The PREPARE and ARRIVE guidelines: for better Science, Welfare and Safety

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norecopa.no/050323

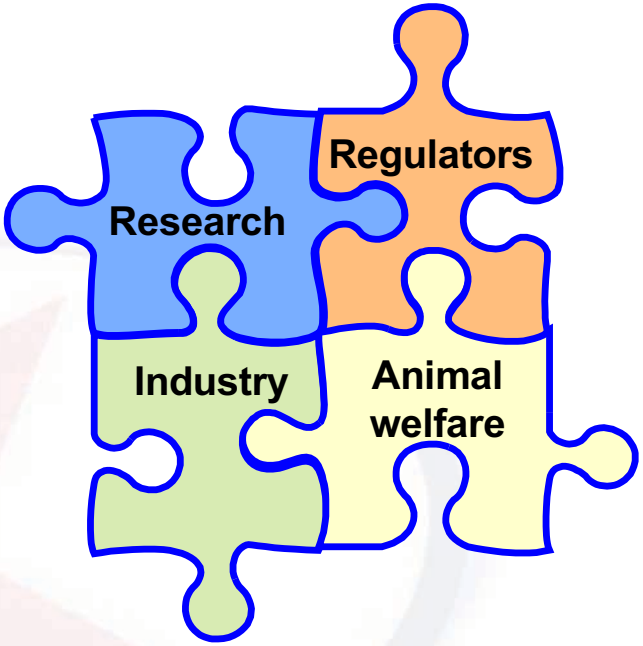
https://norecopa.no

Norecopa is Norway's National *Consensus*-platform,

working to advance ***all the three R's***:

Replacement, Reduction and Refinement

Its Board represents:



Established in 2007

norecopa.no

Disclosures about resources which will be mentioned

- *Webmaster for the Norecopa site - information about global guidelines*
- *Lead author of the 3R Guide database of guidelines*
- *Lead author of the PREPARE guidelines*
- *Manager of the Refinement Wiki*

"...better science"?

- Implementation of all three Rs
- valid data (a true treatment effect)
- reproducible and translatable experiments
- best possible animal welfare
- health & safety (of animals and people)
- a culture of care in the research group
- communication of best practice to others

colourbox.com

Harms and Benefits

- ***The harm*** is experienced **NOW, and is certain**
- **The benefit** is ***in the future***, for ***other animals or humans***, and ***is uncertain***
- ***There are widespread concerns about the standard of animal experiments***

norecopa.no/concerns

We can work to tip the balance

***The 3 Rs* to minimise the harm:**

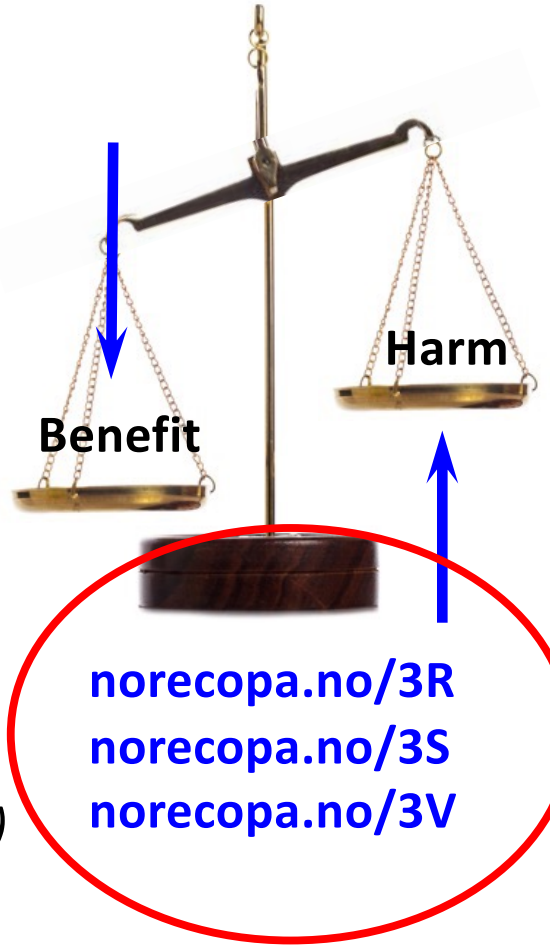
- *Replace the unnecessary experiments*
- *Reduce the number of animals used*
- *Refine the conditions for the animals*

***The 3 Ss* - your commonsense and your heart**

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

***The 3 Vs* to increase the validity of the experiment:**

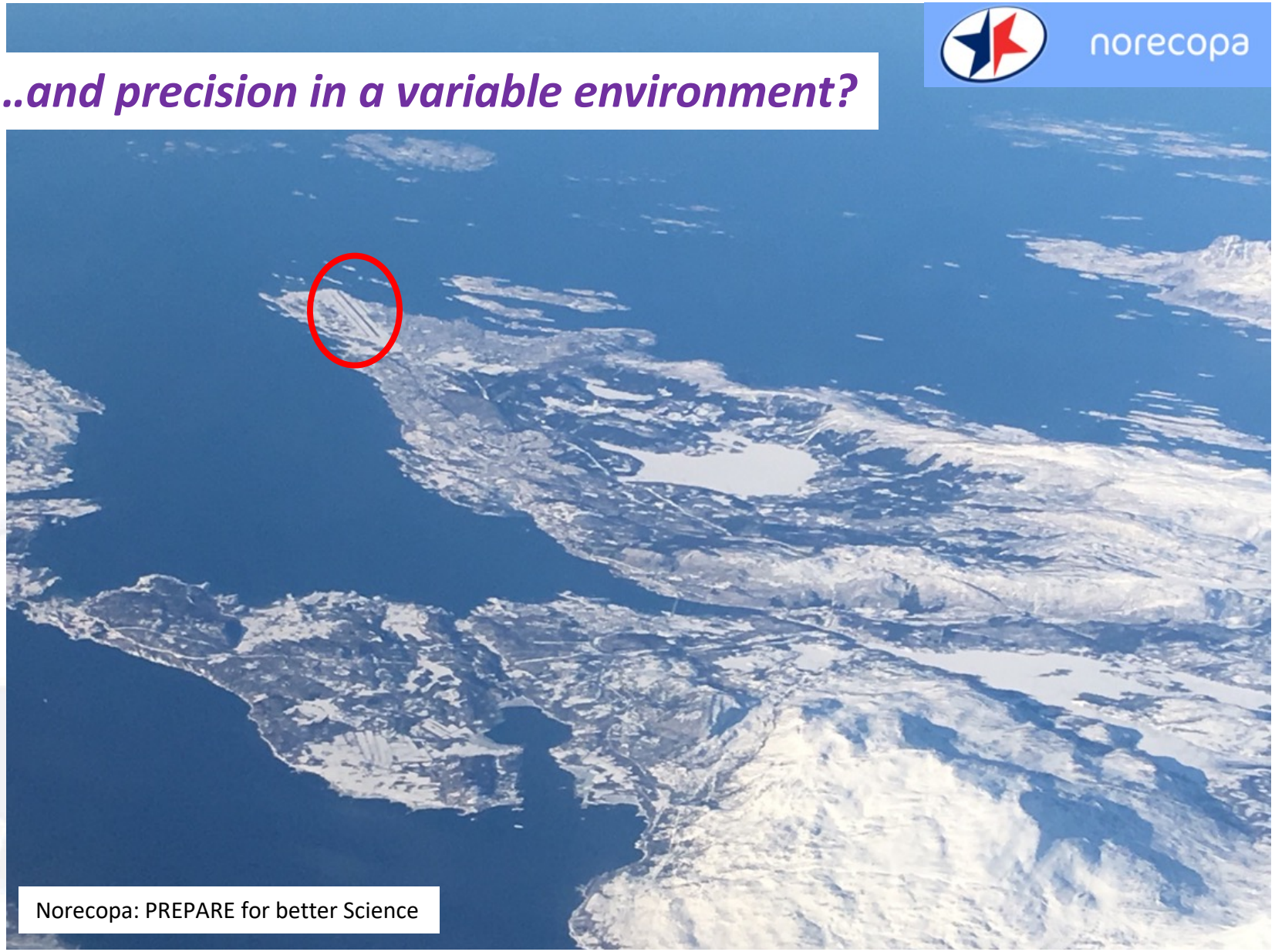
- *Construct Validity (can the model answer the question?*
- *Internal Validity (has the experiment been correctly designed?)*
- *External Validity (are the results translatable to the target group?)*



How do others achieve reproducibility?

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

…and precision in a variable environment?

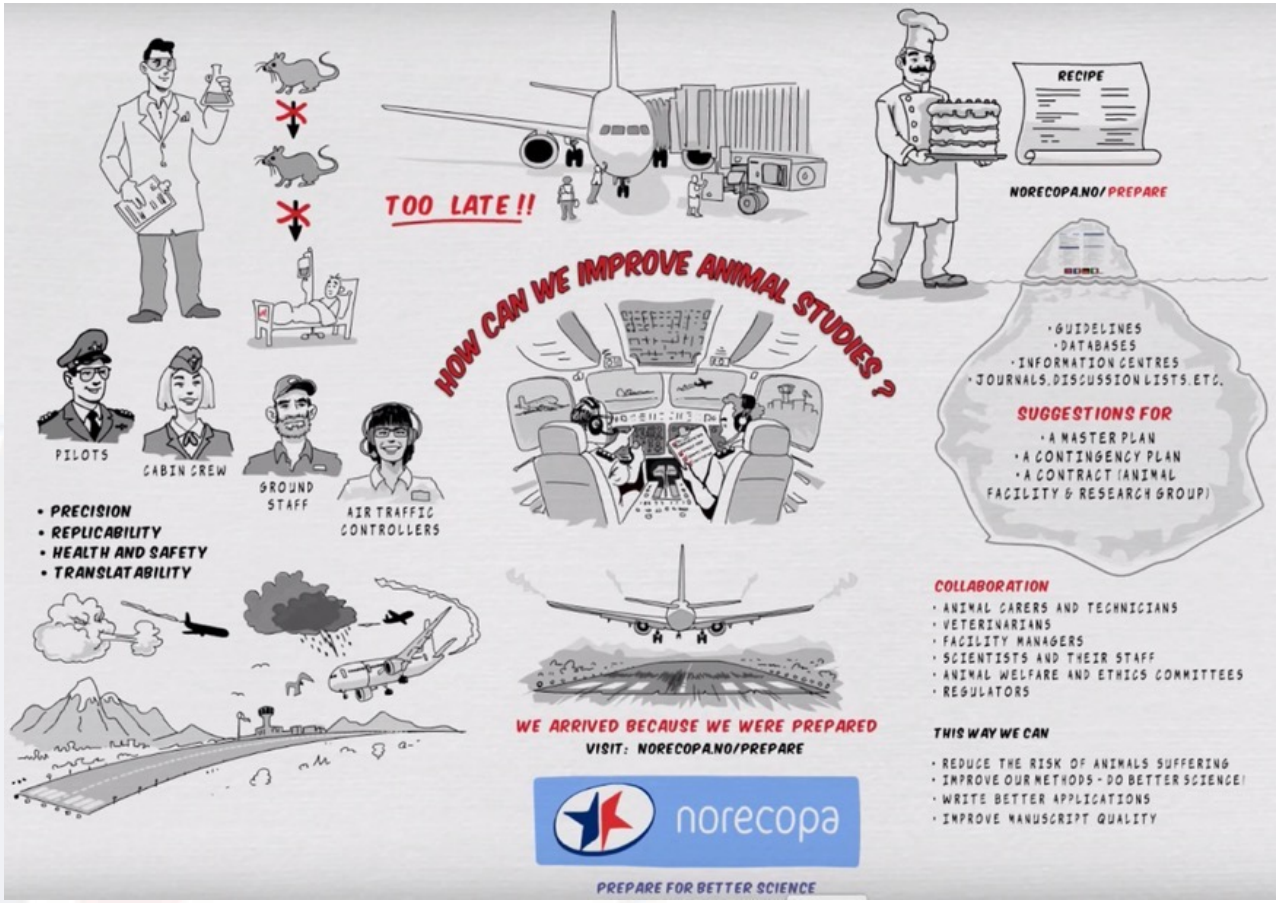


Norecopa: PREPARE for better Science


PILOTS
CABIN CREW
GROUND STAFF
AIR TRAFFIC CONTROLLERS

norecopa.no/PREPARE/film

3-minute whiteboard film



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travelandleisure.com/airlines-airports/what-happens-when-planes-hit-birds

15.25.33	-01.38	Kaptein	Cockpit	V one, rotate
15.25.38	-01.33	Kaptein	Cockpit	positive rate
15.25.39	-01.32	Styrmann	Cockpit	Gear up please
15.25.39	-01.32	Kaptein	Cockpit	Gear up
15.26.37	-00.34	Kaptein	Cockpit	Uh what a view of the Hudson today
15.26.42	-00.29	Styrmann	Cockpit	Yeah
15.27.07	-00.04	Kaptein	Cockpit	After takeoff checklist complete
15.27.10	-00.01	Kaptein	Cockpit	Birds
15.27.11	-00.00	Styrmann	Cockpit	Whoa
15.27.11	00.00			
15.27.12	+00.01	Kaptein	Cockpit	Oh ---
15.27.13	+00.02	Styrmann	Cockpit	Oh yeah
15.27.14	+00.03	Styrmann	Cockpit	Uh oh
15.27.15	+00.04	Kaptein	Cockpit	We got one rol... both of 'em rolling back
15.27.18	+00.07	Kaptein	Cockpit	Ignition, start
15.27.21	+00.10	Kaptein	Cockpit	I'm starting the APU
15.27.23	+00.12	Kaptein	Cockpit	My aircraft
15.27.24	+00.13	Styrmann	Cockpit	Your aircraft
15.27.28	+00.17	Kaptein	Cockpit	Get the QRH... loss of thrust on both engines
15.27.32	+00.21	Kaptein	Radio	Mayday mayday mayday. Uh this is Cactus fifteen thirty [sic] nine, hit birds. We've lost thrust on both engines. We're turning back towards LaGuardia.

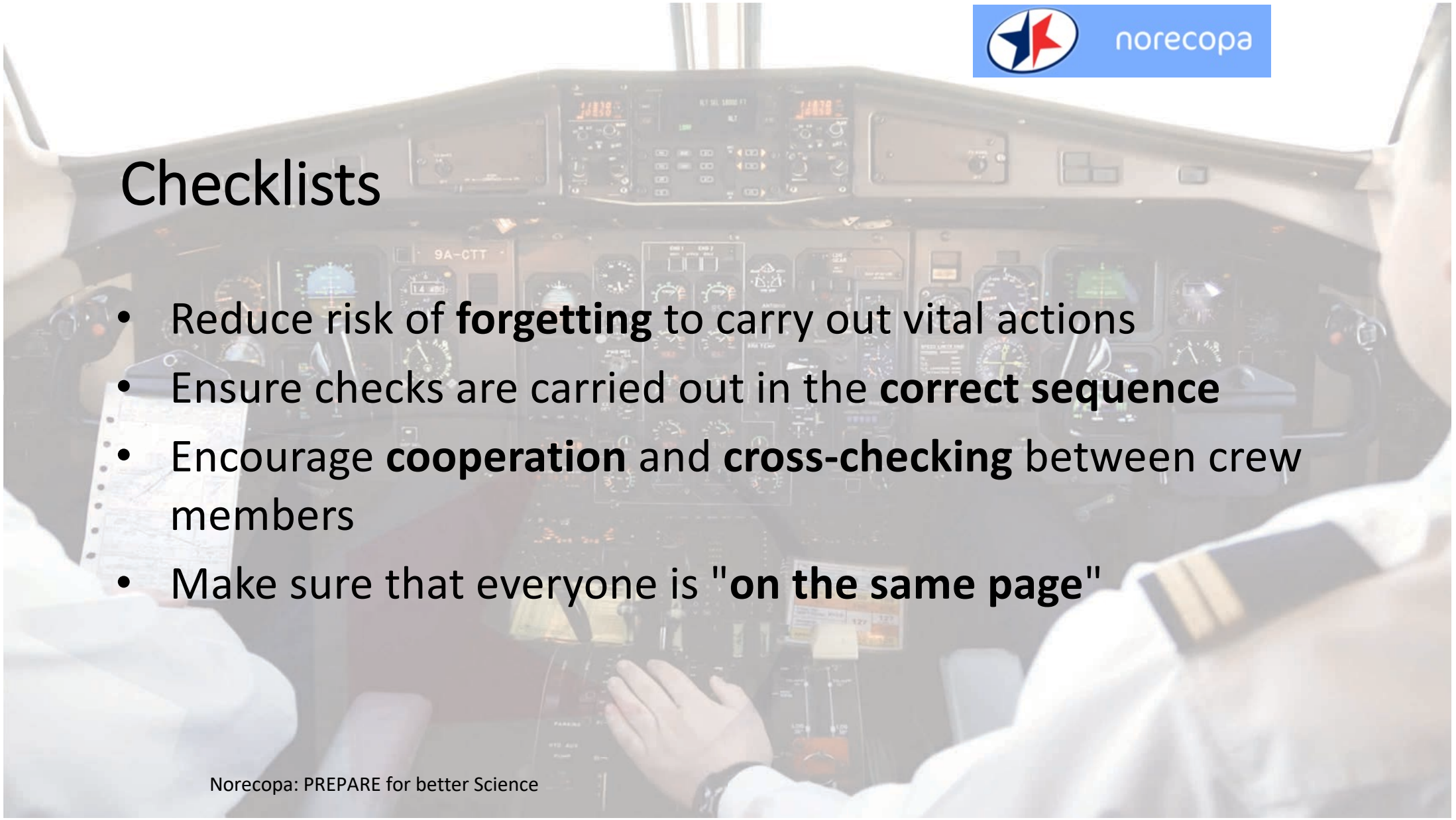
no.wikipedia.org/wiki/US_Airways_Flight_1549

en.wikipedia.org

Hudson River, 2009

All 155 passengers and crew saved

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**"

Rapid evacuation by trained cabin crew saved many lives

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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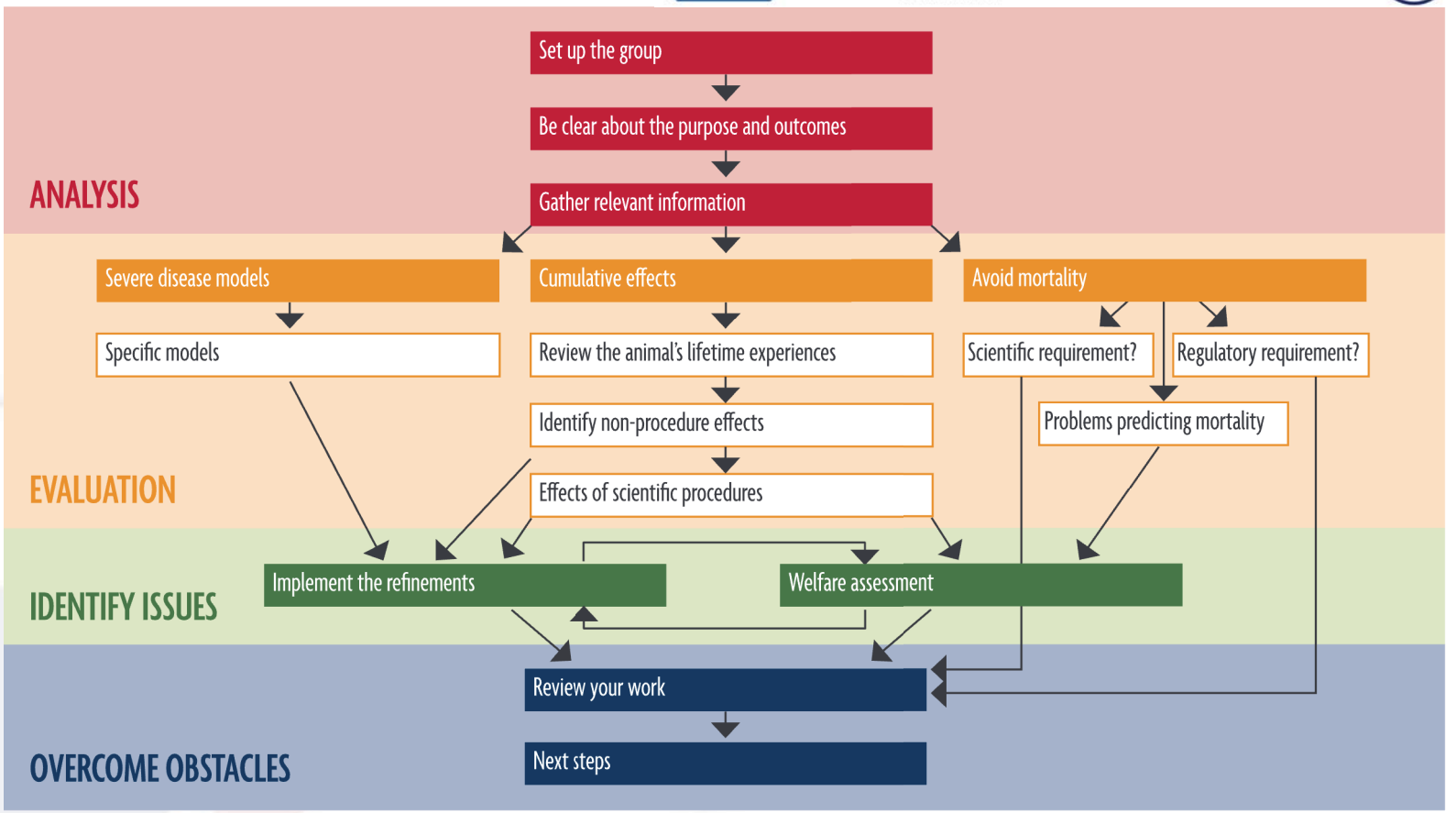
The pathway to better science

Norecopa: PREPARE for better Science

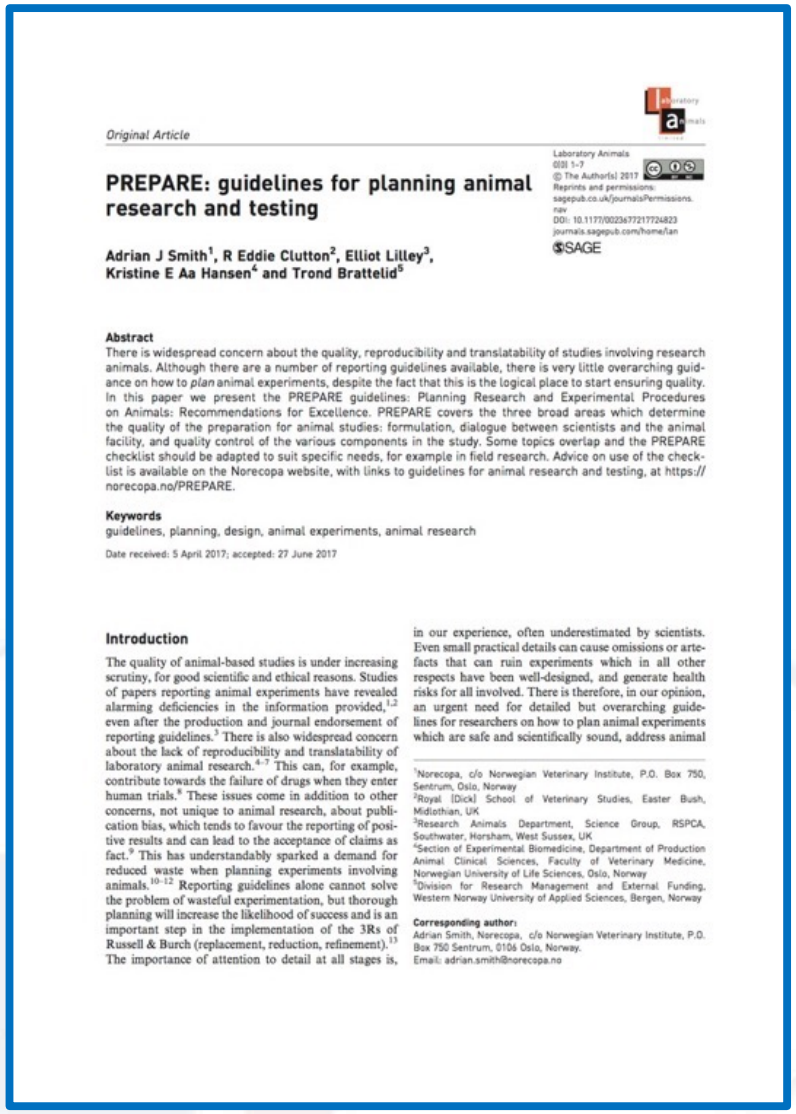
norecopa.no/PREPARE *and*
ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1

A roadmap to reduce severe suffering



focusonseveresuffering.co.uk/roadmap

Norecopa: PREPARE for better Science



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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[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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Over 27,000 views/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

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Systematic Reviews
Synthesis of Evidence from published papers
In vitro / in silico research

norecopa.no/PREPARE/prepare-checklist

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[d] & Trond Bratteli[d]

[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 [illegible]. PREPARE covers the three broad areas which determine the quality of [illegible]:

1. Formulation of the study
2. Dialogue between [illegible]

[illegible] is available on the Norecopa website. The [illegible] will evolve as more species- and situation-specific guidelines are produced, and [illegible] 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.

Animal welfare and 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.
[illegible]	[illegible] sical inspection of the facilities, to evaluate building and equipment standards and needs. [illegible] g levels at times of extra risk.
[illegible]	[illegible] ent competence of staff members and the need for further education or training prior
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(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.
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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 & Bratteli T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*. 2017. DOI: 10.1177/0023677217724823.
2. Kilkenny C, Browne WJ, Cuthill IC *et al.* Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PloS Biology*. 2010; DOI: 10.1371/journal.pbio.1000412.

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

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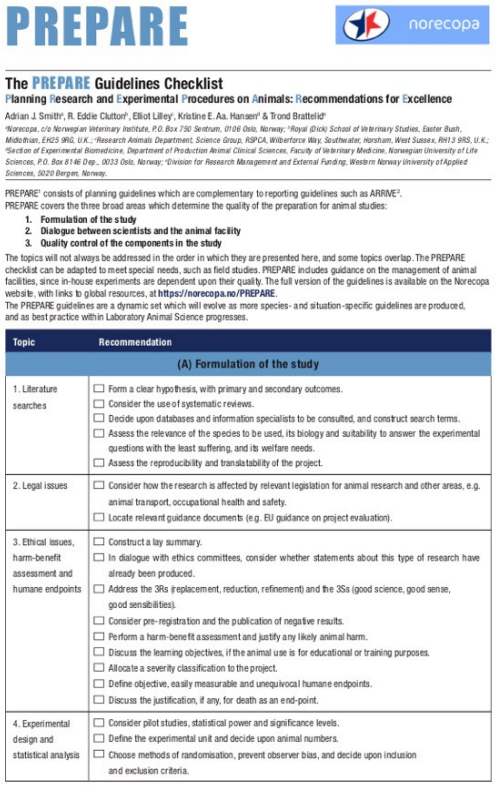
norecopa.no/PREPARE/prepare-checklist

Three versions of the checklist:

1. plain pdf file



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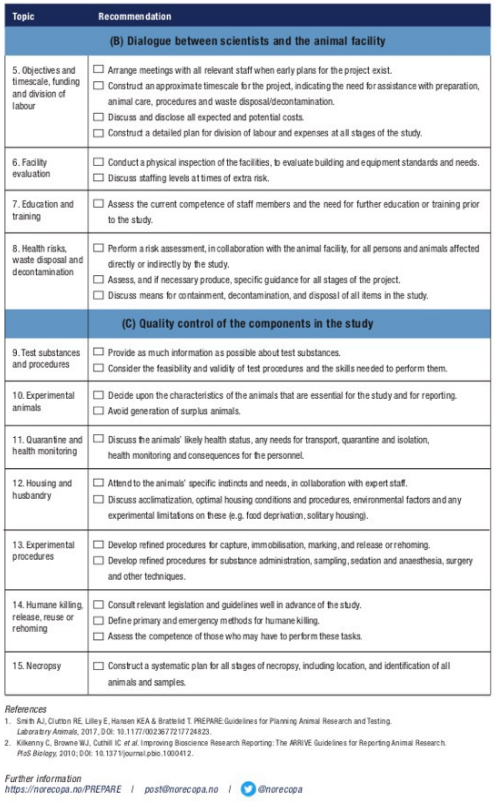

Topic	Recommendation
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6. Facility evaluation	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
7. Education and training	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
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Three versions of the checklist:

2. fillable pdf file

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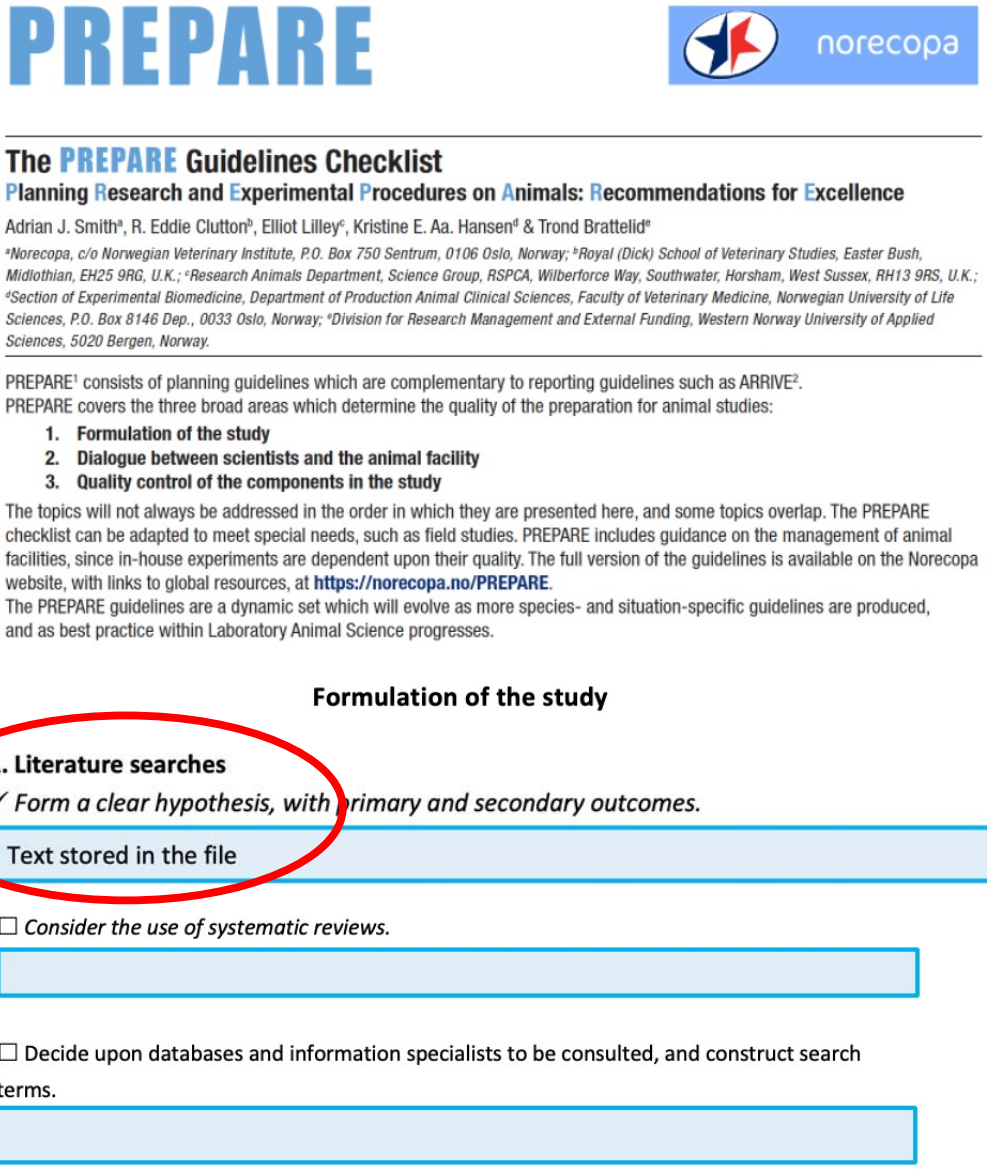

PREPARE

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Formulation of the study

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✓ *Form a clear hypothesis, with primary and secondary outcomes.*

Text stored in the file

☐ *Consider the use of systematic reviews.*

☐ Decide upon databases and information specialists to be consulted, and construct search terms.

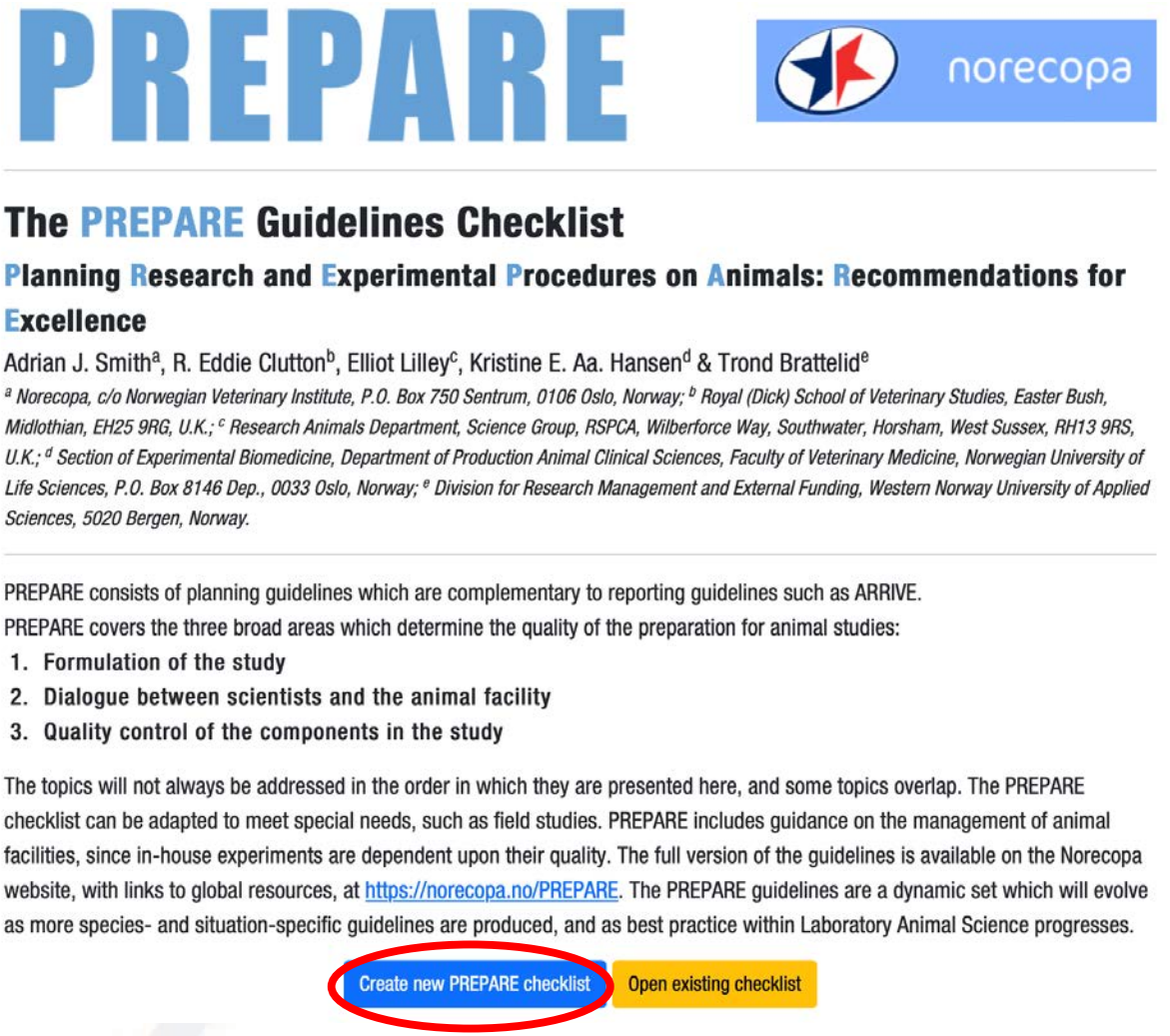
norecopa.no/PREPARE/prepare-checklist

Three versions of the checklist:

3. online version

norecopa.no/PREPARE/Mychecklist

Norecopa: PREPARE for better S



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[d] & Trond Brattelid[e]

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

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

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available 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.

Create new PREPARE checklist Open existing checklist

Your auth code for this checklist is **deeb7d** Please save this code so you are able to open your checklist at a later time. You can also bookmark this page.

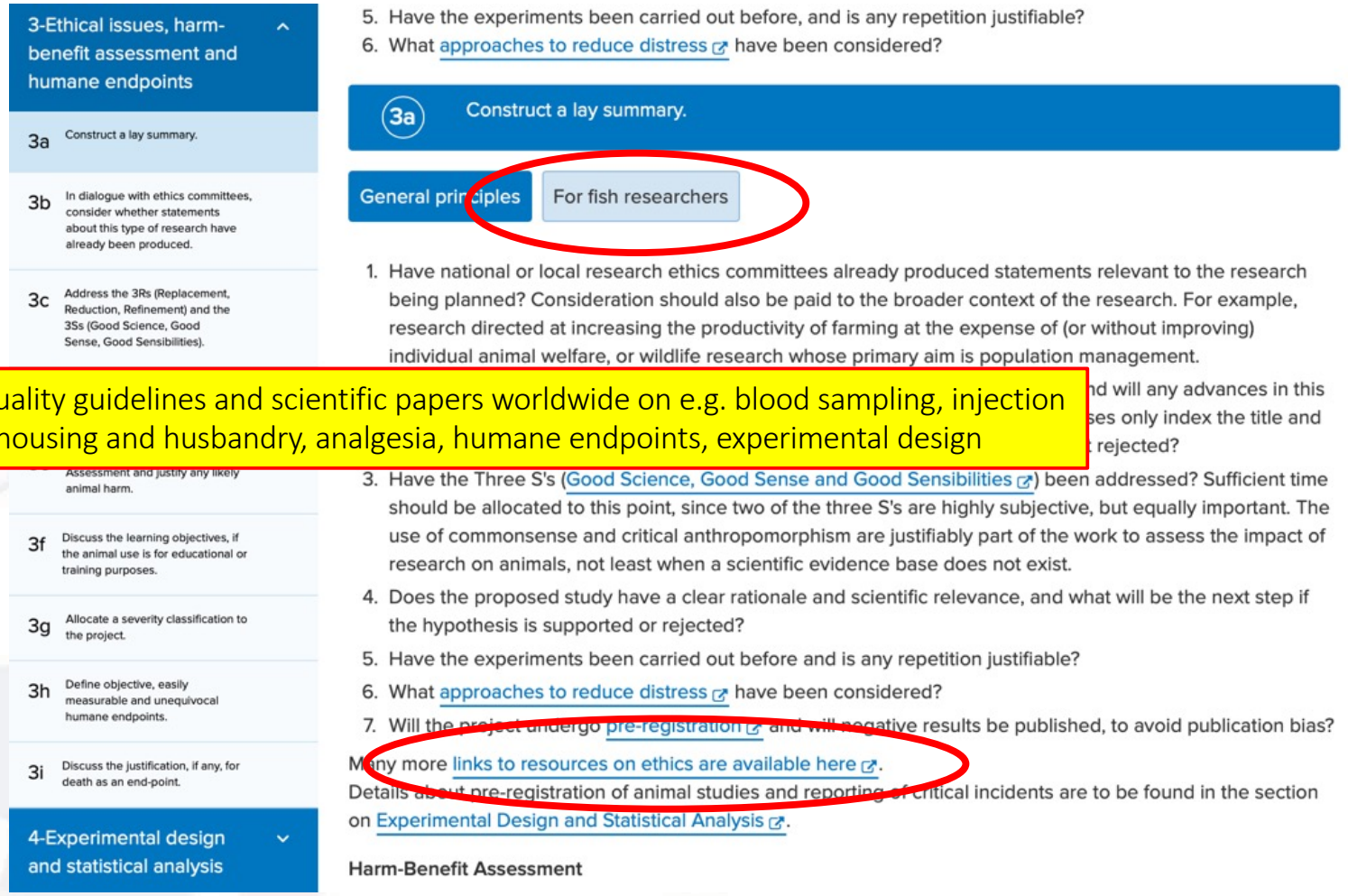
Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	Form a clear hypothesis, with primary and secondary outcomes. Consider the use of systematic reviews. Decide upon databases and information specialists to be consulted, and construct search terms. Assess the relevance of the species 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.

text only stored on author's computer

norecopa.no/prepare/mychecklist?id=deeb7d

Nore

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

Norecopa: PREPARE for better Science

PREPARE is closely linked to

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

approx. 9,000 webpages
350,000 hits annually

7-8 detailed newsletters per year

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

norecopa.no/3RGuide

Links to 415 guidelines

A good practice guide to the administration of substances and removal of blood, including routes and volumes

3R Guide database/c6721 (legacy id: 15079)

This paper provides the researcher in the safety evaluation laboratory with an up-to-date, easy-to-use set of data sheets to aid in the study design process whilst at the same time affording maximum welfare considerations to the experimental animals.

A guide to defining and implementing protocols for the welfare assessment of laboratory animals

3R Guide database/68ba4 (legacy id: 15065)

Eleventh report of the BVAAWF/FRAME/RSPCA/UFAW Joint Working Group on Refinement

A guide to the care and use of native Australian mammals in research and teaching

3R Guide database/502ff (legacy id: 15377)

The Guide supports implementation of the Australian Code for the care and use of animals for scientific purposes (8th edition, 2013) and ensures that the specific and unique needs of Australian native mammals are met when these animals are used for scientific purposes.

AAALAC Position Statements

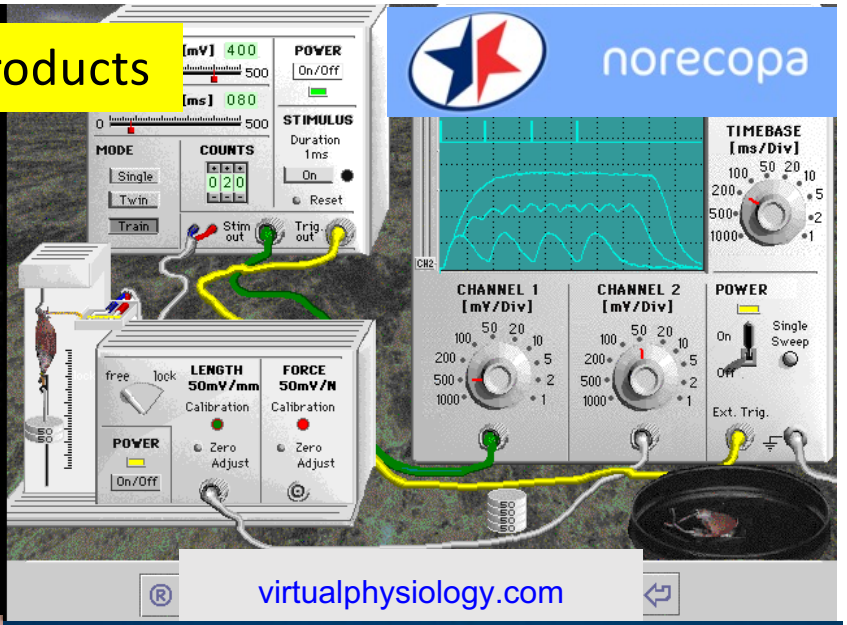
3R Guide database/ef566 (legacy id: 15155)

In connection with its work of accreditation of animal care and use programmes, AAALAC International has issued position statements on a number of key elements in such a programme.

colourbox.com

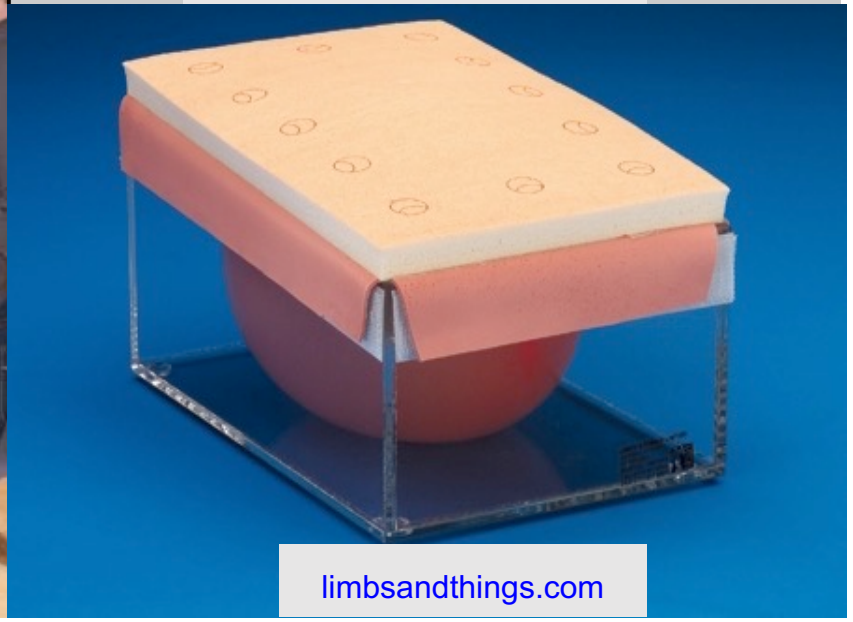
NORINA database: approx. 3,000 products

3dglasshorse.com



virtualphysiology.com

rescuecritters.com



limbsandthings.com

norecopa.no/education-training/films-and-slide-shows

norecopa

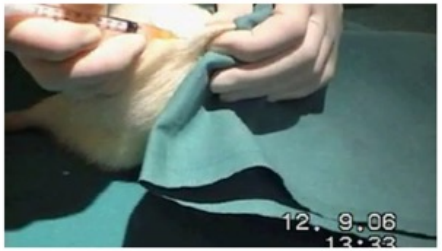
Rat s.c. injection
Norecopa | 1,380 views

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

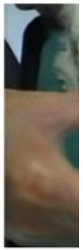
Blood collection from the saphenous vein in the mouse
Norecopa | 6,777 views



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: PREPARE for better Science

RESEARCH ANIMAL TRAINING

researchanimaltraining.com

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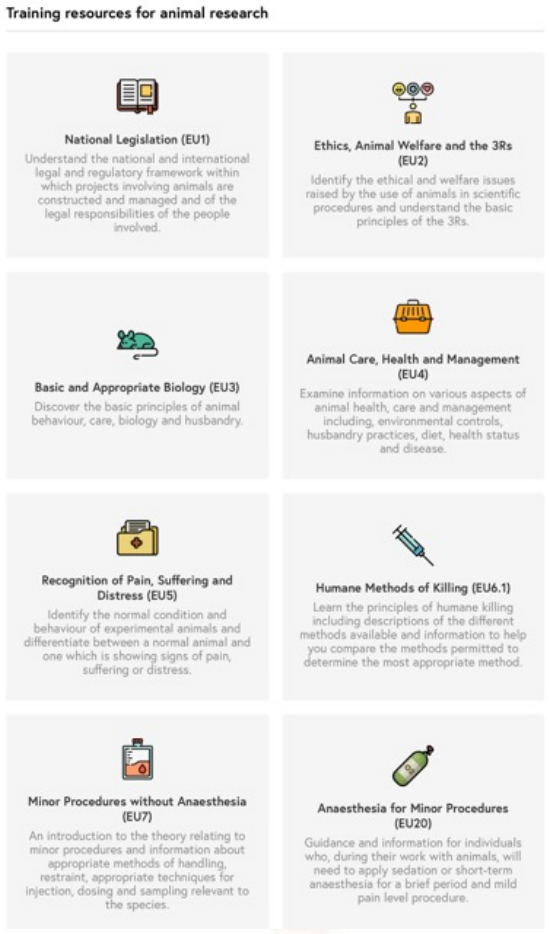
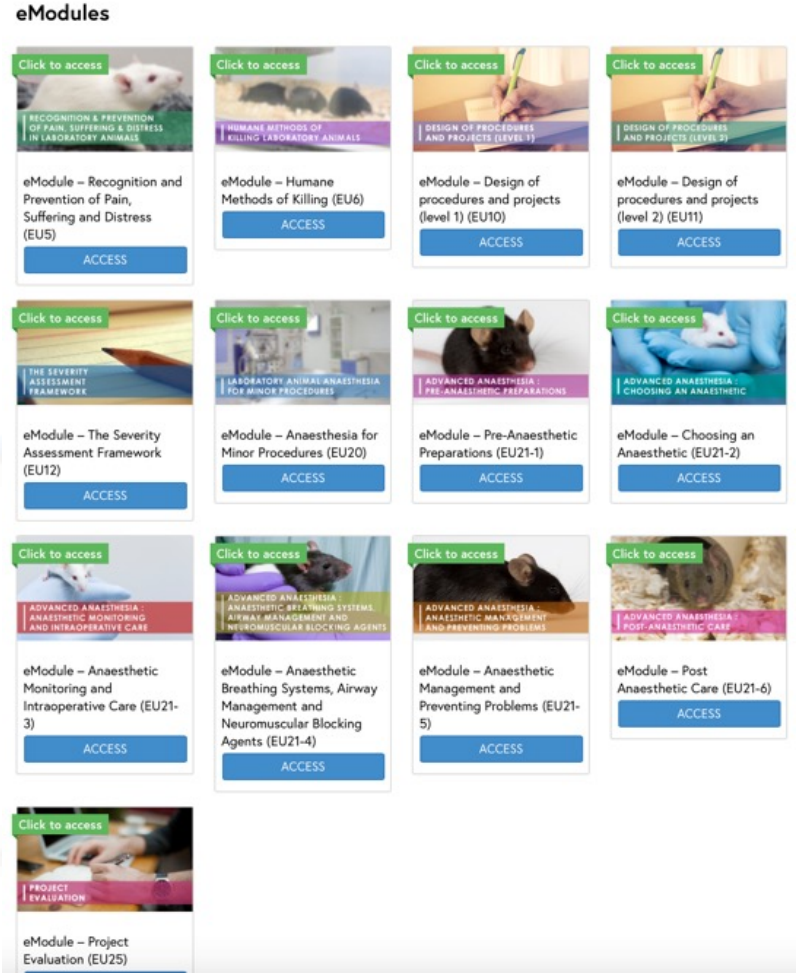




TextBase:

1,500 books related to LAS:

norecopa.no/textbase

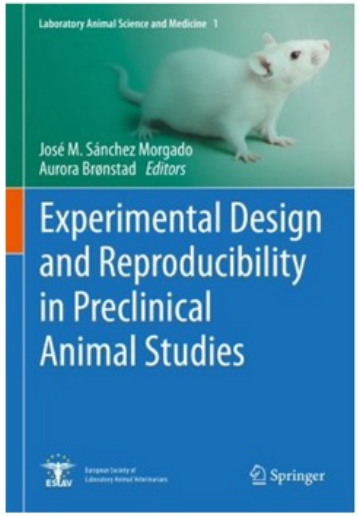
Experimental Design and Reproducibility in Preclinical Animal Studies

By José M. Sánchez Morgado & Aurora Brønstad (Eds.)

Record number: 8619d

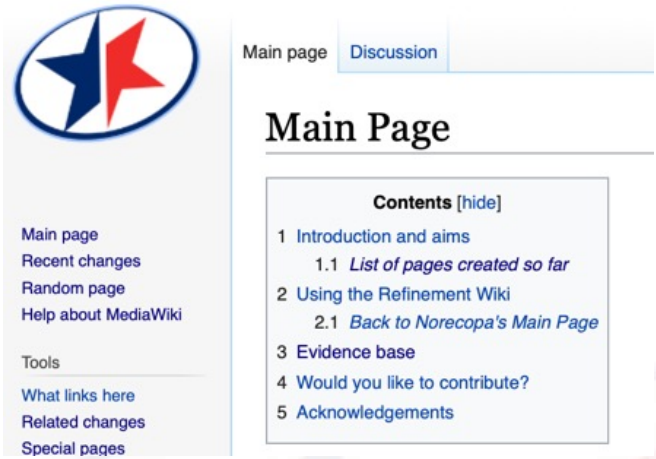
This book provides grounds on how to plan and conduct animal experiments that can be reproduced by others. It touches on factors that may impact the reproducibility of animal studies including: the animal genetic background, the animal microbial flora, environmental and physiological variables affecting the animal, animal welfare, statistics and experimental design, systematic reviews of animal studies, and the publishing process.

The book addresses advanced undergraduates, graduate students and all scientists working with animals.



norecopa.no/textbase/experimental-design-and-reproducibility-in-preclinical-animal-studies

The Refinement Wiki



Susanna Louihimies

wiki.norecopa.no

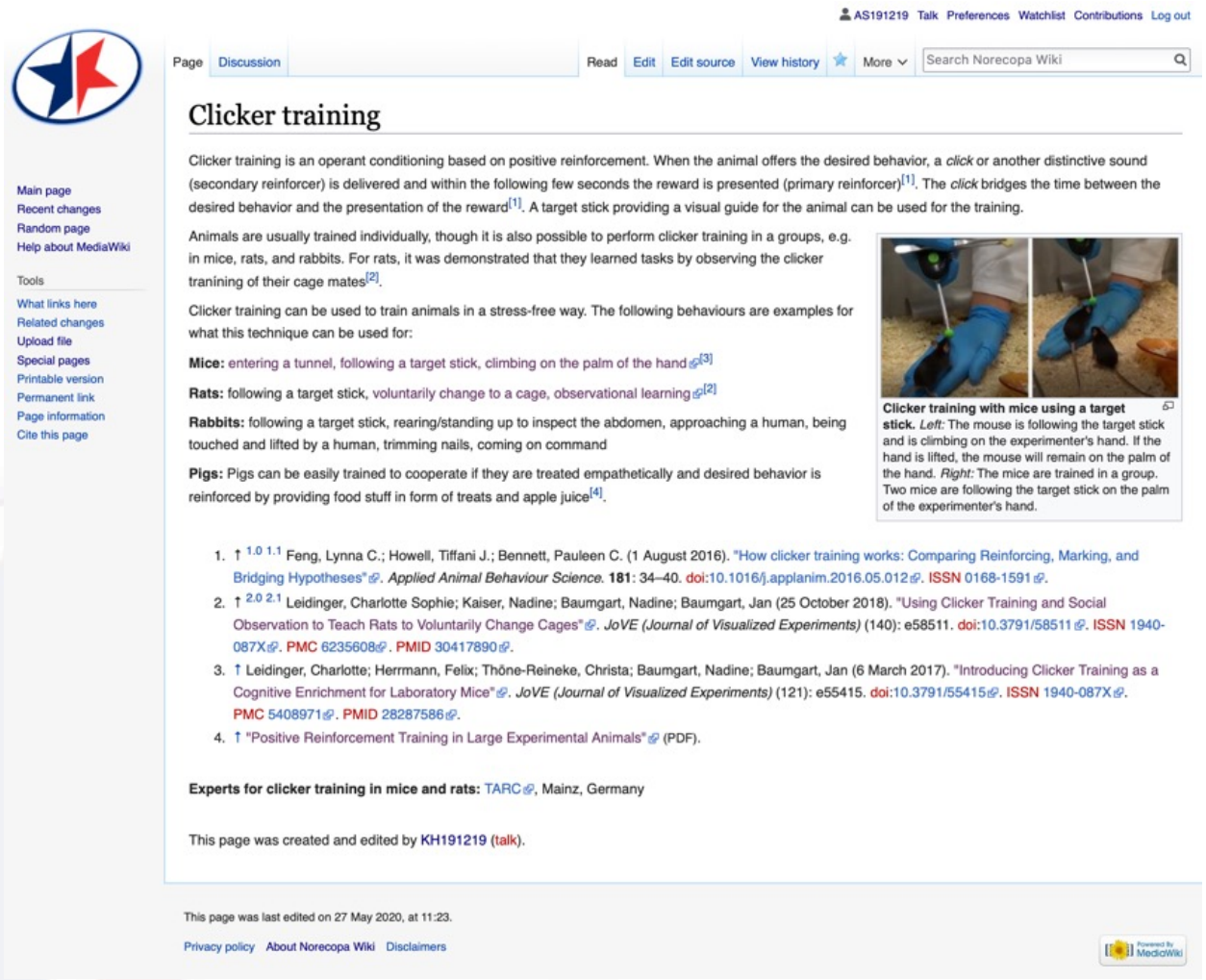
Born from the knowledge that a lot of good ideas on refinement circulate on discussion forums, but never get published.

Designed to be

- a portal for rapid publication and dissemination of these ideas
- a place to identify experts on specific refinement techniques

wiki.norecopa.no

Return to homepage



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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

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

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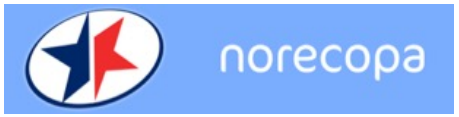


- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- EMLA cream
- Embryo transfer
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- Food crunchers
- General discusson on use of analgesics
- Genotyping mice
- Habituation training
- High-fat diets
- Hot Bead Sterilisers
- Housing nude mice
- Housing research fish
- Humane endpoints
- Hydrodynamic gene delivery
- Intra-ocular injections
- Intranasal administration
- Intraperitoneal injection
- Intraperitoneal pentobarbitone
- Ketamine and alpha-2 agonist combinations
- Long-term anaesthesia in rodents
- Lumpfish
- Main Page
- Marble Burying Test
- Metabolic cages
- Minipumps
- Montanide adjuvant
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Oestrus suppression in ferrets
- Pneumocystis murina
- Recapping needles
- Rotarod Test
- Screening cell lines
- Sedation of cattle
- Splenectomy
- Sterilisation of instruments
- TTEAM and TTouch
- Tail vein injection
- Tramadol
- Transport stress
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing

EU / National

Facility

Project

Procedure

ec.europa.eu/animals-in-science

EU / National

European Commission

ENVIRONMENT

European Commission > Environment > Chemicals > Animals used for scientific purposes

Home | About us | Policies | Funding | Legal compliance | News & outreac

Animals used for scientific purposes

Retrieval and provision of information on the "Three Rs" and alternatives

Accessing accurate, relevant and up-to-date information on the Three Rs is a challenge for all those use of animals.

- Legislation and implementation
  - EU legislative framework
  - Implementation of Directive 2010/63/EU
    - Q&A and guidance documents

- The "Three Rs" and alternative approaches
  - Replacement, Reduction and Refinement – the "Three Rs"
  - Validation, acceptance and use
  - EU activities to advance alternatives
  - Member State activities to advance alternatives
  - Finding and distributing information on alternatives
  - Key resources
    - Search Tools
    - Databases
    - Portals and web-sites
    - Journals
    - Other resources and organisations

Animals used for scientific purposes

Opinions of European Commission Expert Committees related to the use of animals in experiments

ec.europa.eu/environment/chemicals/lab_animals/pubs_guidance_en.htm

Norecopa: PREPARE for better Science

Facility

aaalac INTERNATIONAL

Program Description

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

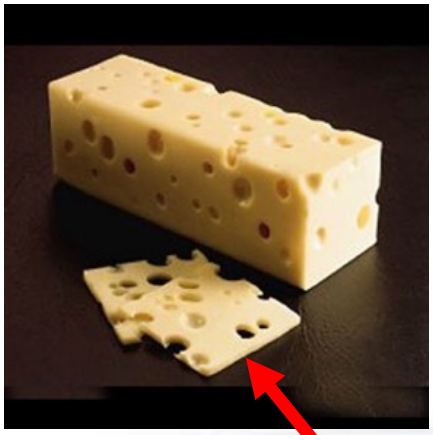
III. Veterinary Care 29
A. Animal Procurement and Transportation 29
1. Animal Procurement 29
2. Transportation of Animals 29
B. Preventive Medicine 29
1. Animal Biosecurity 29
2. Quarantine and Stabilization 29
3. Separation by Health Status and Species 30
C. Clinical Care and Management 30
1. Surveillance, Diagnosis, Treatment and Control of Disease 30
2. Emergency Care 30
3. Clinical Record Keeping 31
4. Diagnostic Resources 31
5. Drug Storage and Control 32
D. Surgery 32
1. Pre-Surgical Planning 32
2. Surgical Facilities 32
3. Surgical Procedures 33
4. Aseptic Technique 33
5. Intraoperative Monitoring 34

63 pages

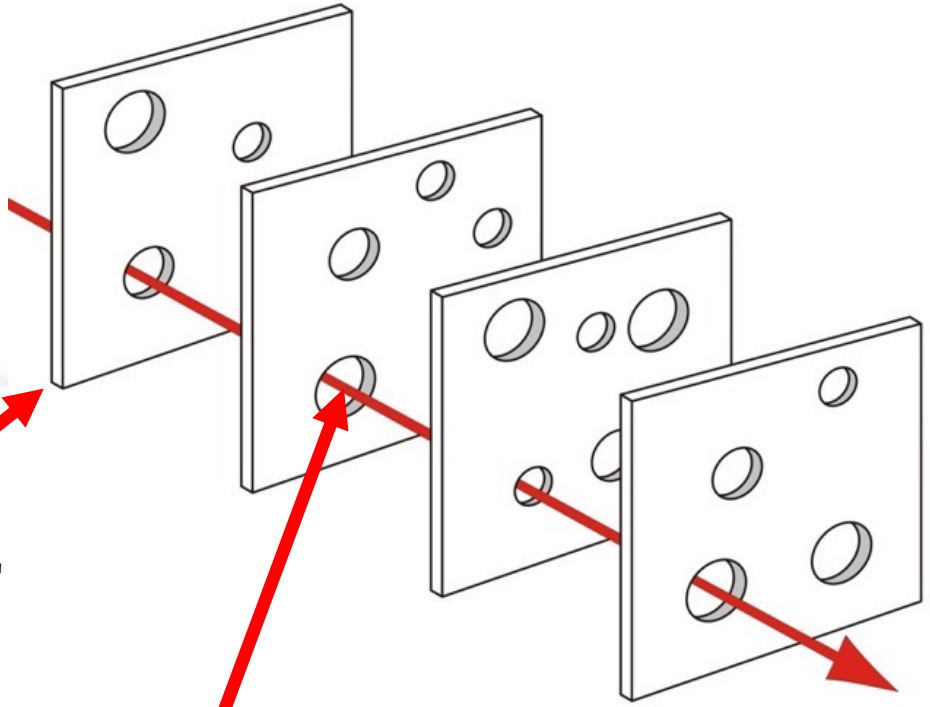
A simple but effective Master Plan

Norecopa: PREPARE for better Science

Threat and Error Management



eaugallecheese.com/Swiss-Cheese



"Layer of defence"
or redundancy

Weakness / hazard

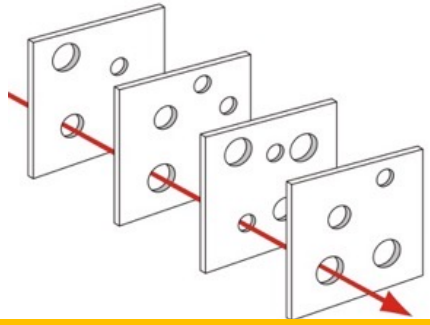
Loss

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
  - 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

Many of these needed revision 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

Contingency and redundancy

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

Work in the spirit of AAALAC,

even if not accredited!

Photo: NMBU

wikipedia


CIRS-LAS Portal
Critical incident reporting system in laboratory animal science
Refine - Reduce - Replace
Homepage
Project
Team
FAQ
Detect a critical incident
Anonymous report
CIRS-LAS.de
Get involved!
We all learn from it!
Expert analysis

Project

A contract between the animal facility and the research group

Division of labour, responsibilities and cost

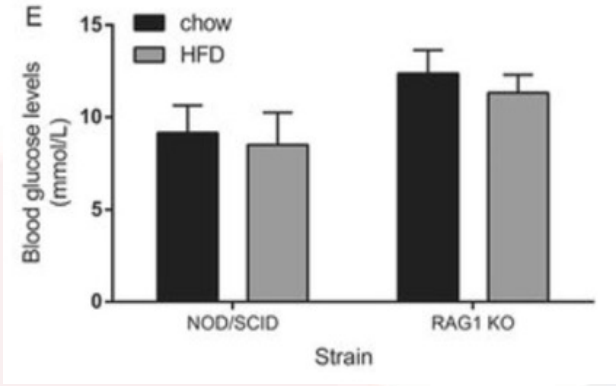
Clarifying all stages of the experiment

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			

Procedure

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

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

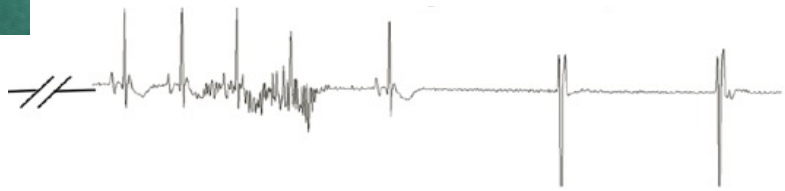
Mice picl
naturally

't act

Ian Johnstor

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

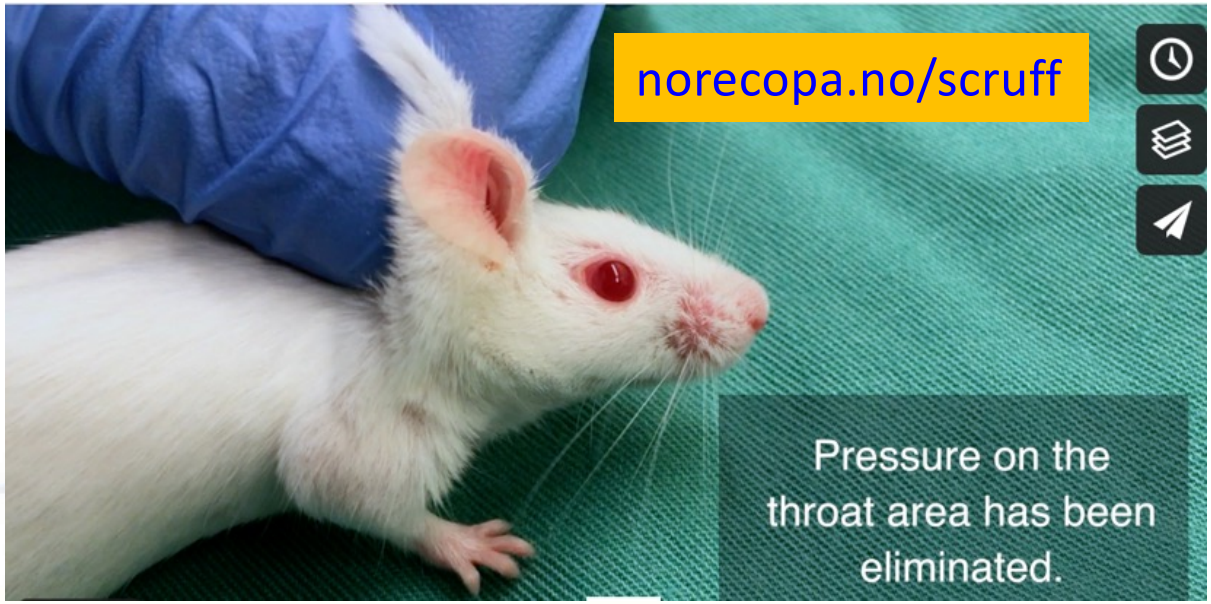
Sinus bradycardia
ventricular escape complexes

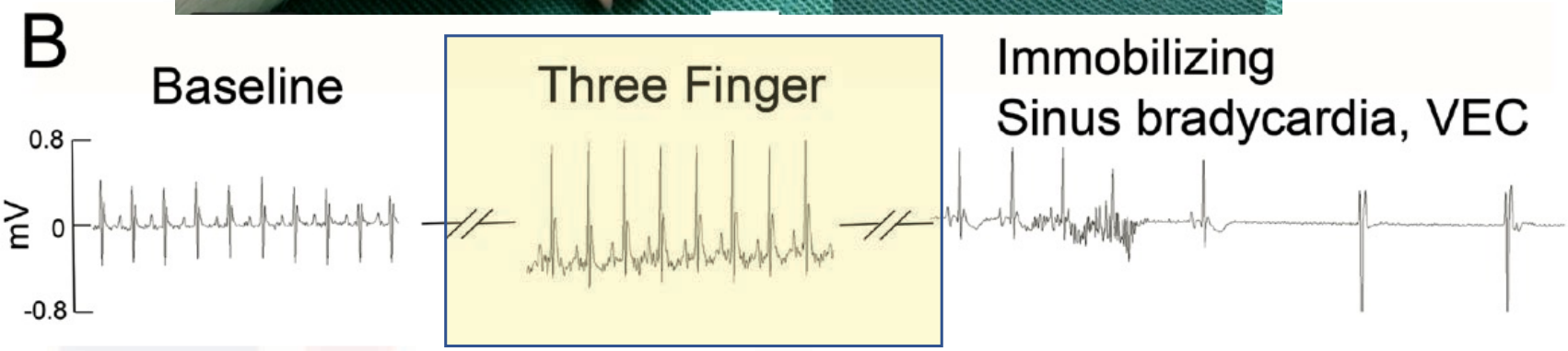


Labitt *et al.*, 26 February 2021

Both sexes and 4 strains of mice, 3 experienced handlers

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.
doi: 10.30802/AALAS-JAALAS-20-000069


norecopa.no/scruff
Pressure on the throat area has been eliminated.


B
Baseline
Three Finger
Immobilizing
Sinus bradycardia, VEC
0.8
mV
0
-0.8

Artefacts caused by poor administration techniques

Photo: NMBU

- *Are you sure that your injection ends up in the same place each time?*
- *Are the injections painful?*
- *Are they realistic? (intramuscular injections in small animals)*

'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

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!

Culture of Care facilitates honest discussion

"because we've always done it that way"

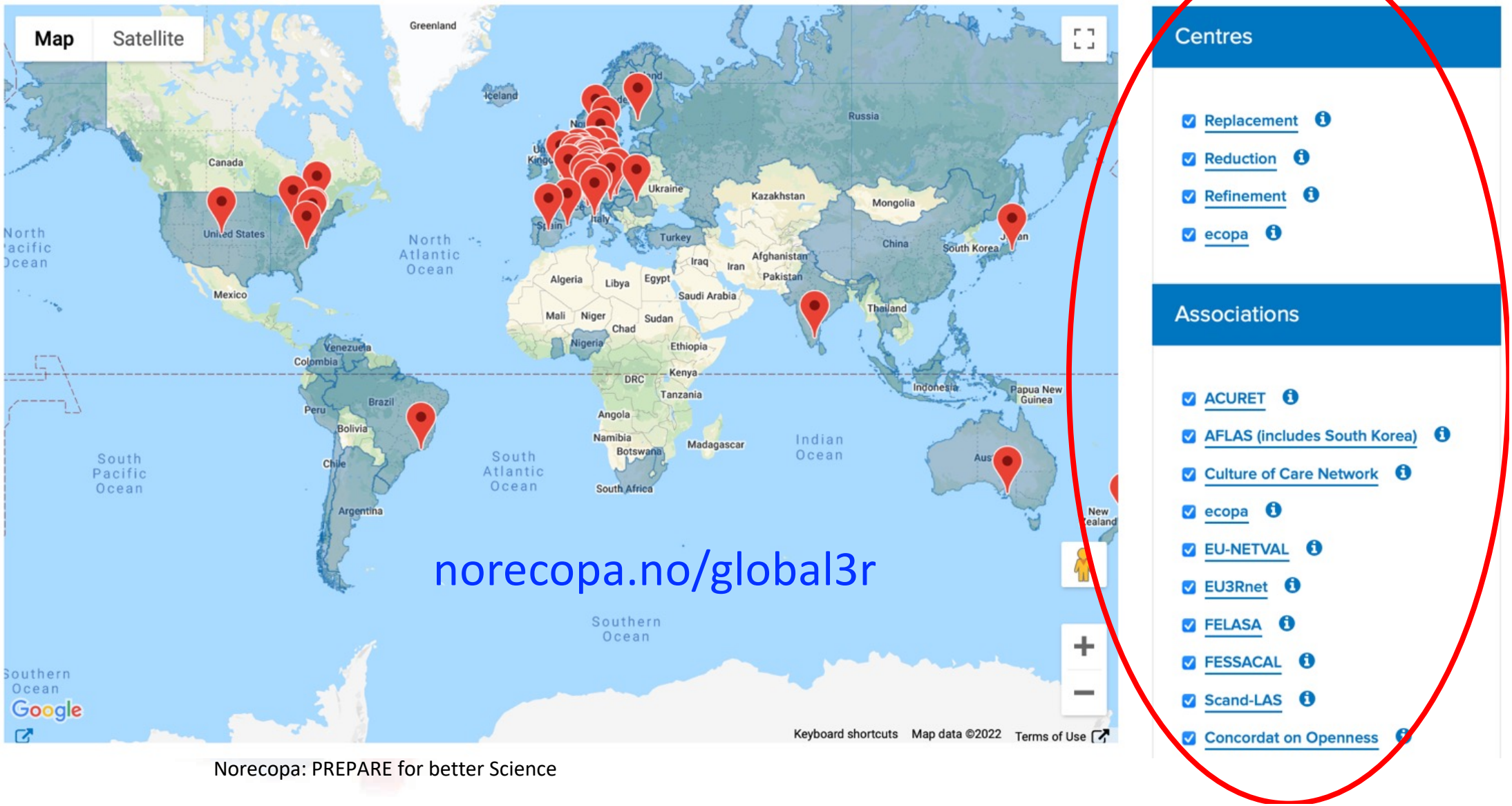
"as often as necessary"

"there are no alternatives"

Closely related to a culture of care is

a **Culture of Challenge** (Louhimies, 2015).

Look for the acceptable, rather than choosing the accepted.



Centres

- Replacement
- Reduction
- Refinement
- ecopa

Associations

- ACURET
- AFLAS (includes South Korea)
- Culture of Care Network
- ecopa
- EU-NETVAL
- EU3Rnet
- FELASA
- FESSACAL
- Scand-LAS
- Concordat on Openness

Norecopa: PREPARE for better Science

The pathway to better science

Norecopa: PREPARE for better Science

norecopa.no/PREPARE *and*
ivd-utrecht.nl/en/news/better-animal-research-through-open-science-1

arriveguidelines.org

The ARRIVE guidelines 2.0

This section of the website provides detailed explanations about each item of the guidelines. Use the left-hand side menu to navigate to each item.

To facilitate a step-wise approach to improving reporting, the guidelines are organised into two prioritised sets:

ARRIVE Essential 10

These ten items are the basic minimum that must be included in any manuscript describing animal research. Without this information readers and reviewers cannot assess the reliability of the findings.

Recommended Set

These items complement the Essential 10 set and add important context to the study described. Reporting the items in both sets represents best practice.

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The ARRIVE guidelines 2019: updated guidelines for reporting animal research

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

Version 1 of 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'

We cannot improve our research by better reporting alone...

...but knowing what you will have to report helps you plan better experiments

reddit.com

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.

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

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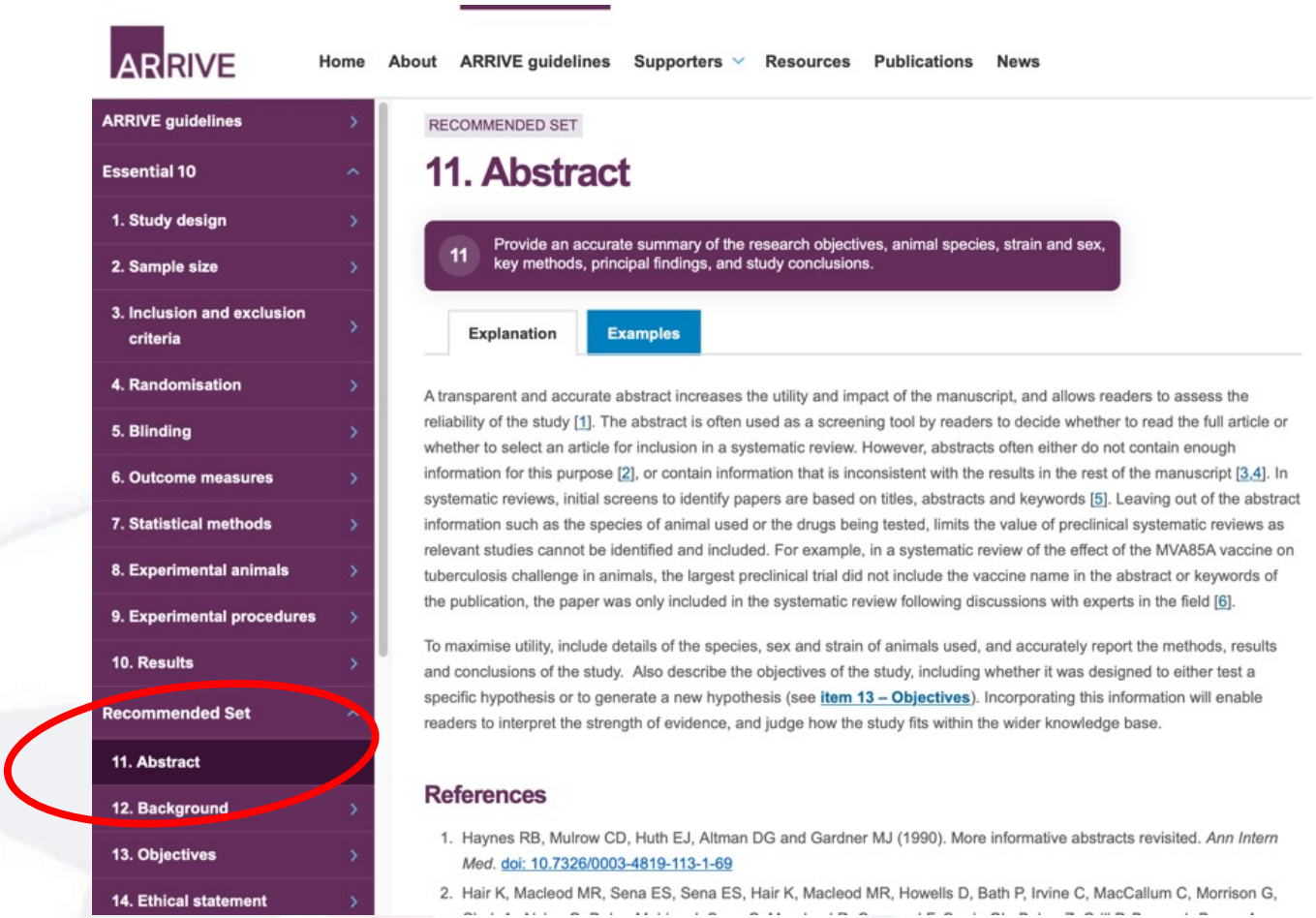
Recommended Set

These items complement the Essential 10 set and add important context to the study described. Reporting the items in both sets represents best practice.

Recommended Set		
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study and the frequency of monitoring.
Interpretation /scientific implications	17	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.
Generalisability /translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.
Data access	20	Provide a statement describing if and where study data are available.
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.

arriveguidelines.org



There are three broad areas which need to be considered when planning animal studies:

1. The suitability of the species or strain as a model of the target organism
2. The ethical issues surrounding their use: 'choosing the right animal for the right reason'. The large increase in use of genetically altered lines has created increasing concern about the suitability of these animals as models of human conditions.
3. Characterisation of the animals. Items to be considered, in collaboration with the supplier, include:
   - Species, strain, line and phenotype (with an explanation of any genetic modifications)
   - Age, developmental stage, sex and weight
   - Stage of oestrous cycle and any previous breeding history
   - Any necessary pre-treatment (e.g. castration for this
   - Name and address of the supplier/breeder, method of capture and transport
   - Health status (e.g. germ-free, gnotobiotic, SP
   - Re-use of animals, which should be justified legislation
   - Any plans for release or re-homing, which m

More resources

- Examples and references from the NC3Rs
- Information on inbred strains of mice and rats
- Strategies to minimise genetic drift and maximise experimental reproducibility in mouse research
- Mouse Locator, UK
- The Collaborative Cross panel of inbred mouse strains
- Nude mice - more than what meets the eye
- The Rat Guide
- Rat Behavior and Biology

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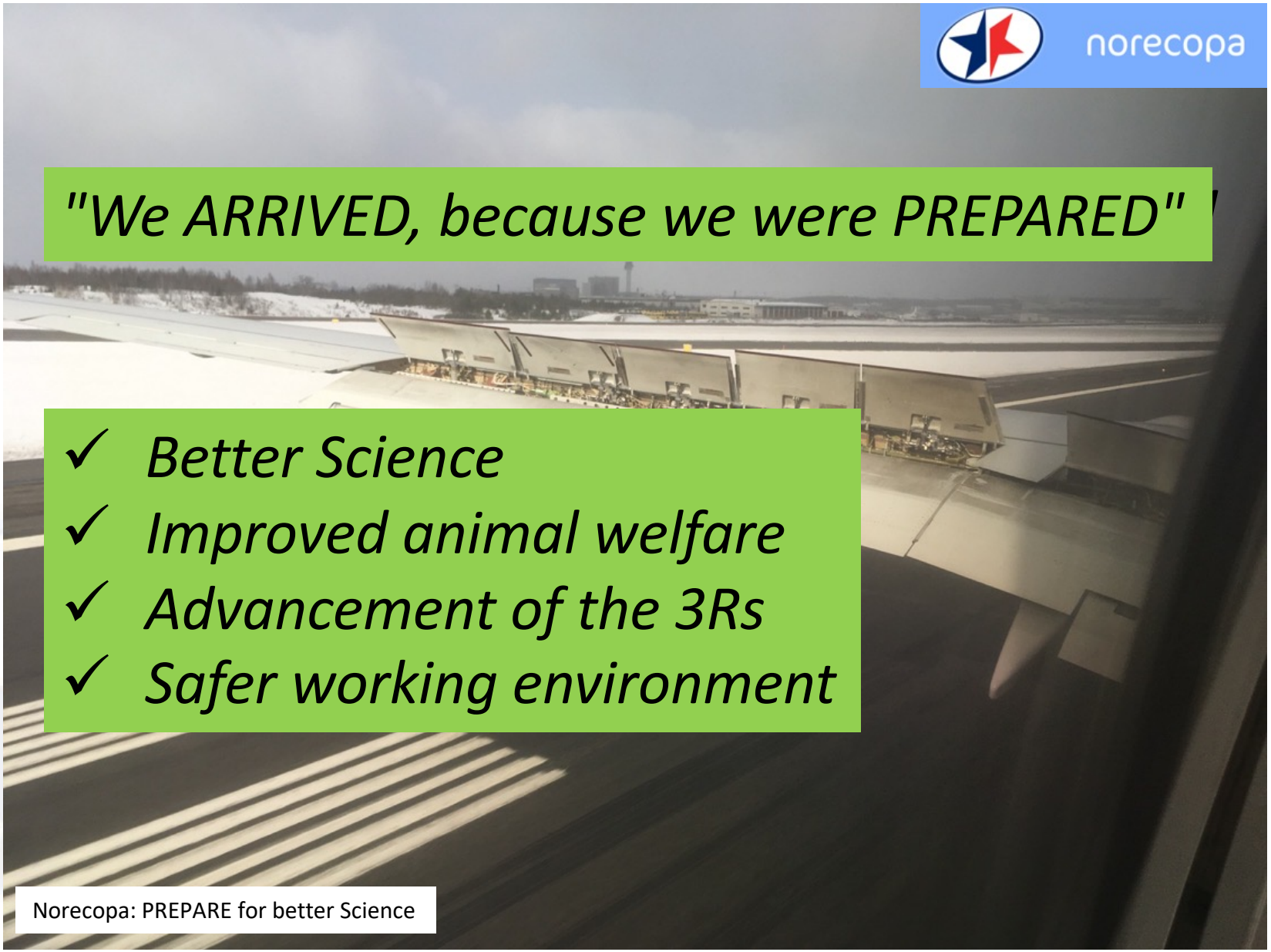
norecopa
"We ARRIVED, because we were PREPARED"
✓ Better Science
✓ Improved animal welfare
✓ Advancement of the 3Rs
✓ Safer working environment
Norecopa: PREPARE for better Science

norecopa.no/Europhysiology

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PREPARE for better Science

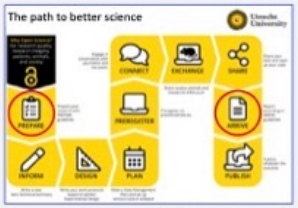
Let's PREPARE together to ARRIVE in better shape: how to plan animal experiments

Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 64, 1431 Ås, Norway
adrian.smith@norecopa.no

What's the problem?

Preclinical *in vivo* research needs to be reproducible and translatable, while maximising the animals' welfare and replacing them with alternatives wherever possible. This can be summed up in **the 3Rs** of Russell & Burch: ***Replace, Reduce & Refine***.

Scientists are usually well aware of ***reporting*** guidelines when publishing research. These are important, but a sub-standard study, like a burnt cake, cannot be improved by a better description. Guidelines for ***planning***, although not mandatory, are of great help in designing better experiments.



norecopa.no/PREPARE

What can Norecopa offer?

Norecopa maintains a comprehensive database of resources for scientists, which include:

- 8,900 searchable webpages of quality 3R resources, with filters to facilitate searching
- the PREPARE guidelines for planning animal experiments, with a checklist in over 30 languages
- links to recordings of webinars covering all aspects of animal research
- an International Webinars & Meetings Calendar
- a collection of 400 guidelines for planning and conducting animal research
- an English-language newsletter with the latest developments within experimental design
- the NORINA database of alternatives to animal use in education and training
- a Refinement Wiki

Examples of Norecopa's resources:

PREPARE covers:

- ✓ *Formulation of a study*
- ✓ *Dialogue between scientists and the animal facility*
- ✓ *Quality control of the components in the study*

norecopa.no/PREPARE

The Refinement Wiki
wiki.norecopa.no

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Thanks to Norecopa's main sponsors:

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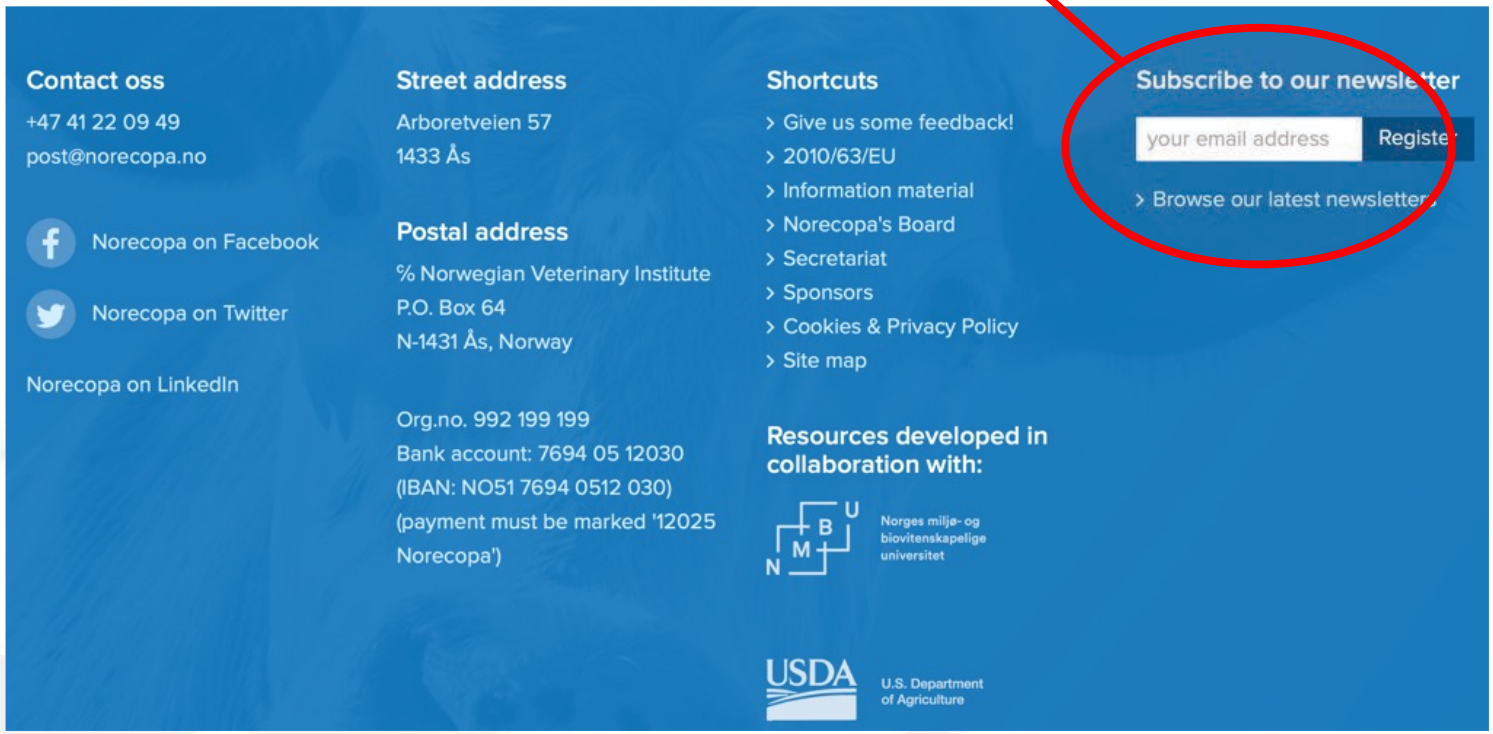
- Norwegian Society for Animal Protection (Dyrebeskyttelsen Norge)
- Norwegian Animal Protection Alliance (Dyrevernalliansen)
- Novo Nordisk
- Sanofi
- Scottish Accreditation Board (SAB)
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture (USDA)

Graphics: colourbox.com

norecopa.no/050323

English-language newsletters



Thank you for listening!