Norecopa: A hub of international resources

norecopa.no/WC11

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

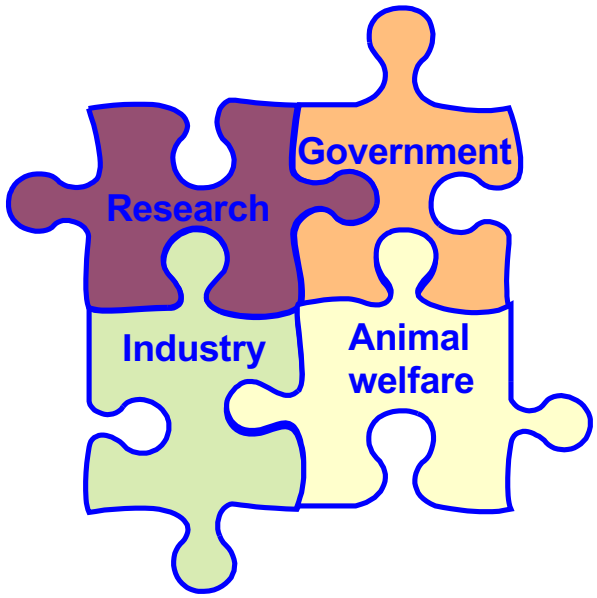
The background for the foundation of Norecopa

peta.org

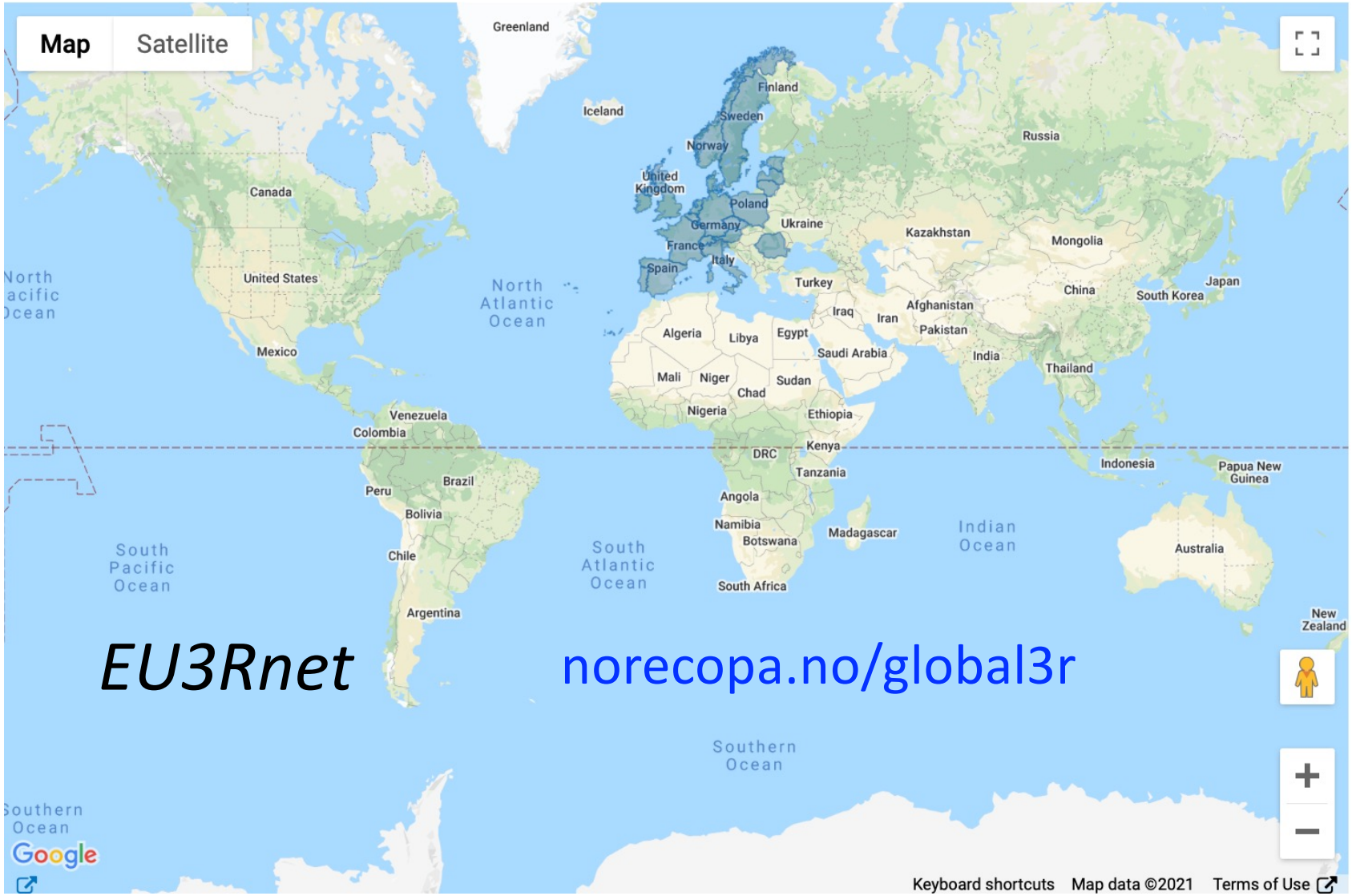
fbresearch.org

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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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

Norecopa: PREPARE for better Science


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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
Application of cardiac myocyte cell lines as models for heart diseases, webinar (Anna Koncz), 8 July 2021
Berlin 3R seminar series: Refinement and Reduction, 8 July 2021
How to perform a systematic review in biomedical research; lessons to improve reproducibility and rigour, webinar (Shona Lang), 9 July 2021
Zebrafish as experimental model for research, webinar series, 8, 9, 15 & 16 July 2021
VetBioNet Summer School: Animal Infectious Disease Research: Good Practice Approaches, Ethics & 3Rs by Design, 12-14 July 2021
KALAS International Symposium, Jeju Island, 14-17 July 2021
Berlin 3R seminar series: Replacement and Refinement, 17 July 2021
Norecopa: A National Consensus Platform working to advance the 3Rs internationally, webinar (Adrian Smith), 19 July 2021
Animal Research: Critical, Challenging & Creative Thinking Course, 19-22 July 2021
August 2021
Course in Animal, General, and Plant Biosafety and Biosecurity, Fort Collins, 2-6 August 2021
ISAE2020 (54th Congress of the International Society for Applied Biology), Bangalore, 2-6 August 2021
4th International TCPF Preclinical Imaging Symposium, virtual event, 11-12 August 2021
EPAA Satellite Training on Skin Sensitisation - Case Studies on DA, Maastricht, 22 August 2021
11th World Congress on Alternatives and Animal Use in the Life Sciences, virtual event, 23 August - 2 September 2021
ASAB Summer Virtual Meeting, 23-25 August 2021

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

Norecopa: PREPARE for better Science

Norecopa's 3R Prize – approx. $ 3,300










norecopa.no/about-norecopa/3r-prize

https://norecopa.no/meetings

International consensus meetings

Harmonisation of the Care and Use of:

- *Fish (2005)*
- *Wildlife (2008)*
- *Fish (2009)*
- *Agricultural animals (2012)*
- *Wildlife (2017)*

All the presentations and consensus statements on the web: a lasting resource

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.

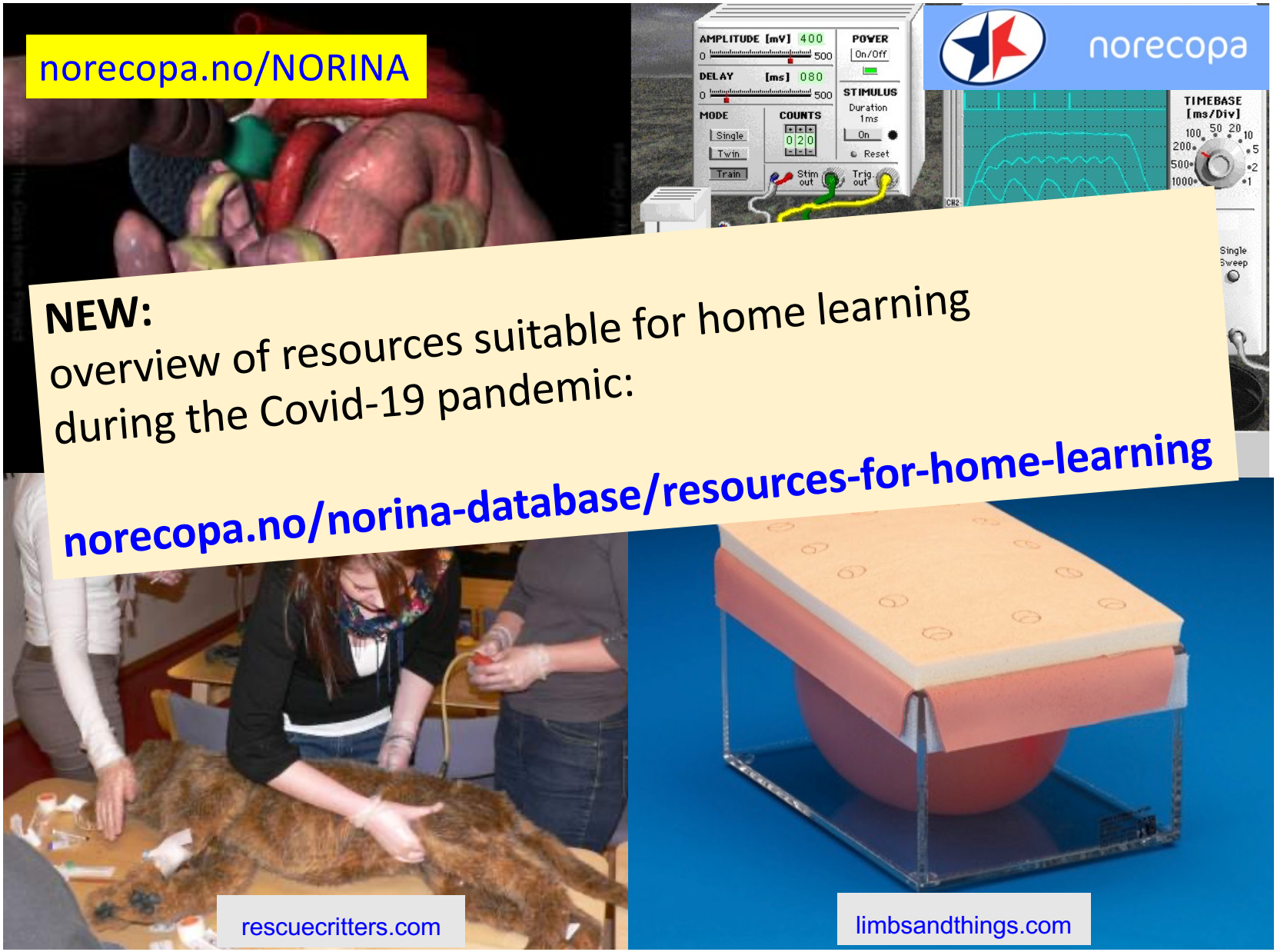
The Norecopa website also includes four other collections:

- 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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NEW:
overview of resources suitable for home learning
during the Covid-19 pandemic:
norecopa.no/norina-database/resources-for-home-learning
rescuecritters.com
limbsandthings.com

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]

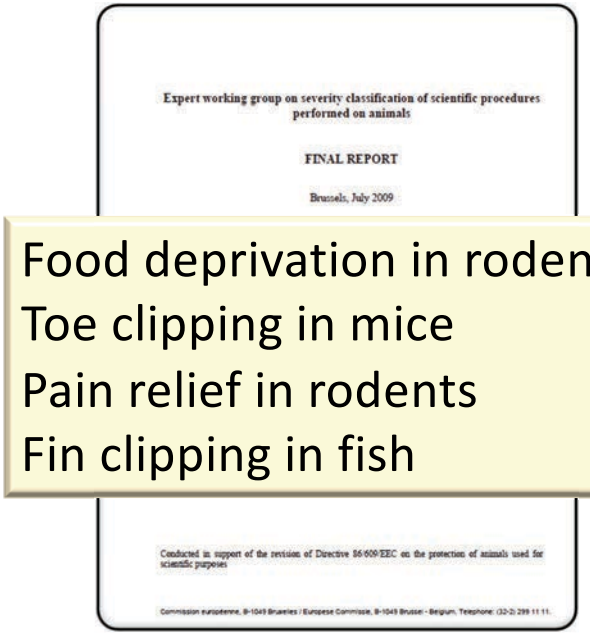
Abstract

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 - 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

The PREPARE guidelines

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

Separate presentation about PREPARE:
Thursday 26 August - 3.00-5.00 p.m. S-311
norecopa.no/WC11-PREPARE

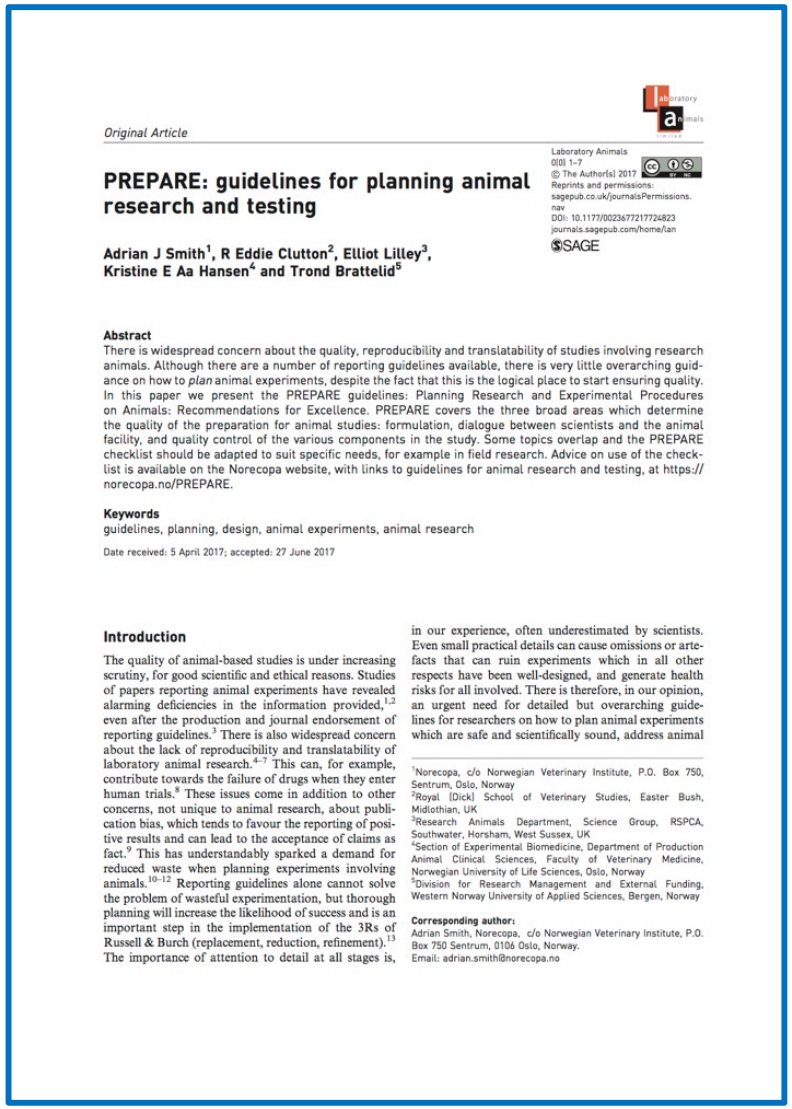
PREPARE was born out of two frustrations

"We can solve the reproducibility crisis by

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

- **better reporting"**

reddit.com



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
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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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[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

Norecopa: PREPARE for better Science

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

https://doi.org/10.1177/0023677217724823

Over 19,000 downloads from the journal website so far

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

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

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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

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PREPARE

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The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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

PREPARE[1] consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE[2].
PREPARE covers the three broad areas which determine the quality of the preparation for animal 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 on the Norecopa website, with links to global resources, at **https://norecopa.no/PREPARE**.
The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

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
3. Ethical issues	☐ [illegible] science, good sense, ☐ [illegible] 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!

Let us know if you would like another language!

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 [illegible]
[illegible]	[illegible] factors and any [illegible] housing).
[illegible] 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.

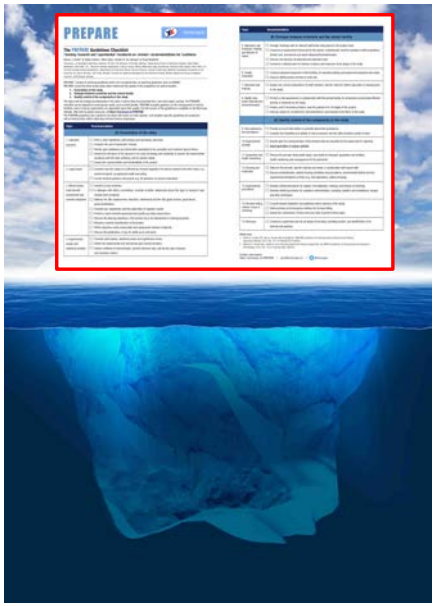
References

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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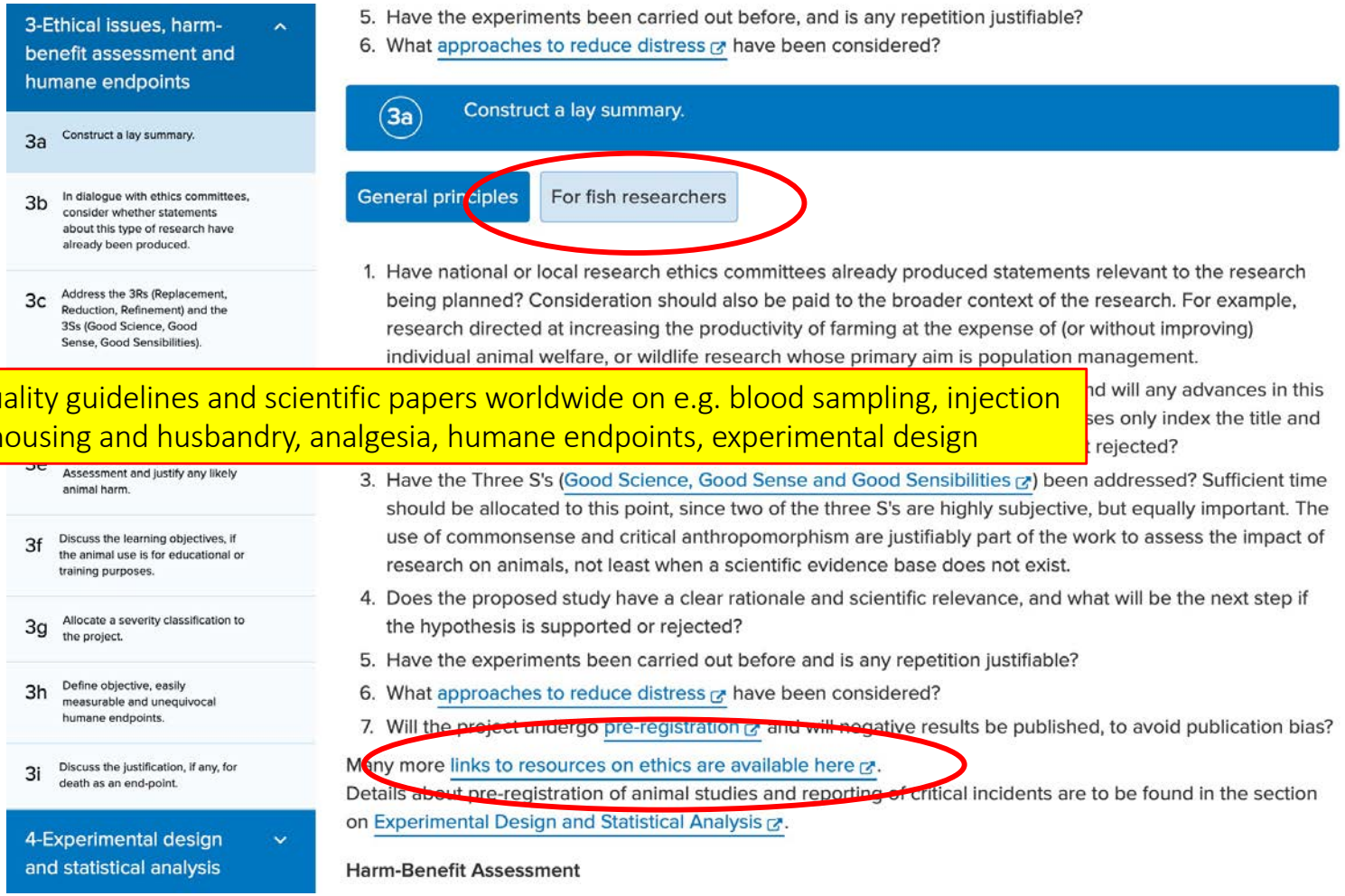

Links to quality guidelines and scientific papers worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design

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"We ARRIVED, because we were PREPARED" !
✓ Better Science
✓ Improved animal welfare
✓ Advancement of the 3Rs
✓ Safer working environment
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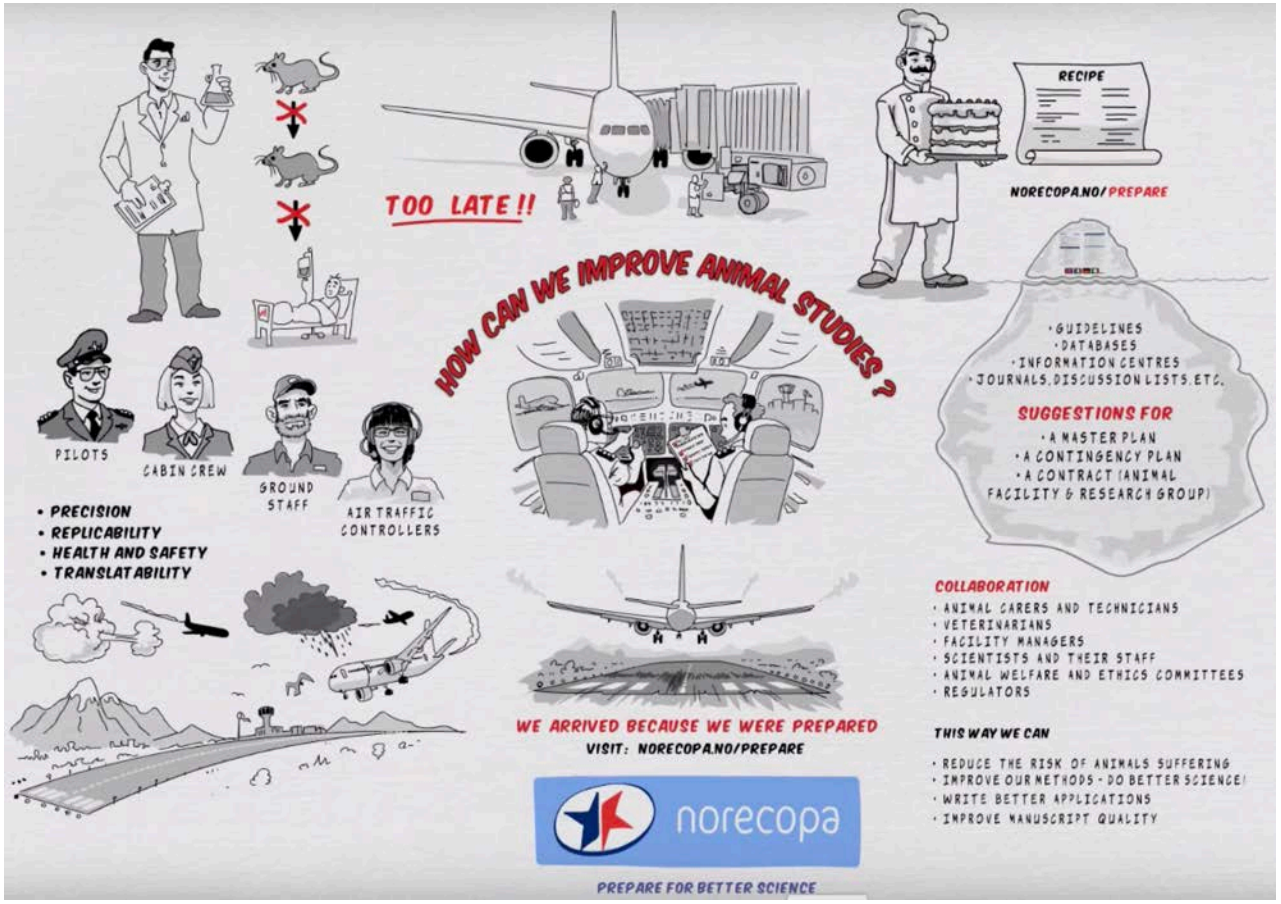
BRAINER
Norecopa: PREPARE for better Science

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

3-minute cartoon film



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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.

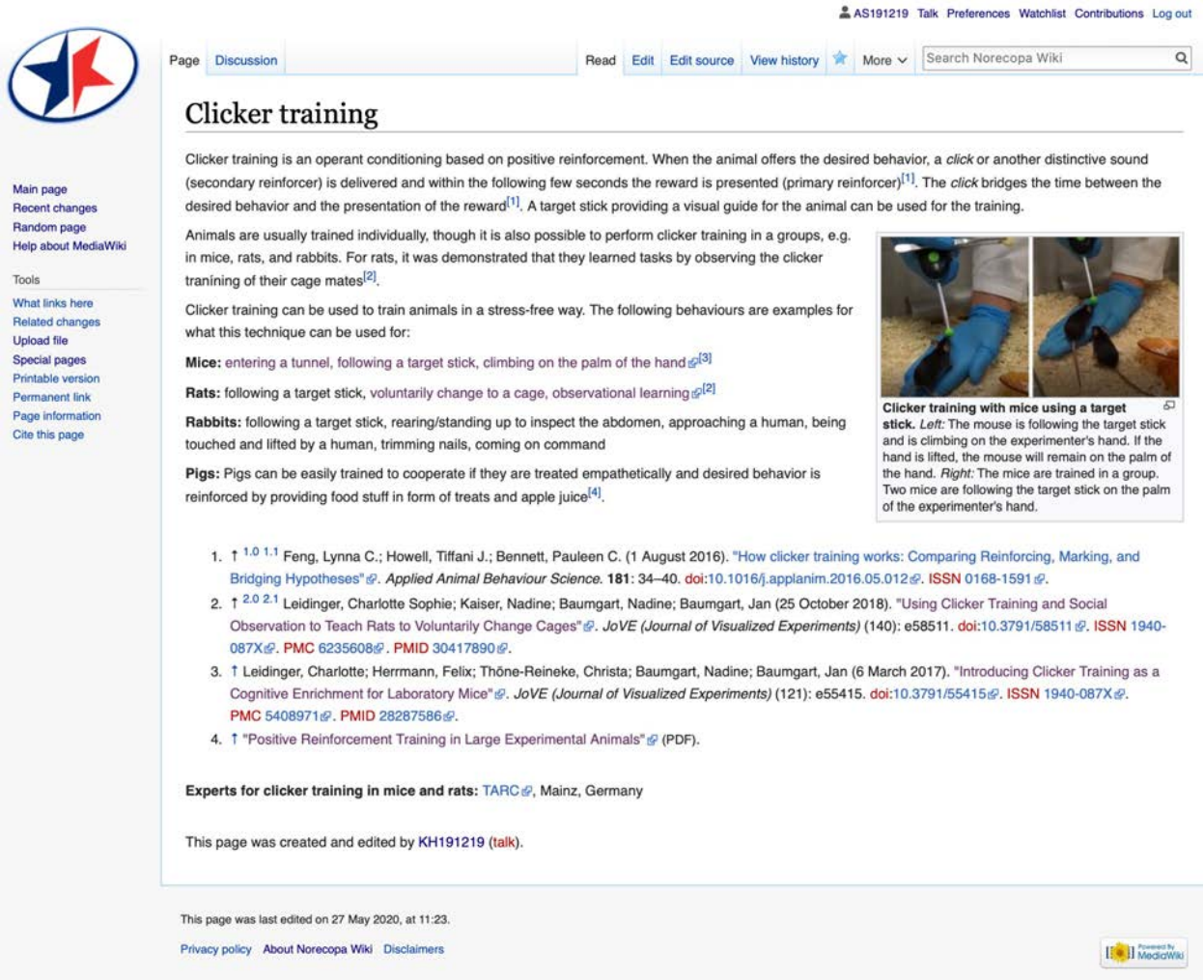
Designed to be

- 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

Separate presentation: Tuesday 31 August 6.30-8.30 p.m. CEST (session S301).
Pdf of the slides available at https://norecopa.no/WC11-wiki

Refinement Wiki

wiki.norecopa.no



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Clicker training

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

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

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

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

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

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

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

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

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

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

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

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Culture of Care

The International Culture of Care Network

norecopa.no/coc

A demonstrable commitment, throughout the establishment, to improving:

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

It goes beyond simply complying with the law!


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The Research Council of Norway

3R Flag

- **Frameworks for classifying the welfare of farmed Atlantic salmon based upon severity assessment (2021-2025)**
- **SPHERTOX: Hepatic 3D spheroids, the next generation of testing in toxicology (2021-2025)**
- **ENRICH Fish (2015-2017): to improve the rearing conditions and welfare of Atlantic salmon used in laboratory experiments**
- **3R-KART: A 3R-strategy for fish to establish suggestions for a platform for increasing implementation of the 3Rs in Norwegian fish research (2010-2012)**
- **Fish in Research - environmental requirements and welfare indicators in fish (2009)**

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Graphics: colourbox.com

PREPARING, CARING, SHARING and FLAGGING

The scientific and welfare benefits of increased collaboration and transparency

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

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

Ensure that scientists and animal care staff collaborate closely from day one, to ensure all aspects of a study that potentially uses animals have been addressed
norecopa.no/PREPARE

Promote examples of improvements in the care and use of animals, for example by using the Refinement Wiki
norecopa.no/wiki

Encourage a strong Culture of Care around animal research, promoting mutual respect, animal and human wellbeing, and safety
norecopa.no/coc

Highlight advances made within the 3Rs in scientific papers, if necessary in a separate methodology paper
norecopa.no/3R

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

Thanks to Per Trystad for the artwork.

norecopa ***PREPARE for better Science***

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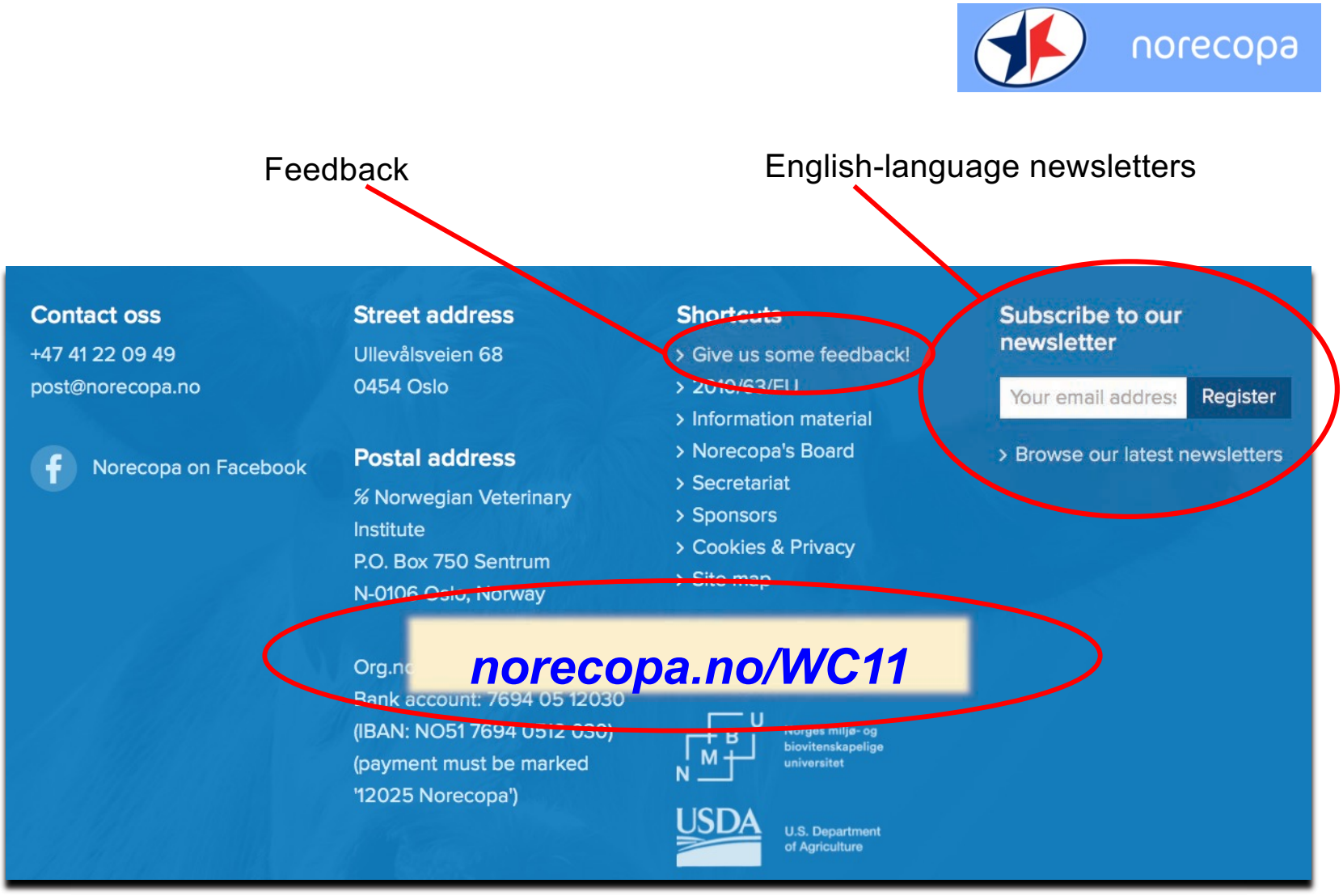
Thursday 26 August Session S311, 3.00-5.00 p.m.
The PREPARE guidelines **norecopa.no/WC11-PREPARE**

Friday 27 August Session S113, 3.00-5.00 p.m.
Wildlife research **norecopa.no/WC11-wildlife**

Tuesday 31 August Session S301, 6.30-8.30 p.m.
The Refinement Wiki **norecopa.no/WC11-wiki**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