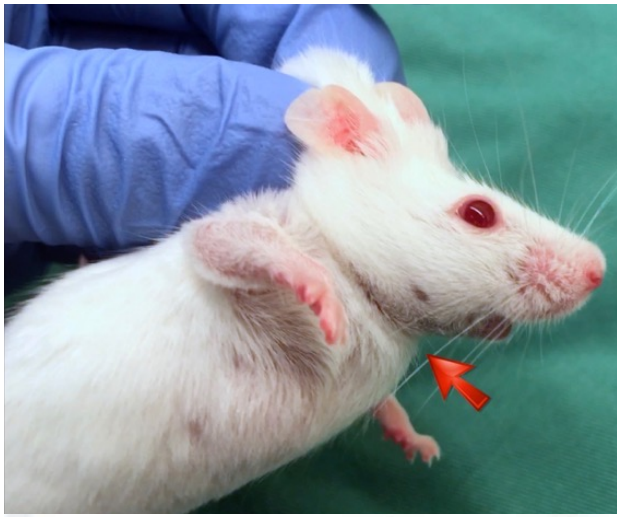
Ian Johnstor

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

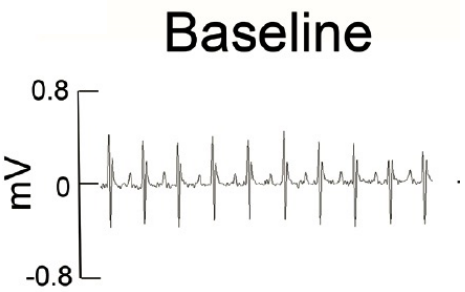
Refinement of scruffing mice

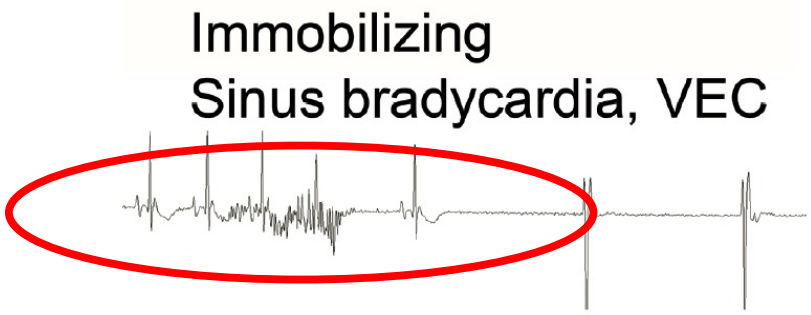
norecopa

norecopa.no/scruff



Three fingers better than two





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

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

medipoint.com/html/for_use_on_mice.html

theodora.com/rodent_laboratory/blood_collection.html

vimeo.com/486368886

photo:NMBU

The best blood sampling techniques are those where you can:

- ✓ see the blood vessel
- ✓ regulate the amount of blood you remove
- ✓ stop the bleeding easily (including internal bleeding)
- ✓ avoid damage to the surrounding tissue
- ✓ collect samples rapidly, to avoid artefacts due to mechanical stress, temperature changes, differing lengths of sampling time

3R literature can be 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 papers with explicit 3R-terms when they index them
- We have no single ”Journal of Alternatives”

3R improvements are often not highlighted in the scientific literature

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

photo:NMBU

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

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

Annelise 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.

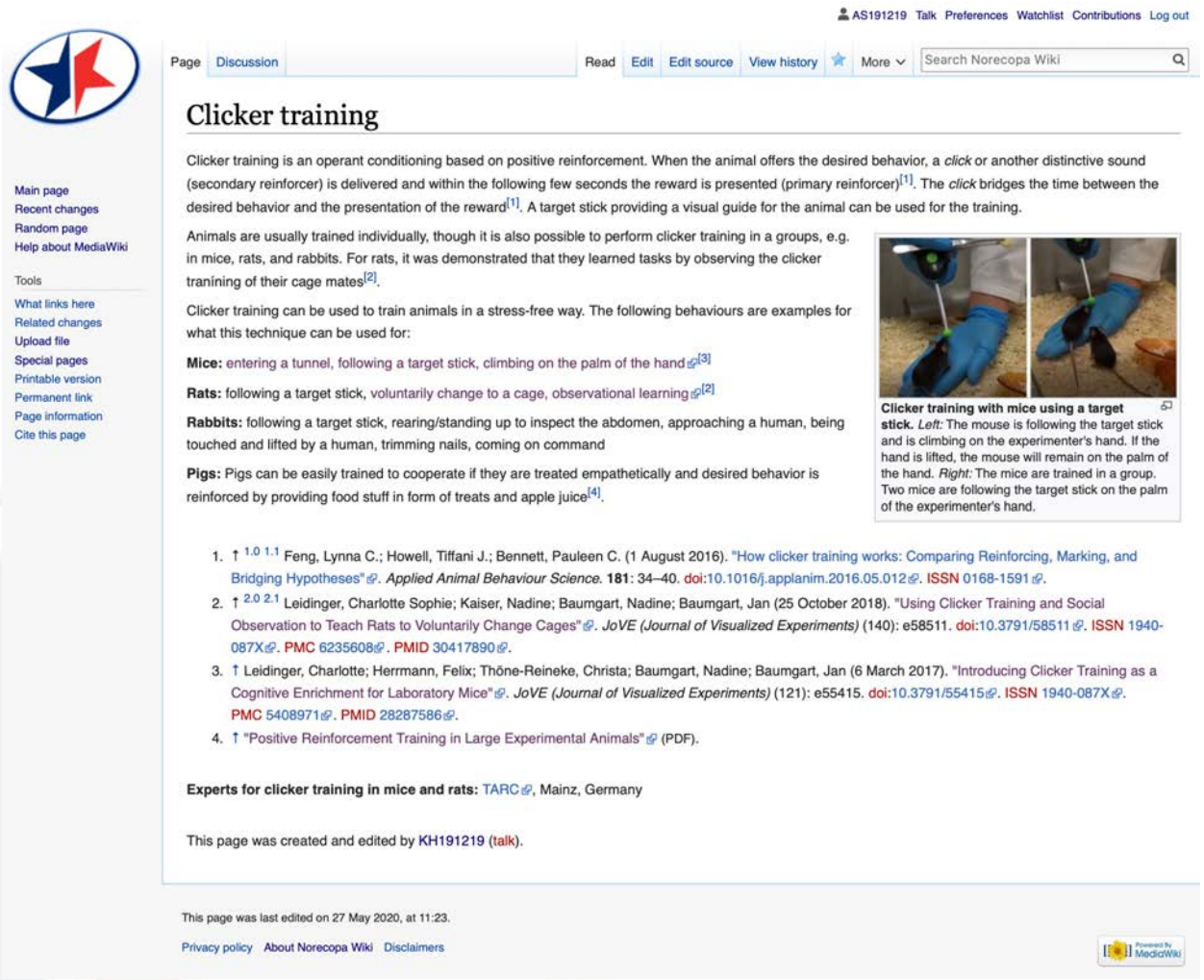
Keywords Saphenous vein; blood sampling; mouse; rat; hamster; gerbil; guineapig; rodent; ferret; mink

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

Not necessarily a high-impact journal.

wiki.norecopa.no

Return to homepage



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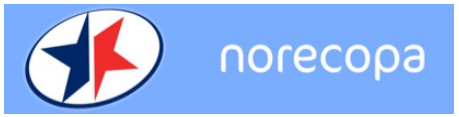
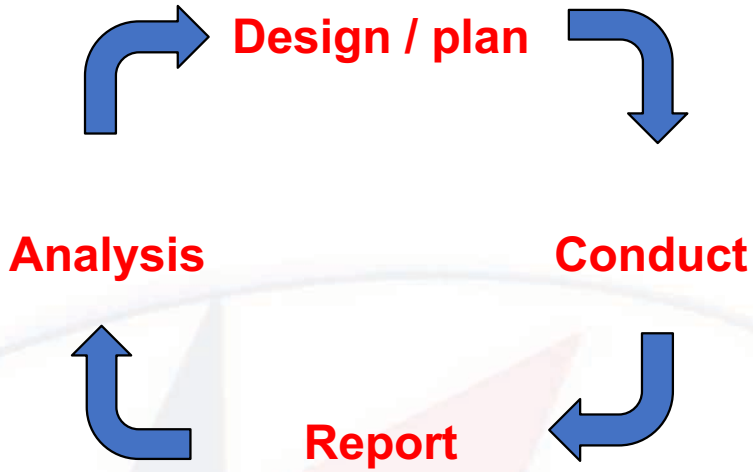
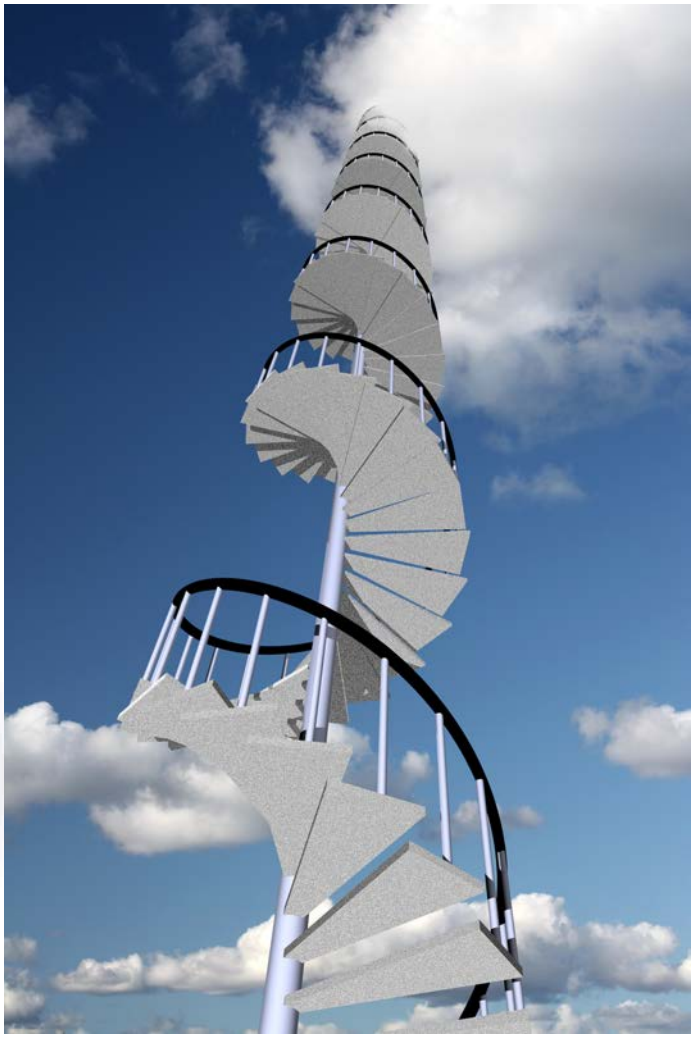


Pages created as of today

- 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
- Marble Burying Test
- 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

Quality assurance





Aggregation of marginal gains – *not rocket science*

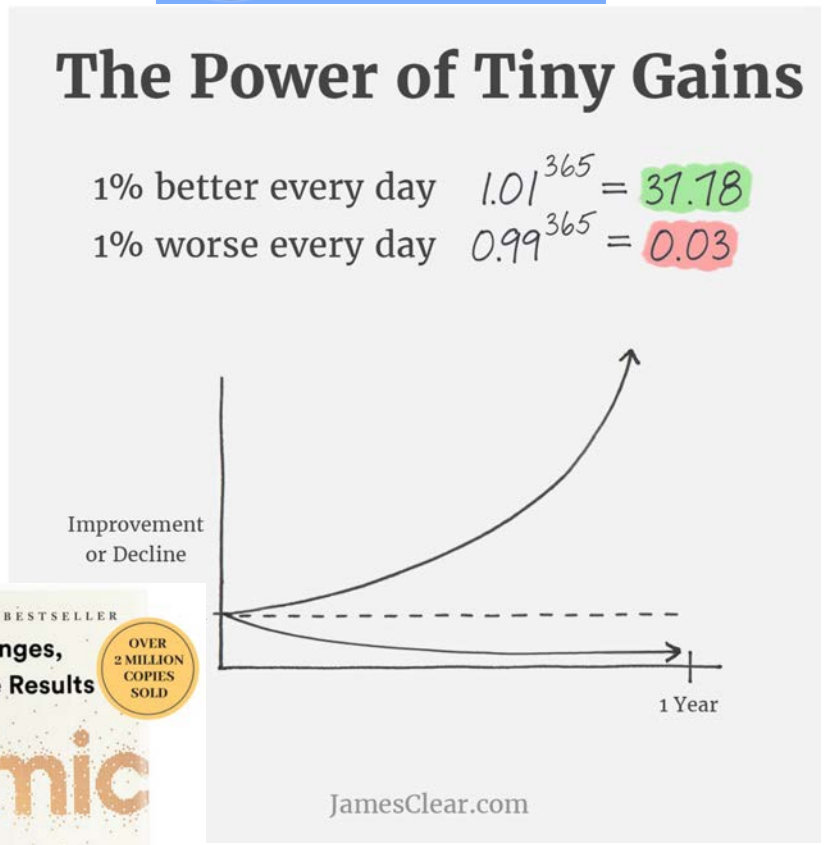
Instead of hoping for a paradigm shift (= immediate animal replacement):

Small improvements of many small components

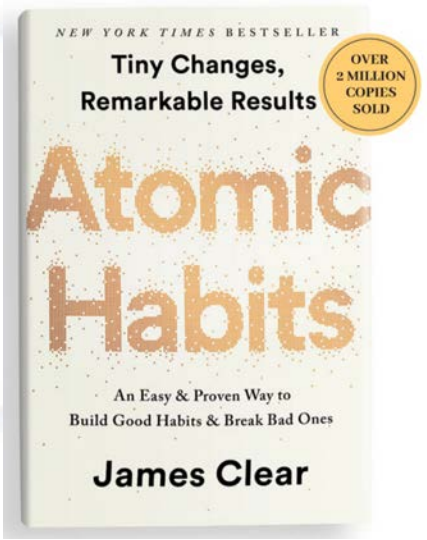
1908-2003: UK cycling team won only 1 gold medal and never won the Tour de France

2003: hired Dave Brailsford

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



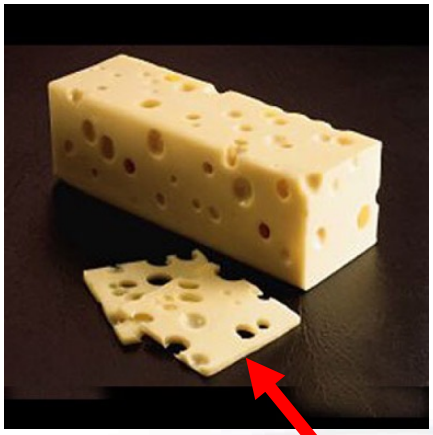
jamesclear.com/marginal-gains



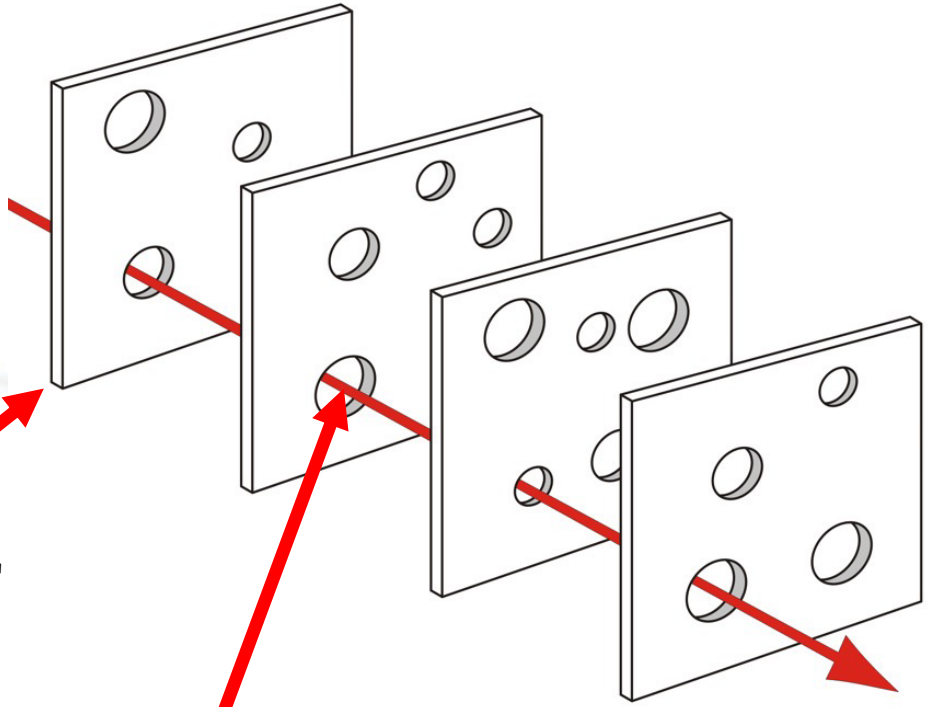
Lab animal perspective:

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

Threat and Error Management



eaugallecheese.com/Swiss-Cheese



"Layer of defence"
or redundancy

Weakness / hazard

Loss

wikipedia.org/wiki/Swiss_cheese_model

Contingency and redundancy

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

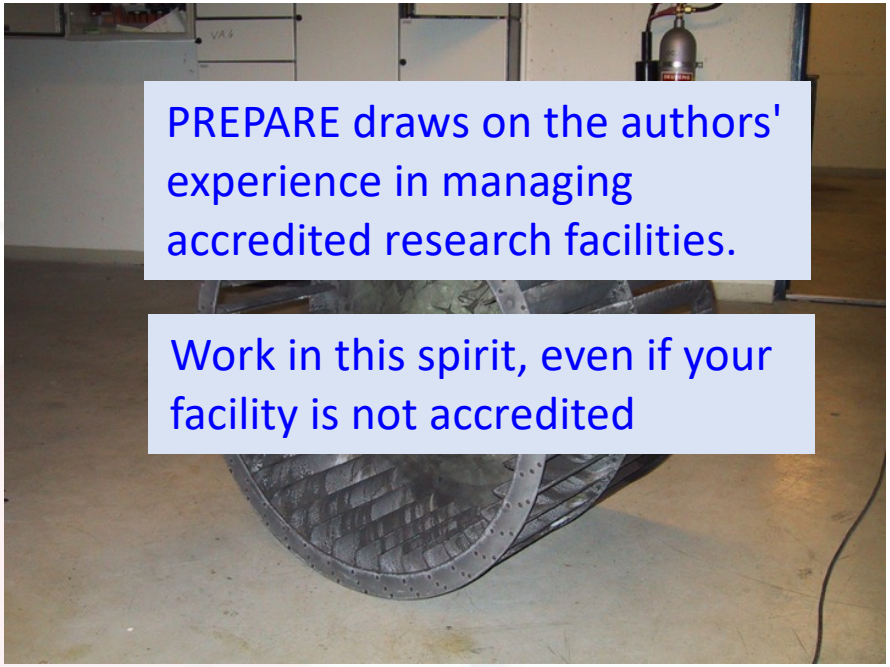


Photo: NMBU

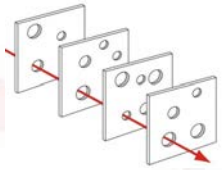
NASA

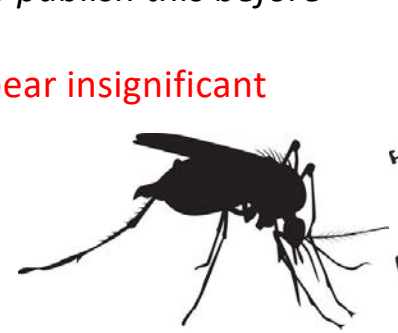
cbsnews.com

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

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!

A Culture of Care is anchored in the EU Directive 2010/63

Recital 31 states:

Animal-welfare considerations should be given the highest priority in the context of animal keeping, breeding and use. Breeders, suppliers and users should therefore have an ***animal-welfare body*** *in place with the primary task of focusing on giving advice on animal-welfare issues. The body should also follow the development and outcome of projects at establishment level,* ***foster a climate of care*** *and provide tools for the practical application and timely implementation of recent technical and scientific developments in relation to the principles of replacement, reduction and refinement...*

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The International Culture of Care Network

A Quick Start Guide and more resources

norecopa.no/CoC

"because we've always done it that way"

"as often as necessary"

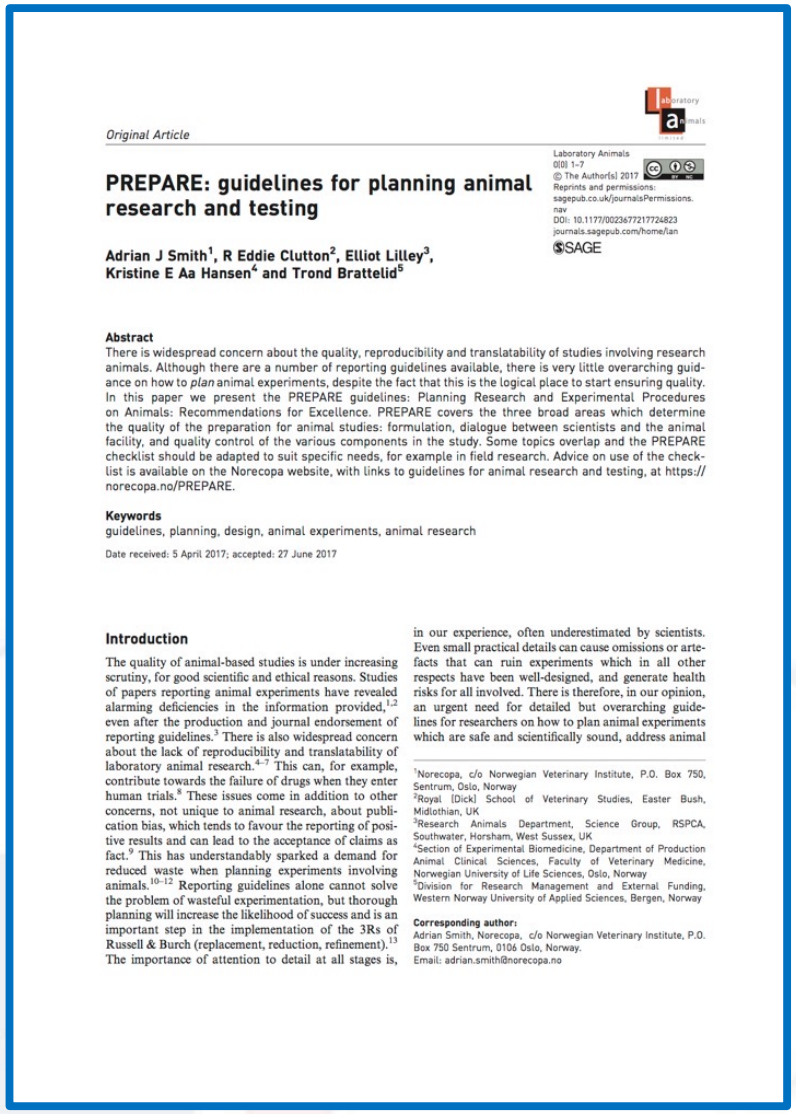
"there are no alternatives"

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

Closely related to a culture of care is the concept of a **Culture of Challenge** (Louhimies, 2015)**.**

Look for the acceptable, rather than choosing the accepted.

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



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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Over 12,000 downloads from the journal website so far

Also downloadable from 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

norecopa

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[a] & Trond Brattelid[a]

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

PREPARE[1] consists of planning guidelines which are complemer
PREPARE covers the three broad areas which determine the qua

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
checklist can be adapted to meet special needs, such as field stud
facilities, since in-house experiments are dependent upon their qu
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.

Three Rs

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.
(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 evaluation	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
7. Education and training	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health 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

Norecopa: PREPARE for better Science

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

norecopa.no/PREPARE

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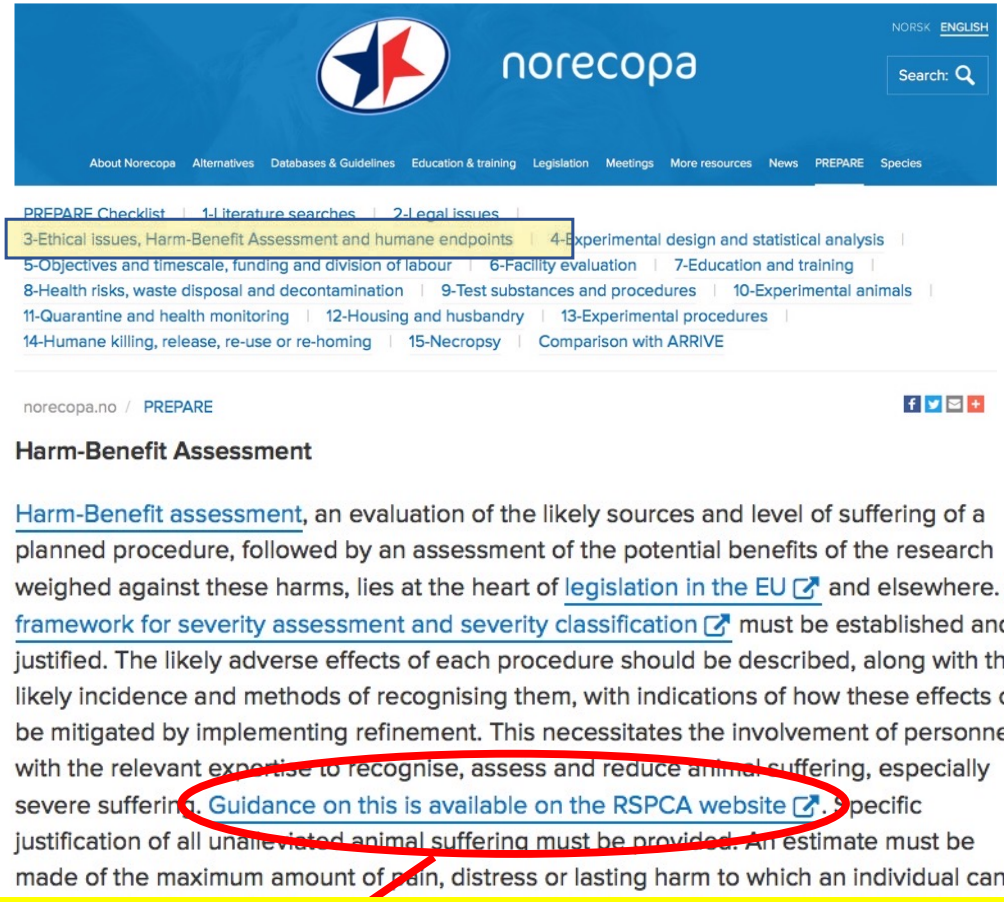
norecopa.no/PREPARE



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

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!

Photo: NMBU

63 pages

A simple but effective Master Plan

Norecopa: PREPARE for better Science

A contract between the animal facility and the research group

Division of labour, responsibilities and cost

Clarifying all stages of the experiment

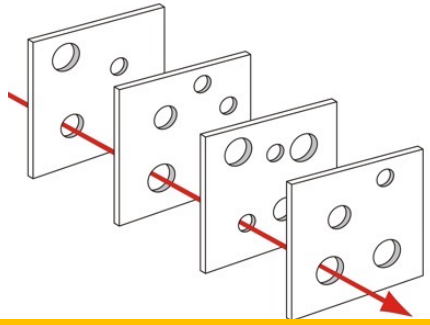
Ensuring that all necessary data are recorded

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

A Contingency Plan, based upon risk assessment

- Access to emergency services (police, fire, medical and veterinary help, security guards, personnel transport in cases of acute illness)
- Means of communication with staff members at all levels
- SOPs for acute illness, including
  - serious haemorrhages
  - fainting
  - corrosive injuries
  - and forms for reporting such injuries
- Firefighting, evacuation of personnel and animals
- Access to specialist services (e.g. ventilation system, plumbing, electrical installations, suppliers of equipment)
- Routines in cases of power failure, water leaks and (if applicable) natural disasters such as flooding
- Routines for emergency killing of animals
- Routines in cases of threats to the facility or personnel

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



Temporary staff at weekends and holidays

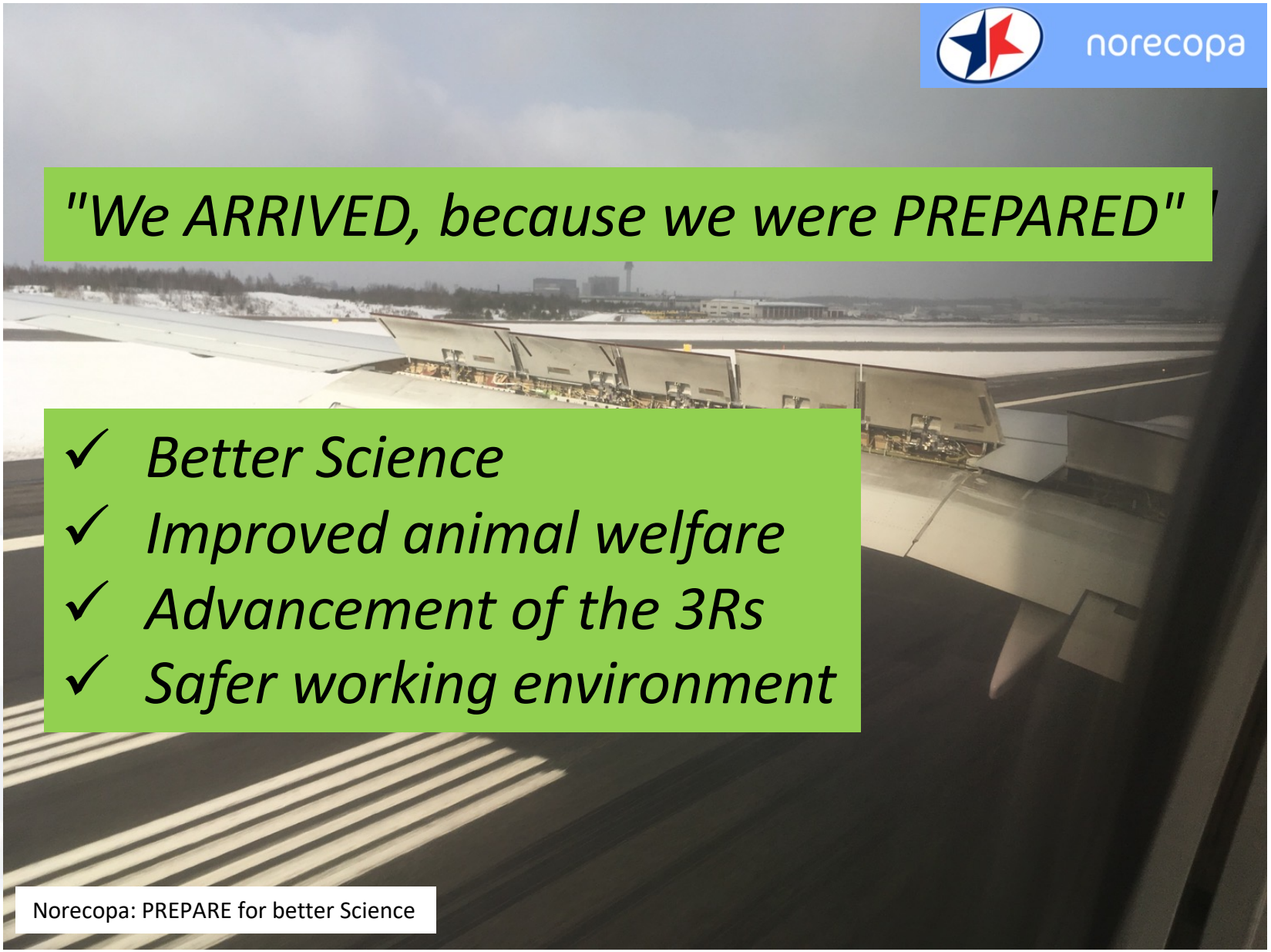
https://norecopa.no/prepare/6-facility-evaluation/master-plan-and-sops/contingency-plan

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

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

PREPARE encourages scientists to collaborate with animal carers and technicians from Day 1

- they have a right to know and will be more motivated
- they know the possibilities (and limitations) in the animal facility
- they often possess a large range of practical skills and are good at lateral thinking
- they know the animals best
- the animals know them best
- lack of involvement creates anxiety, depression and opposition to animal research, as well as limiting creativity which might improve the experiments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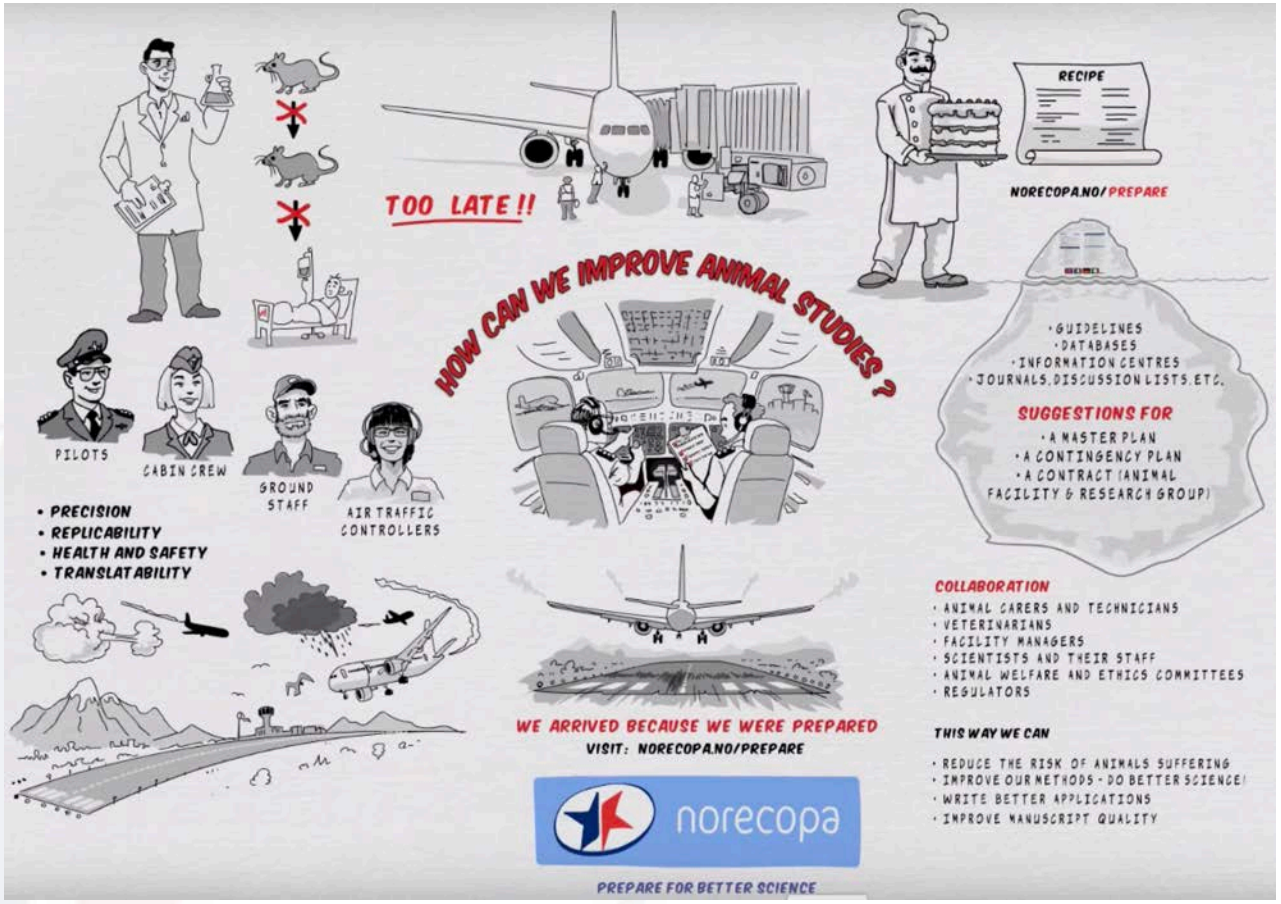
"We ARRIVED, because we were PREPARED"
✓ Better Science
✓ Improved animal welfare
✓ Advancement of the 3Rs
✓ Safer working environment
Norecopa: PREPARE for better Science

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

3-minute cartoon film



Norecopa: PREPARE for better Science

Overall planning:
PREPARE guidelines

Specific details:
EDA + statistician
Other guidelines e.g.
- acclimatisation
- health monitoring
- pain control

Culture of Care

Reporting
Guidelines e.g. ARRIVE, GSPC
Refinement Wiki

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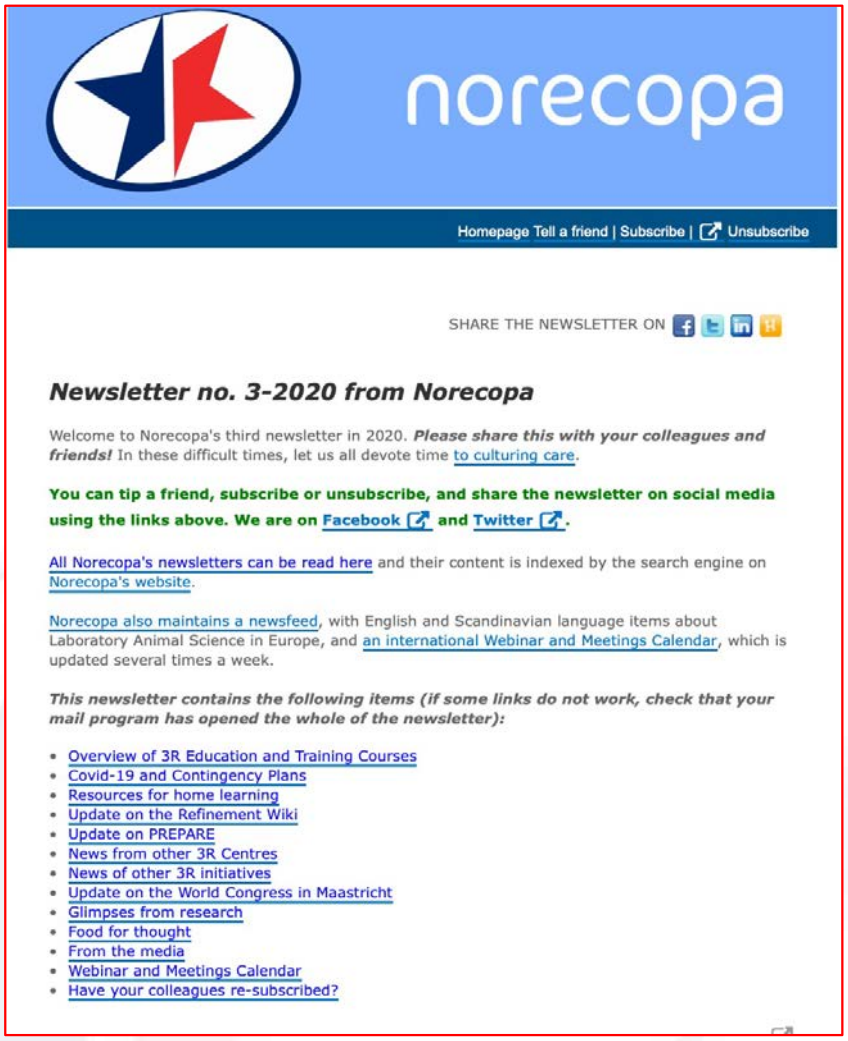
Thanks to Norecopa's main sponsors:

- Standing Committee on Business Affairs, Norwegian Parliament
- Norwegian Ministries of Agriculture and Fisheries
- Research Council of Norway
- Laboratory Animals Ltd.
- Architect Finn Rahn's Legacy
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Society for Animal Protection (Dyrebeskyttelsen Norge)
- Norwegian Animal Protection Alliance (Dyrevernalliansen)
- Novo Nordisk
- Sanofi
- Scottish Accreditation Board (SAB)
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture (USDA)

Graphics: colourbox.com



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