Improving Our Scientific Output and Animal Welfare? The PREPARE Guidelines for Planning Animal Studies

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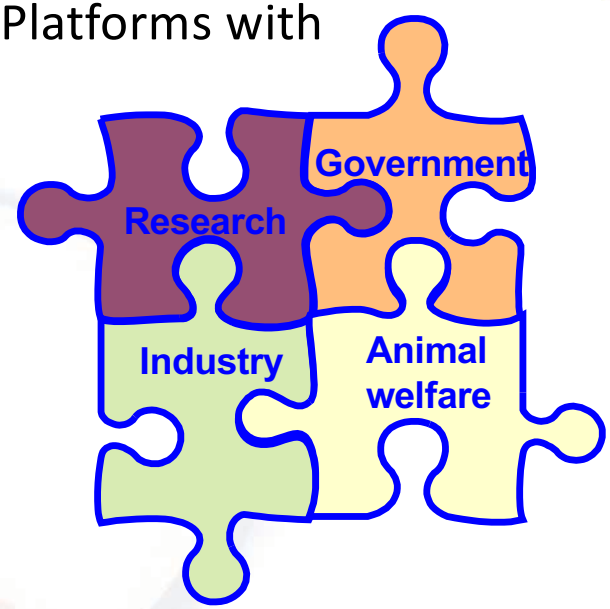
Norecopa is a National Consensus Platform for the 3Rs:
***Replacement**, **Reduction** and **Refinement** of animal experiments*

*A member of **ecopa**:*
European Consensus-Platform for Alternatives
which recognises National Consensus Platforms with
4 stakeholders equally represented:

ecopa.eu



Norecopa: PREPARE for better Science

”better science?"

- replacement if possible
- reduction and refinement if not possible to replace
- valid data (a true treatment effect)
- reproducible and translatable experiments
- best possible animal welfare
- health & safety (of animals and people)
- a culture of care at the animal facility
- communication of best practice to others

colourbox.com

40-slide powerpoint presentation about the 3Rs

ccac.ca

All three Rs of Russell and Burch:

Replacement, Reduction & Refinement

English, Czech, French, German and Spanish versions
Free download from norecopa.no/3Rs

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More than 3Rs

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

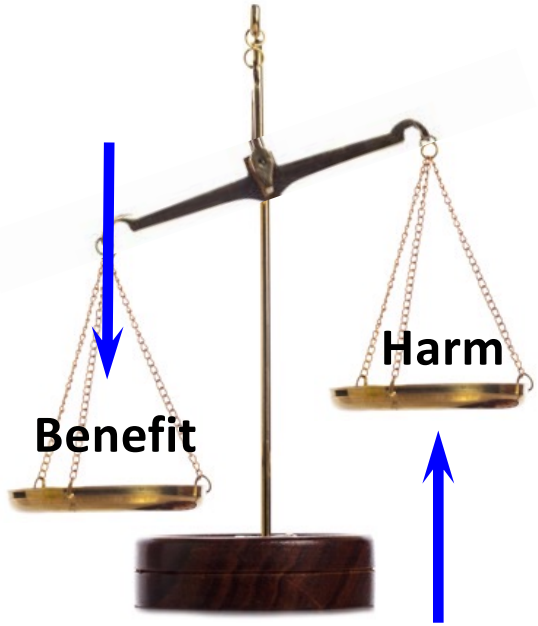
- *Replace the unnecessary experiments*
- *Reduce the number of animals used*
- *Refine the conditions for the animals*

***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?)*



norecopa.no/3R
norecopa.no/3S
norecopa.no/3V

The pathway to better science

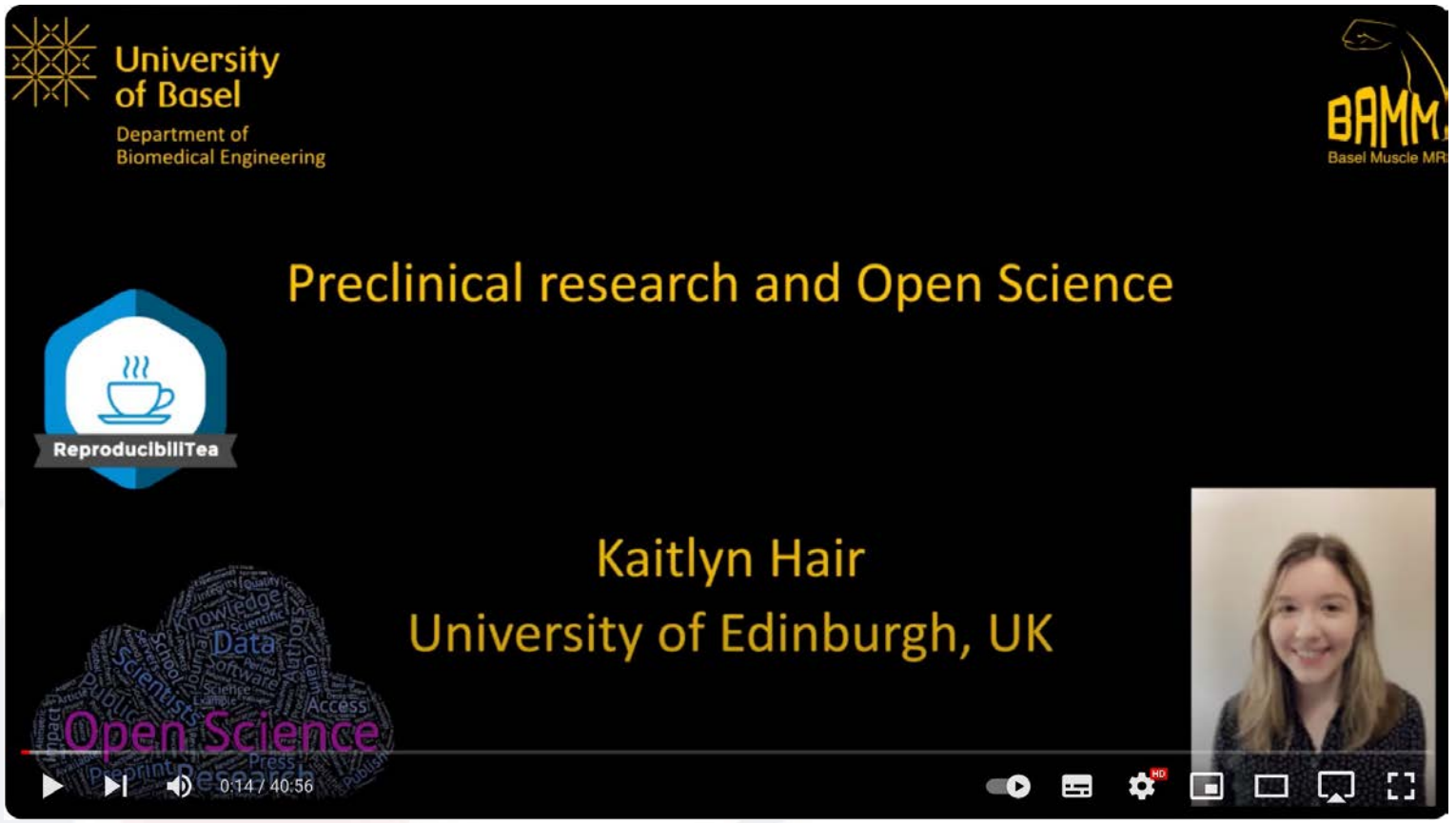
Norecopa: PREPARE for better Science

norecopa.no/PREPARE *and*
https://riojournal.com/article/105198

We cannot improve our research by

better reporting alone...

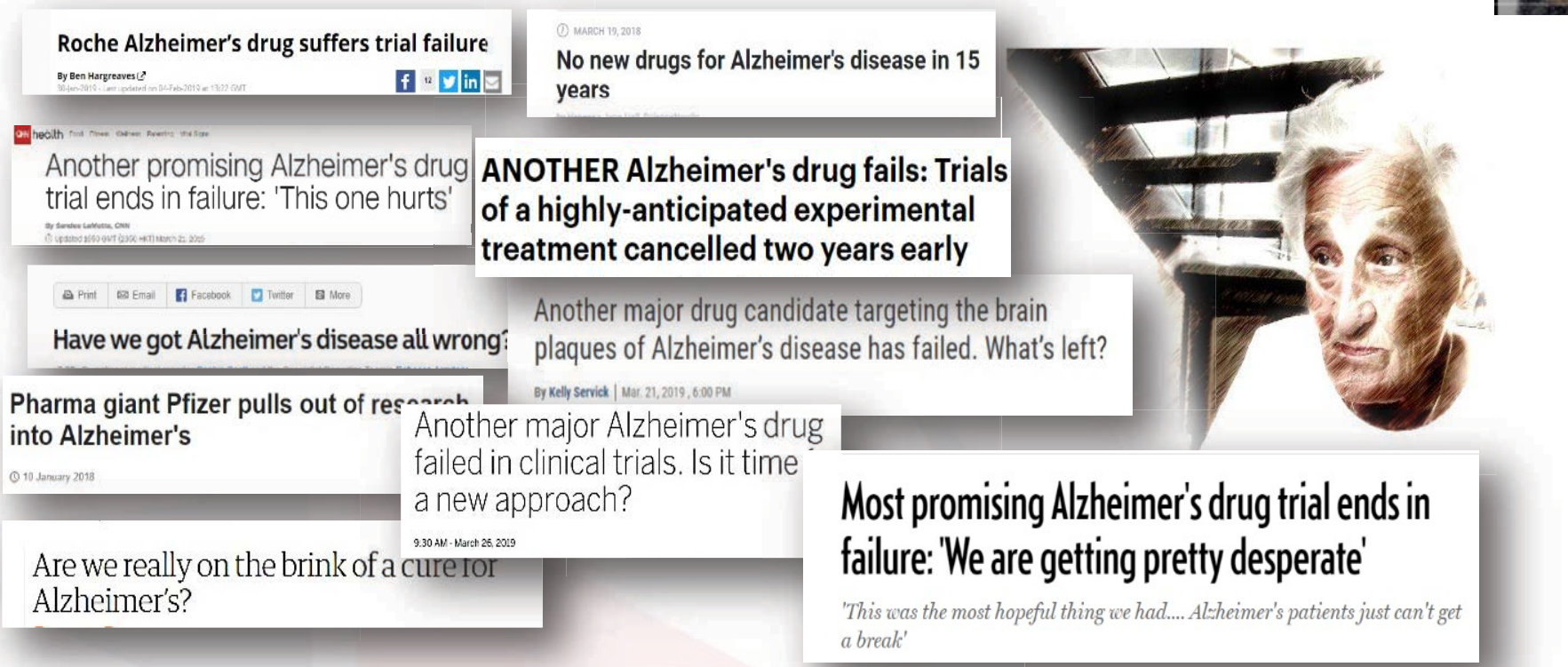
reddit.com



https://www.youtube.com/watch?v=6lC7RNVZNLM
slides: https://osf.io/8j7hr

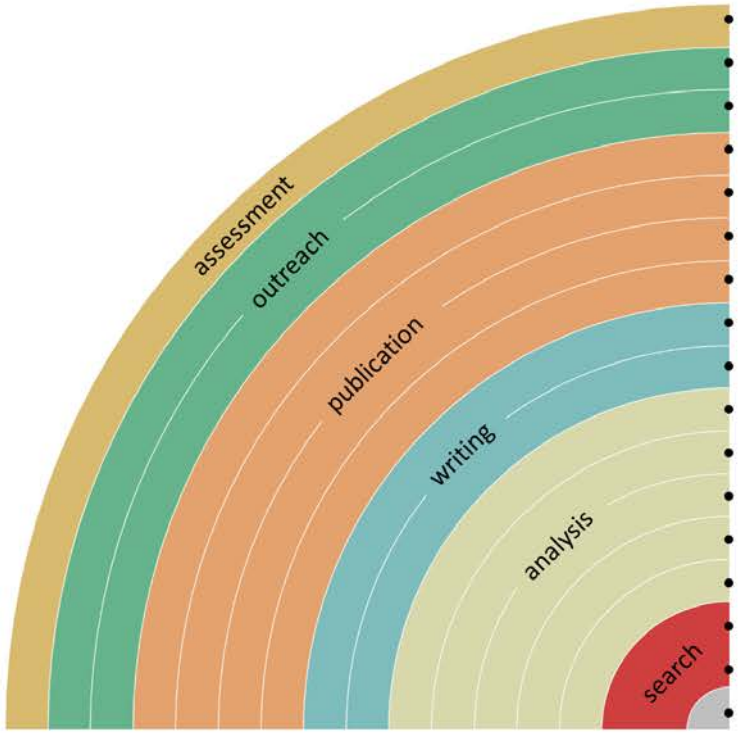
Norecopa: PREPARE for better Science

Preclinical research: lost in translation



Since the millennium,
400+ trials have failed (Rinaldi, 2018).

You can make your workflow more open by …



- adding alternative evaluation, e.g. with altmetrics
- communicating through social media, e.g. Twitter
- sharing posters & presentations, e.g. at FigShare
- using open licenses, e.g. CC0 or CC-BY
- publishing open access, 'green' or 'gold'
- using open peer review, e.g. at journals or PubPeer
- sharing preprints, e.g. at OSF, arXiv or bioRxiv
- using actionable formats, e.g. with Jupyter or CoCalc
- open XML-drafting, e.g. at Overleaf or Authorea
- sharing protocols & workfl., e.g. at Protocols.io
- sharing notebooks, e.g. at OpenNotebookScience
- sharing code, e.g. at GitHub with GNU/MIT license
- sharing data, e.g. at Dryad, Zenodo or Dataverse
- pre-registering, e.g. at OSF or AsPredicted
- commenting openly, e.g. with Hypothes.is
- using shared reference libraries, e.g. with Zotero
- sharing (grant) proposals, e.g. at RIO

DOI: 10.5281/zenodo.1147025

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

approx. 10,000 webpages
approx. 1,000 hits per day

7-8 detailed newsletters per year

November 2024

- NAMs workshop for early career scientists, 19 November 2024
- LASA Annual Meeting, West Midlands, 18-20 November 2024
- Anaesthesia and perioperative care of laboratory rodents and rabbits, Flaire Consultants workshop, online, 19-21 November 2024
- The Seminar for Transparent and Open Science, webinar (Rafael Munoz-Tamayo), 20 November 2024
- Re-wilding mice reveals otherwise hidden behavioral and physiological effects in lab mice, webinar (Matthew Zipple), 20 November 2024
- Fish Welfare and Aquatic Facilities, CCAC webinar, 20 (English) & 2
- Born to be wild: Wildlings, a novel translational research model for hur
- RSPCA's 6th International Focus on Severe Suffering Meeting, near Paris, 20-21 November 2024
- DSI European User Group meeting, Barcelona, 20-21 November 2024
- Writing Non-Technical Summaries, webinar (Wendy Jarrett), 21 November 2024
- The OBSERVE guidelines for the refinement of rodent cancer models, webinar (Stéphanie de Vleeshauwer), 21 November 2024
- FC3R 3R days, near Paris, 21-22 November 2024
- Anaesthesia
- Recognition,
- OpenTox virtual conference, 25-29 November 2024
- What Happens when Mouse Genetics are Overlooked? Establishing a Mouse Genetic Monitoring Program, webinar (Viola Galligioni), 26 November 2024
- SGV annual meeting: Advancing Laboratory Animal Science, Lausanne, 26-27 November 2024
- 3Rs and Ethics by Design Course, online, 26-27 November 2024 (fully booked, but requests can be made here)
- Rethinking experimental animal behavior, webinar (Abhilashi Joshi), 27 November 2024
- Semi-natural environments may enhance both animal welfare and external validity of the observations, webinar (Anders Ågmo), 27 November 2024
- 31st Annual Rodent Welfare Group Meeting, Bristol, 28 November 2024

norecopa.no/meetings/meetings-calendar

+ webpages for recorded meetings, including a page sorted by the PREPARE topics

Databases & Guidelines

- 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 five 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 papers, published in 2020
  - Non-animal models for cardiovascular diseases, citing over 400 models, identified in a literature review of over 14,000 papers, published in 2022

The EU Commission has now published 30 datasets of this type.

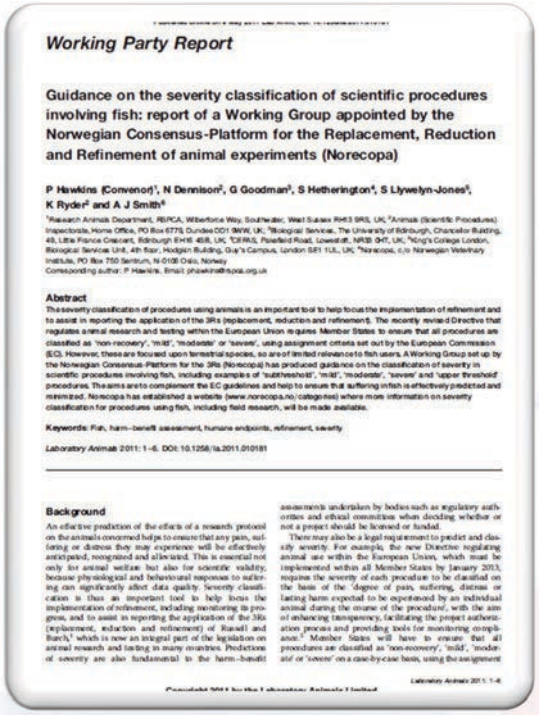
Here is an alphabetical global list of all the databases cited on the Norecopa website.

norecopa.no/databases-guidelines

links to over 70 other databases

3R-Guide (over 400 guidelines for implementation of the 3Rs)

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]

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Abstract

The 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 aim is 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/categorise) 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

AVMA Guidelines for the Euthanasia of Animals: 2020 Edition*

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*The AVMA Panel on Euthanasia develops the content of the guidelines, with support from its working groups. The panel is required to do a comprehensive review and update of the report at least every 10 years, although more frequent major revisions are possible based on substantive information gleaned from new research and experience with practical implementation. To ensure the guidelines remain as up-to-date as possible, interim revisions (reaffirmed, substantive updates, but of a less extensive nature than a major revision) are also recommended.

A Gold Standard Publication Checklist to Improve the Quality of Animal Studies, to Fully Integrate the Three Rs, and to Make Systematic Reviews More Feasible

Carlijn R. Hooijmans, Marlies Leenaars and Merel Ritskes-Hoitinga

Radboud University Nijmegen Medical Centre, Central Animal Laboratory and 3R Research Centre, Nijmegen, The Netherlands

Summary — Systematic reviews are generally regarded by professionals in the field of evidence-based medicine as the highest level of medical evidence, and they are already standard practice for clinical studies. However, they are not yet widely used nor undertaken in the field of animal experimentation, even though there is a lot to be gained from the process. Therefore, a gold standard publication checklist (GSPC) for animal studies is presented in this paper. The items on the checklist have been selected on the basis of a literature analysis and the resulting scientific evidence that these factors are decisive in determining the outcome of animal studies. In order to make future systematic reviews and meta-analyses of animal studies possible, to allow others to replicate and build on work previously published, diminish the number of animals needed in animal experimentation (reduction), improve animal welfare (refinement) and, above all, improve the quality of scientific papers on animal experimentation, this publication checklist needs to be used and followed. We have discussed and optimised this GSPC through feedback from interviews with experts in the field of animal experimentation. From these interviews, it became clear that scientists will adopt this GSPC when journals demand it. The GSPC was compared with the current instructions for authors from nine different journals, selected on the basis that they featured a high number of publications on animal studies. In general, the journals' demands for the description of the animal studies are so limited that it is not possible to repeat the studies, let alone carry out a systematic review. By using the GSPC for animal studies, the quality of scientific papers will be improved. The use of the GSPC and the concomitant improvement in the quality of scientific papers will also contribute to decreased variation and increased standardisation and, as a consequence, a reduction in the numbers of animals used and a more reliable outcome of animal studies. It is of major importance that journal editors become convinced of and adopt these recommendations, because only then will scientists follow these guidelines to the full extent.

Key words: *animal experimentation, meta-analysis, publication checklist, scientific quality, systematic review*

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Introduction

A systematic review (SR) is a literature review focused on a single question which tries to identify, appraise, select and synthesise all available high-quality research evidence relevant to that question (1). SRs are generally regarded by evidence-based medicine professionals as the highest level of medical evidence, and they are already standard practice in clinical studies. However, SRs are not yet widely used nor undertaken in the animal experimentation field, although there would be a lot to be gained from the process. A systematic approach to incorporate all available relevant literature into the design of an animal experiment is a prerequisite for research which is of high scientific quality. Good science, from a scientific as well as an animal welfare point of view, is the basis of the book, *The Principles of Humane Experimental Technique*, by Russell and Burch (2). In this book, they recommend that the Three Rs principles (*Refinement, Reduction* and *Replacement*) should be applied whenever possible in animal studies. Besides producing high-quality research, SRs of animal experiments will result in direct implementation of the Three Rs. SRs may provide the proper argumentation to decide which animal model will give the best answer to the (clinical) research question (3, 4) and to detect whether there are gaps in scientific knowledge that require new animal experiments (*replacement and refinement*). This will also aid in preventing unnecessary duplication of animal experiments (*reduction*), and thus discourage unnecessary animal use and time loss. A SR of animal studies will also lead to a better interpretation of the already existing scientific results from animal experiments, through which a better

Tim Allen, USDA

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TextBase:

1,500 books related to Lab Animal Science, welfare and alternatives:

norecopa.no/textbase

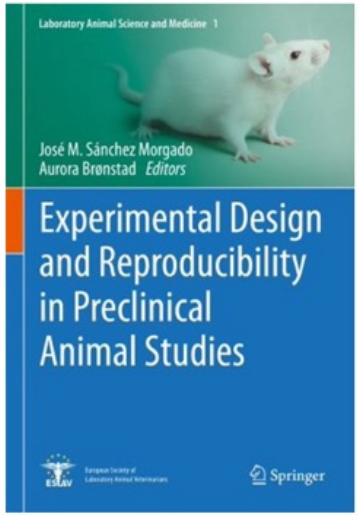
Experimental Design and Reproducibility in Preclinical Animal Studies

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

Record number: 8619d

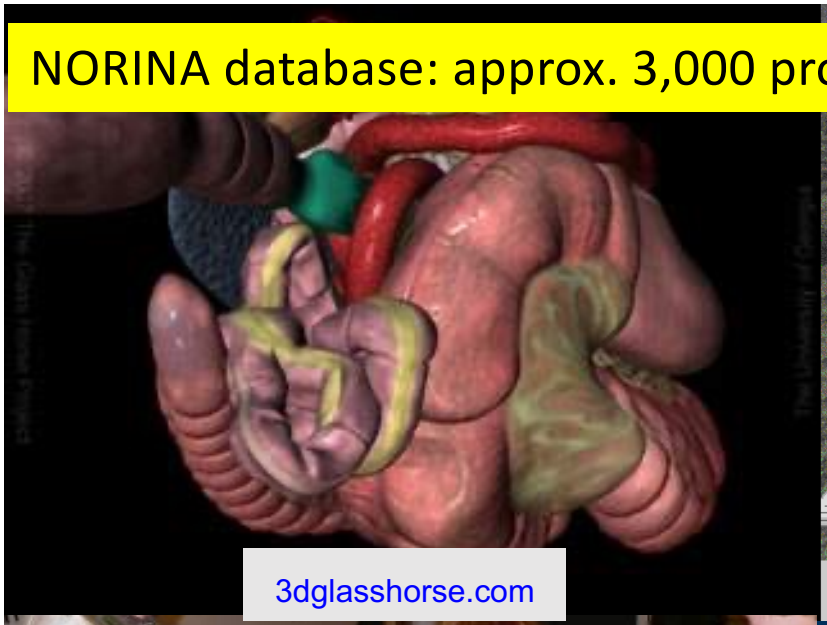
This book provides grounds on how to plan and conduct animal experiments that can be reproduced by others. It touches on factors that may impact the reproducibility of animal studies including: the animal genetic background, the animal microbial flora, environmental and physiological variables affecting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

NORINA database: approx. 3,000 products



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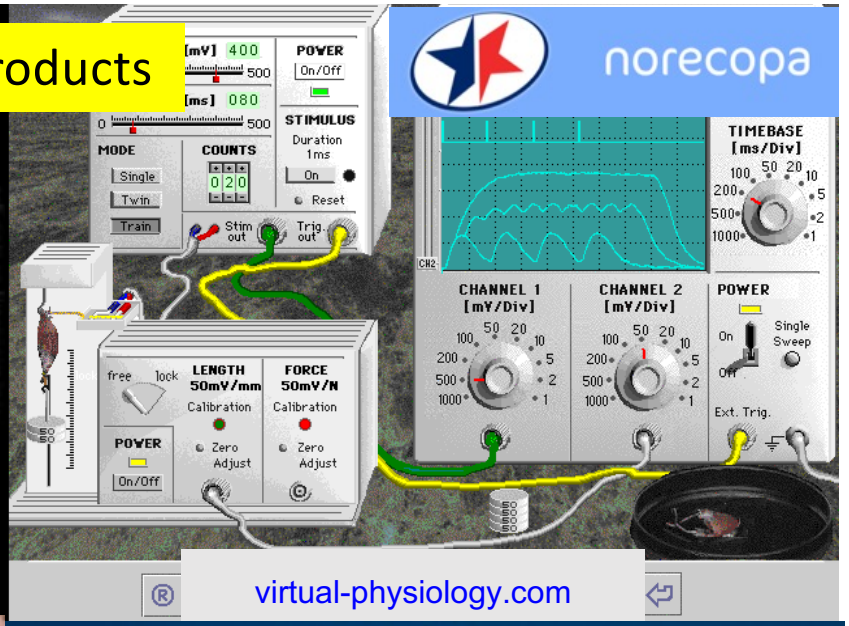

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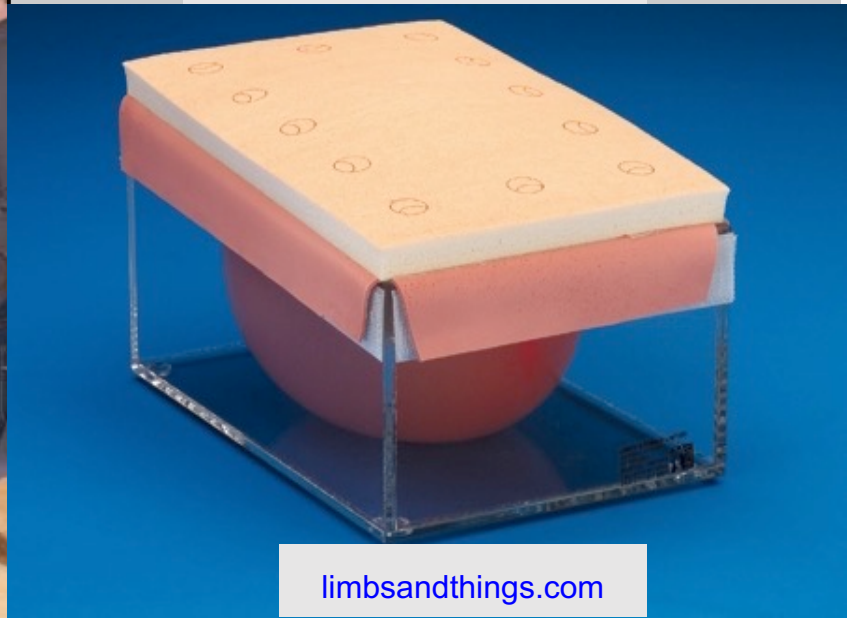
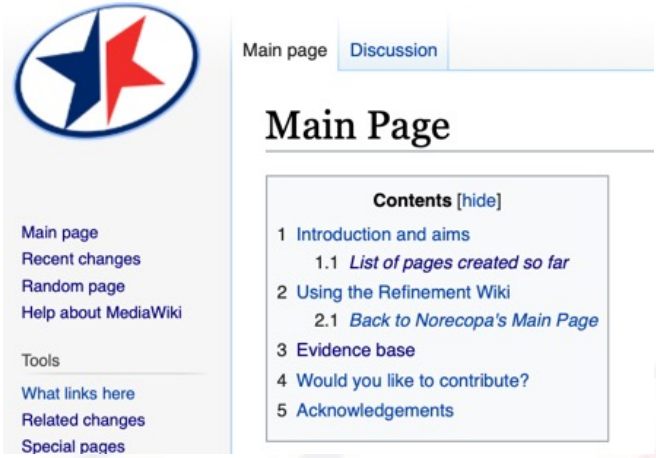


limbsandthings.com

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

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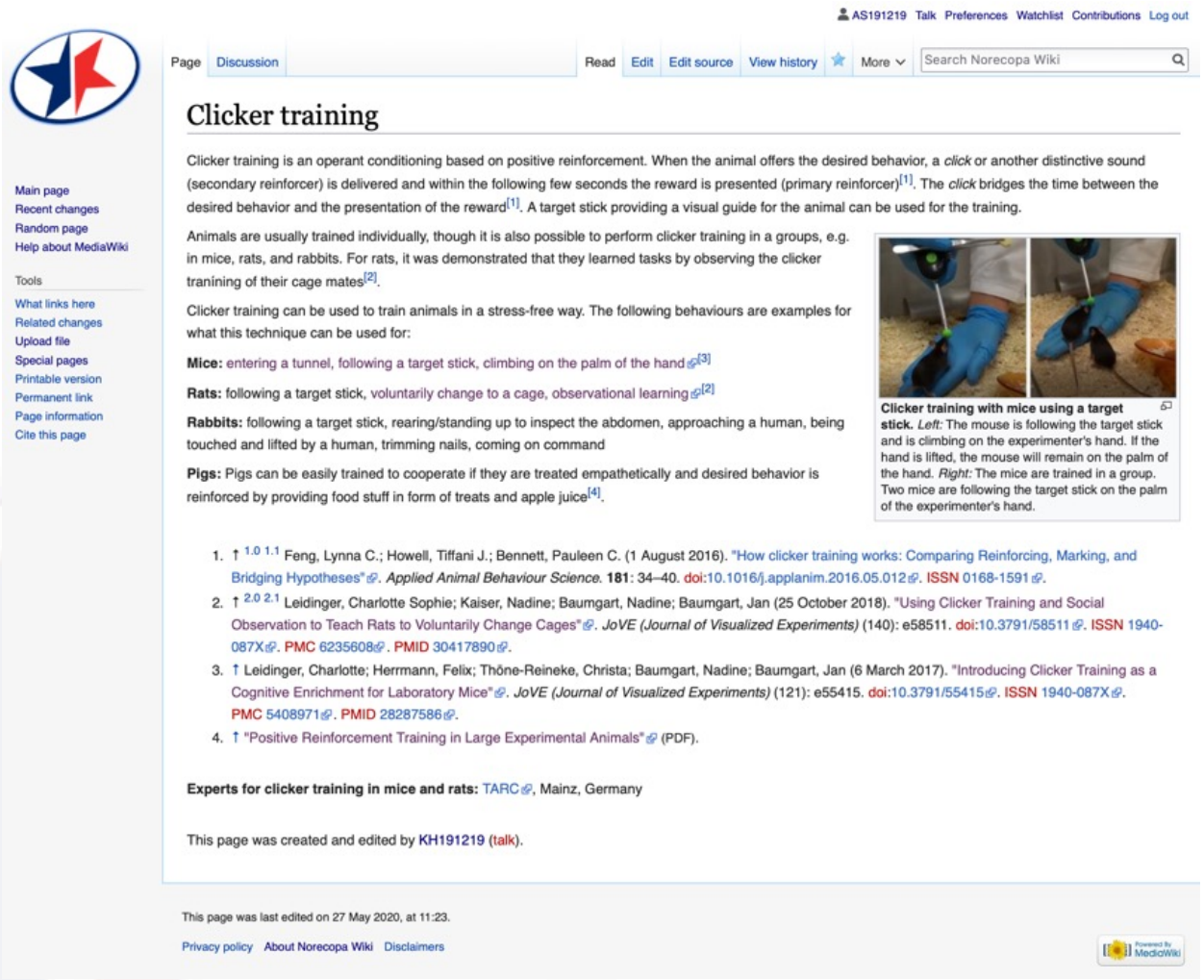

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Clicker training

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

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

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

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

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

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

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

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

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

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

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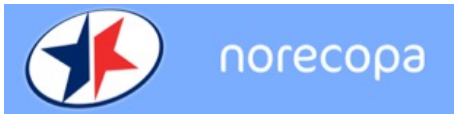

- Acclimatisation
- Adrian Smith
- Alphaxalone
- Anaesthesia in neonates
- Analgesia
- Asepsis
- Blood sampling of hamsters
- Blood sampling of pigs
- Blood sampling of rainbow trout
- Breeding strategies for mice
- Clicker training
- Contingency plans
- Decapitation
- Dehydration
- Detecting early onset 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)
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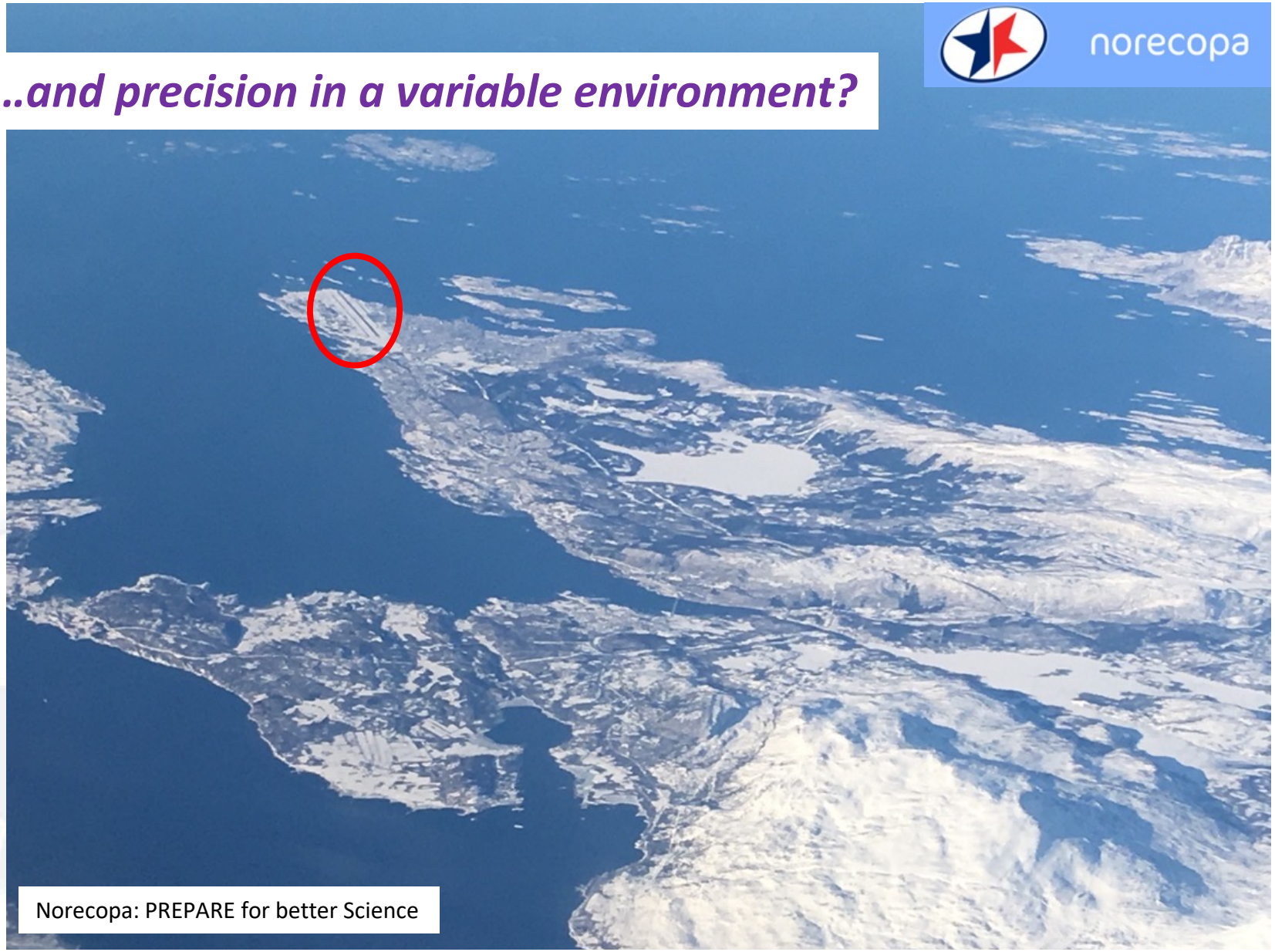
- Habituation training
- Health monitoring
- High-fat diets
- Hot Bead Sterilisers
- Housing nude mice
- Housing research fish
- Humane endpoints
- Hydrodynamic gene delivery
- Intra-ocular injections
- Intranasal administration
- Intraperitoneal injection
- Intraperitoneal pentobarbitone
- Irradiation for haematology studies
- Ketamine and alpha-2 agonist combinations
- Long-term anaesthesia in rodents
- Lumpfish
- MDA (micropipette-guided drug administration) Method
- Main Page
- Marble Burying Test
- Metabolic cages
- Microchipping rats and mice
- Minipumps
- Montanide adjuvant
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Non-invasive genetic sampling in wildlife research
- Oestrus suppression in ferrets
- Pneumocystis murina
- Recapping needles
- Refinement of oral gavage
- Rotarod Test
- Screening cell lines
- Sedation of cattle
- Splenectomy
- Sterilisation of instruments
- TTEAM and TTouch
- Tail vein injection
- Tamoxifen
- Tamoxifen information sheet V4.pdf
- The use of DMSO
- Tramadol
- Transport stress
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality
- Xenopus laevis
- Zebrafish swabbing

How do others achieve success and reproducibility?

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

…and precision in a variable environment?



Norecopa: PREPARE for better Science

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.

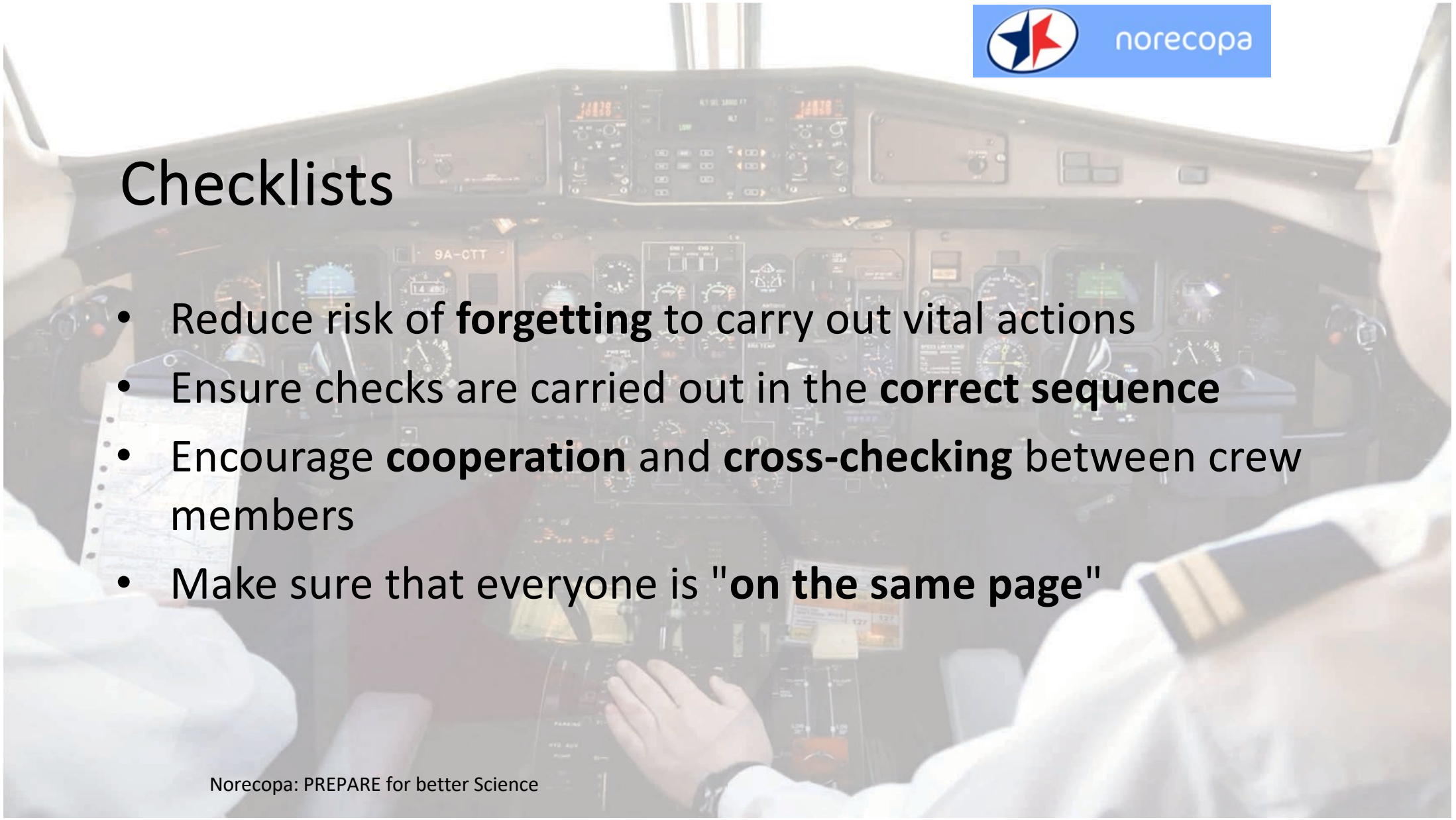
no.wikipedia.org/wiki/US_Airways_Flight_1549

en.wikipedia.org

Hudson River, 2009

All 155 passengers and crew saved

10-15 checklists even on short routine flights



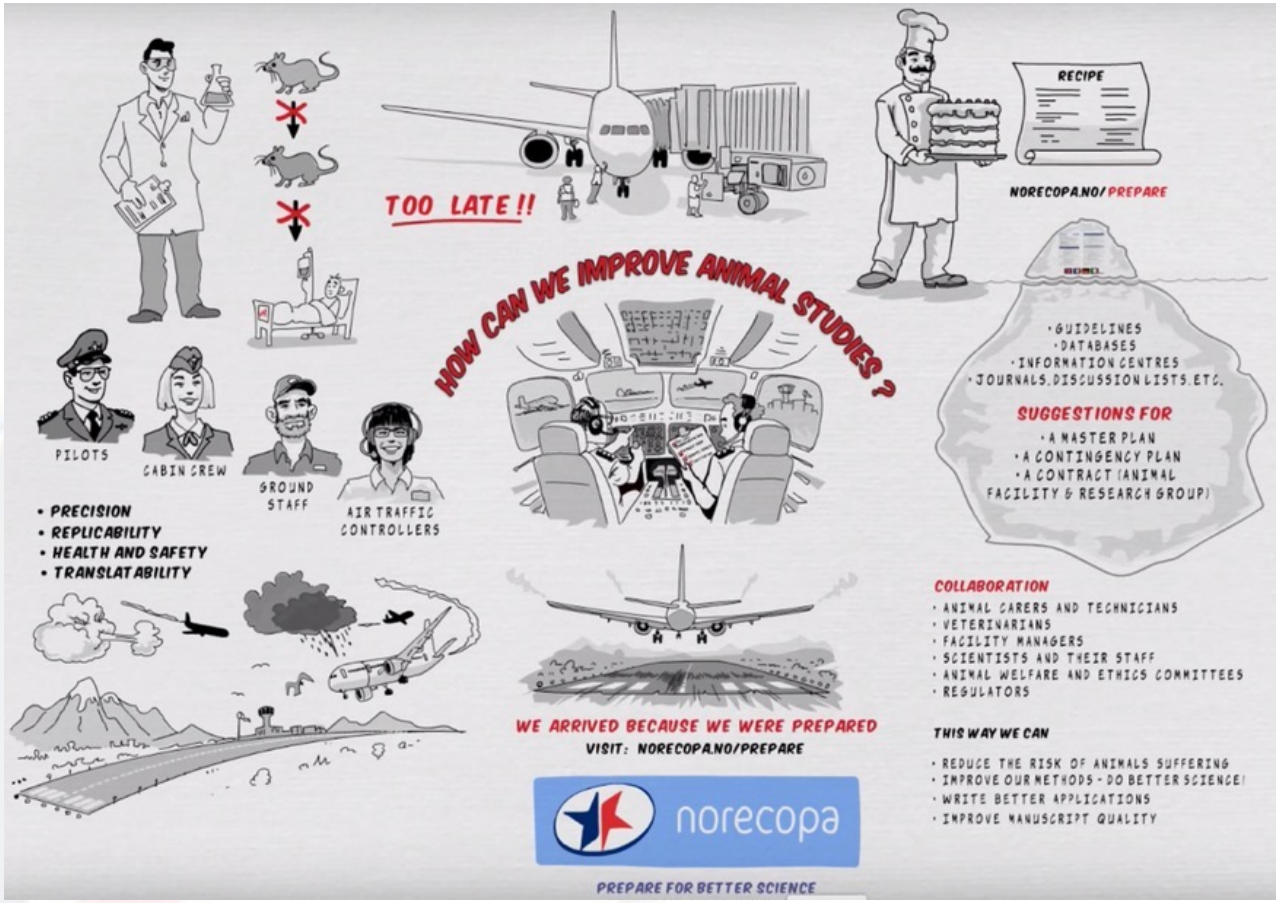
Checklists

- 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

norecopa.no/PREPARE/film

3-minute whiteboard film



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Surgical Safety Checklist

World Health Organization | Patient Safety
A World Alliance for Safer Health Care

Before induction of anaesthesia
(with at least nurse and anaesthetist)

Has the patient confirmed his/her identity, site, procedure, and consent?
- ☐ Yes

Is the site marked?
- ☐ Yes
- ☐ Not applicable

Is the anaesthesia machine and medication check complete?
- ☐ Yes

Is the pulse oximeter on the patient and functioning?
- ☐ Yes

Does the patient have a:

Known allergy?
- ☐ No
- ☐ Yes

Difficult airway or aspiration risk?
- ☐ No
- ☐ Yes, and equipment/assistance available

Risk of >500ml blood loss (7ml/kg in children)?
- ☐ No
- ☐ Yes, and two IVs/central access and fluids planned

Before skin incision
(with nurse, anaesthetist and surgeon)

- ☐ **Confirm all team members have introduced themselves by name and role.**
- ☐ **Confirm the patient's name, procedure, and where the incision will be made.**

Has antibiotic prophylaxis been given within the last 60 minutes?
- ☐ Yes
- ☐ Not applicable

Anticipated Critical Events

To Surgeon:
- ☐ What are the critical or non-routine steps?
- ☐ How long will the case take?
- ☐ What is the anticipated blood loss?

To Anaesthetist:
- ☐ Are there any patient-specific concerns?

To Nursing Team:
- ☐ Has sterility (including indicator results) been confirmed?
- ☐ Are there equipment issues or any concerns?

Is essential imaging displayed?
- ☐ Yes
- ☐ Not applicable

Before patient leaves operating room
(with nurse, anaesthetist and surgeon)

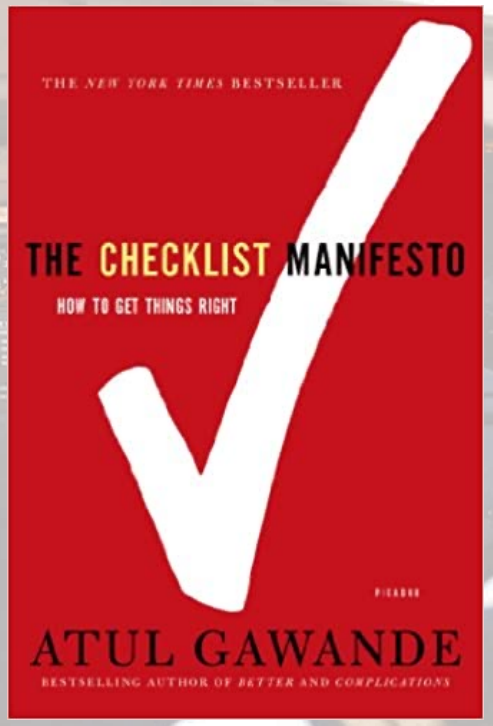
Nurse Verbally Confirms:
- ☐ The name of the procedure
- ☐ Completion of instrument, sponge and needle counts
- ☐ Specimen labelling (read specimen labels aloud, including patient name)
- ☐ Whether there are any equipment problems to be addressed

To Surgeon, Anaesthetist and Nurse:
- ☐ What are the key concerns for recovery and management of this patient?

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

Revised 1 / 2009

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



amazon.com/gp/product/0312430000

Norecopa: PREPARE for better Science

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

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

Culture of Care facilitates honest discussion along the path

"because we've always done it that way"

"as often as necessary"

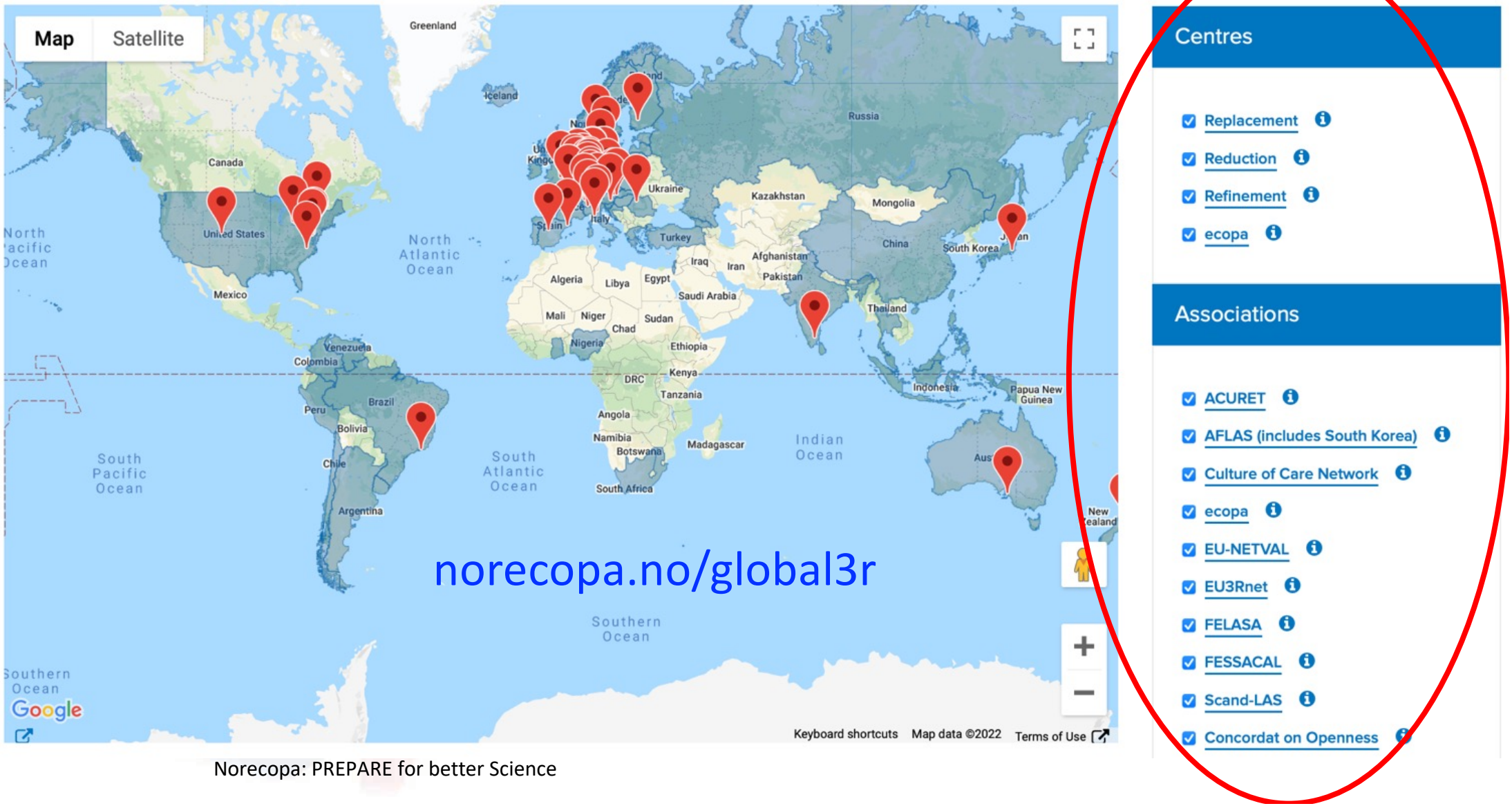
"there are no alternatives"

Closely related to a culture of care is

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

Look for the acceptable, rather than choosing the accepted.


Map
Satellite
Greenland
Iceland
Finland
Sweden
Norway
Russia
United Kingdom
Poland
Germany
Ukraine
Kazakhstan
Mongolia
France
Italy
Spain
Turkey
China
Japan
South Korea
Canada
United States
North Atlantic Ocean
Iraq
Iran
Afghanistan
Pakistan
Algeria
Libya
Egypt
Saudi Arabia
India
Thailand
Mexico
Mali
Niger
Sudan
Chad
Nigeria
Ethiopia
Venezuela
Colombia
Kenya
DRC
Tanzania
Indonesia
Papua New Guinea
Brazil
Peru
Angola
Bolivia
Namibia
Botswana
Madagascar
Indian Ocean
South Pacific Ocean
South Atlantic Ocean
Chile
Australia
South Africa
Argentina
New Zealand
norecopa.no/coc
Culture of Care Network
Google
Keyboard shortcuts
Map data ©2022
Terms of Use



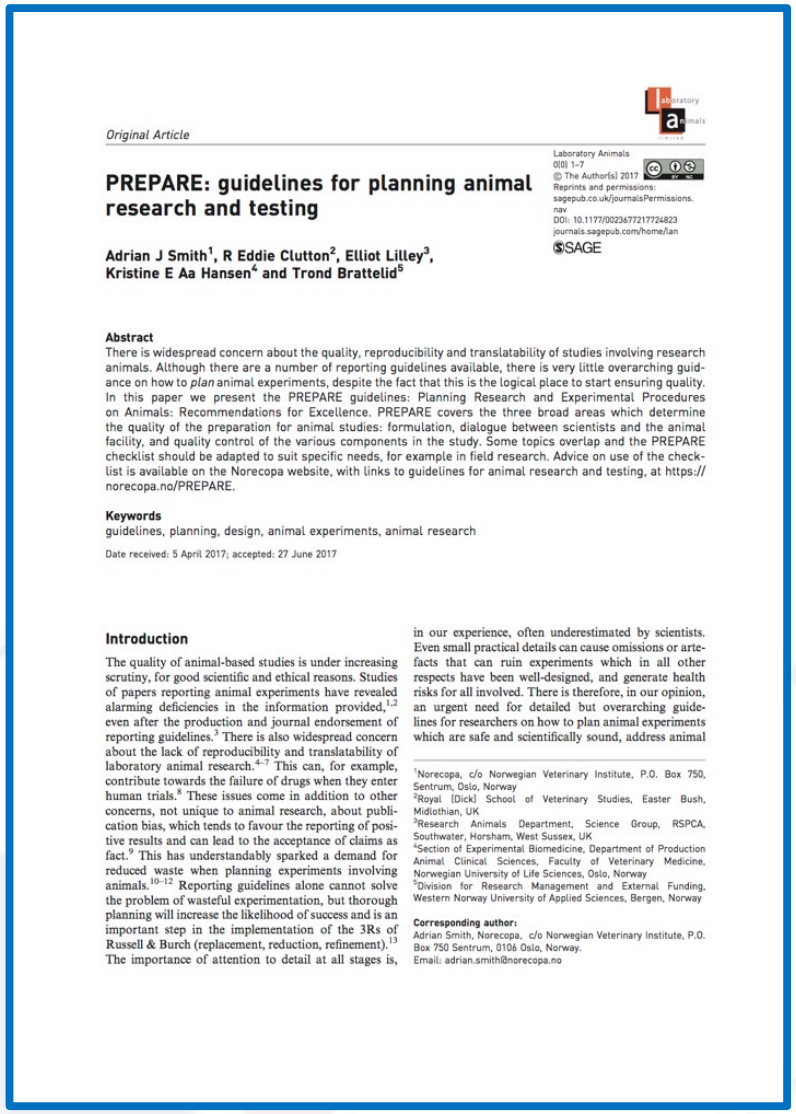
Centres

- 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



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
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Norecopa: PREPARE for better Science

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https://doi.org/10.1177/0023677217724823

38,000 views/downloads from the

journal website so far

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

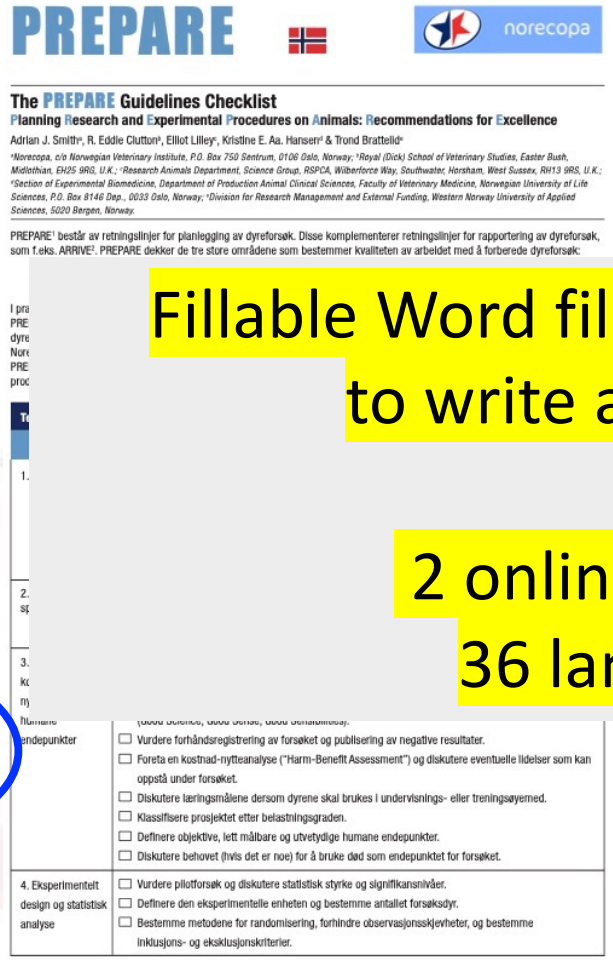
5. Objectives and timescale, funding and division of labour
6. Facility evaluation
7. Education and training
8. Health risks, waste disposal and decontamination

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

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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 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[1] består av retningslinjer for planlegging av dyreforsøk. Disse komplementerer retningslinjer for rapportering av dyreforsøk, som f.eks. ARRIVE[2]. PREPARE dekker de tre store områdene som bestemmer kvaliteten av arbeidet med å forberede dyreforsøk:

Tema	Anbefaling
	(B) Dialogen mellom forskerne og dyreavdelingen
5. Mål og tidshorisont, finansiering og arbeidsfordeling	☐ Arrangere møter med alle relevante personell når tidlige planer for prosjektet foreligger. ☐ Lag en omtrentlig tidsramme for prosjektet, som viser behovene for assistanse med forberedelser, dyrestell, prosedyrer og avfallshåndtering/dekontaminasjon. ☐ Diskutere og legge frem alle forventede og potensielle kostnader. ☐ Lage en detaljert plan for fordelingen av både arbeidsoppgavene og utgiftene, på alle stadiene i forsøket.
6. Evaluering av dyreavdelingen	☐ Foreta en fysisk inspeksjon av fasilitetene, for å evaluere bygningsmassen, standarden på utstyret og spesielle behov. ☐ Diskutere bemanningsbehovet ved perioder med ekstra risiko.
7. Utdanning og	☐ Vurdere den nåværende kompetansen hos personalet og evaluere behovet for videreutdanning og
endepunkter	☐ Vurdere forhåndsregistrering av forsøket og publisering av negative resultater. ☐ Foreta en kostnad-nytteanalyse ("Harm-Benefit Assessment") og diskutere eventuelle lidelser som kan oppstå under forsøket. ☐ Diskutere læringsmålene dersom dyrene skal brukes i undervisnings- eller treningsøyemed. ☐ Klassifisere prosjektet etter belastningsgraden. ☐ Definere objektive, lett målbare og utvetydige humane endepunkter. ☐ Diskutere behovet (hvis det er noe) for å bruke død som endepunktet for forsøket.
4. Eksperimentelt design og statistisk analyse	☐ Vurdere pilotforsøk og diskutere statistisk styrke og signifikansnivåer. ☐ Definere den eksperimentelle enheten og bestemme antallet forsøksdyr. ☐ Bestemme metodene for randomisering, forhindre observasjonsskjevheter, og bestemme inklusjons- og eksklusjonskriterier.
14. Human avliving, frisettelse eller omplassering	☐ Konsultere relevant lovgivning og retningslinjer i god tid før studiet. ☐ Definere de primære metodene for avliving, samt metoder som kan brukes i en nødssituasjon. ☐ Evaluere kompetansen til personene som må foreta disse handlingene.
15. Obduksjon	☐ Lage en systematisk plan for alle stadiene i obduksjonen, inkl. hvor den skal foregå, og identifikasjon av alle dyrene og prøvene som tas.

Referanser

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.

Mer informasjon
https://norecopa.no/PREPARE / post@norecopa.no / @norecopa

Fillable Word file that can be used to write a Study Plan

2 online versions
36 languages

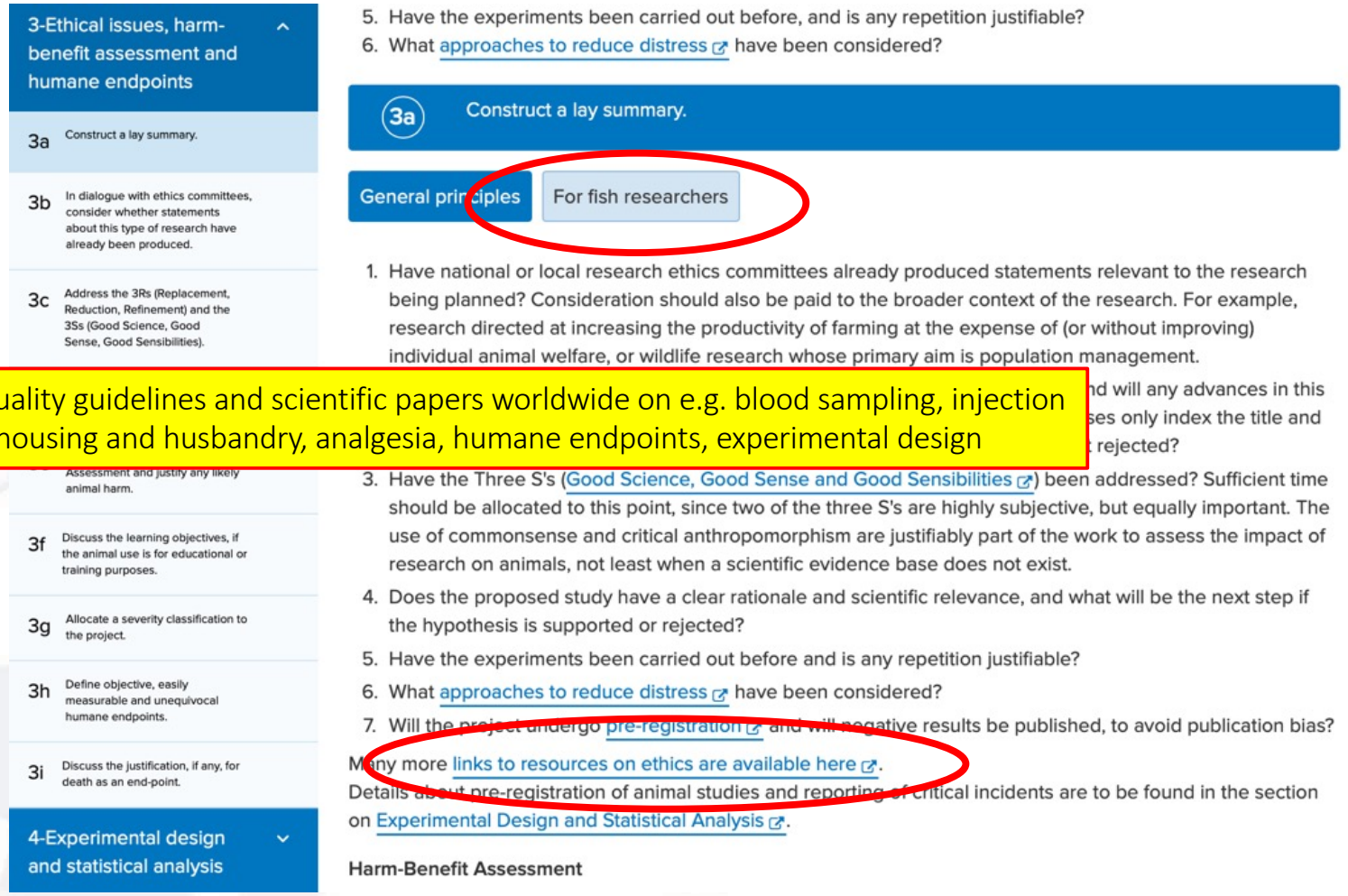
Norecopa: PREPARE for better Science

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

norecopa.no/PREPARE

Norecopa: PREPARE for better Science

norecopa.no/PREPARE



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

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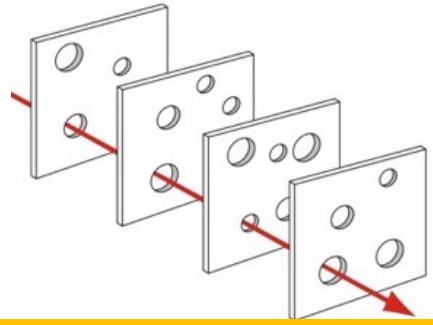
A simple but effective Master Plan

norecopa.no/more-resources/master-plan-and-sops

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

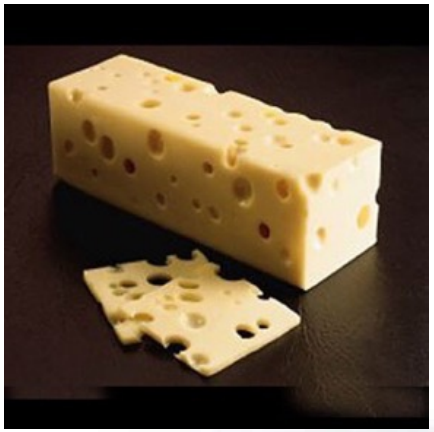
Many of these needed revision in the light of Covid-19
norecopa.no/be-prepared



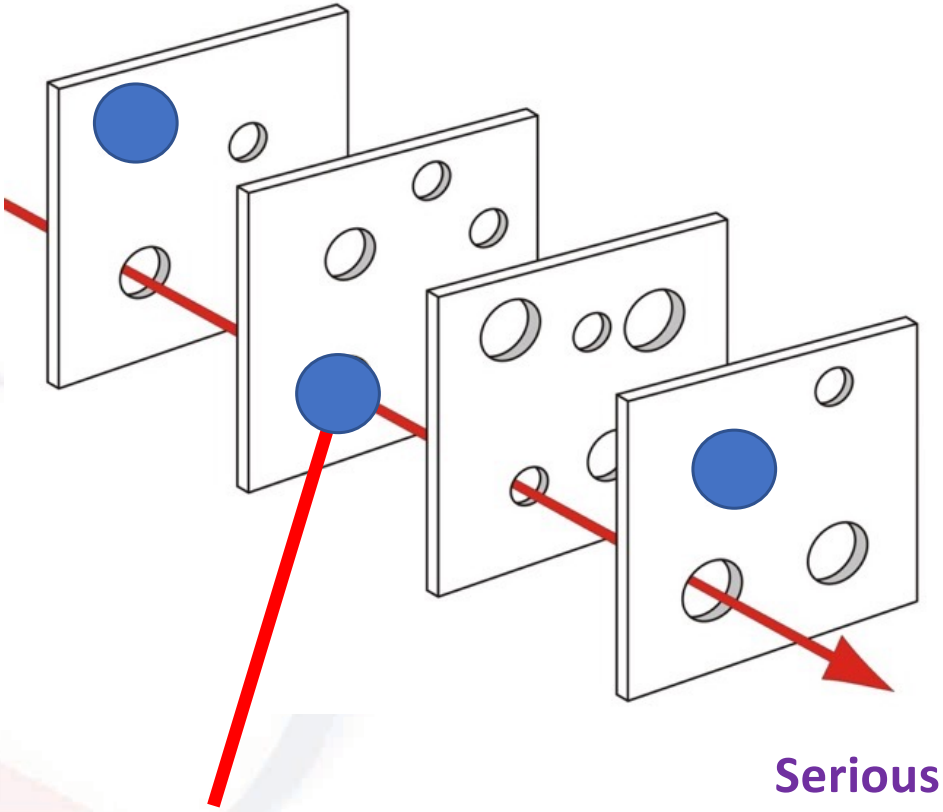
Temporary staff at weekends and holidays

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

“Threat and Error Management”



eaugallecheese.com/Swiss-Cheese



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

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

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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

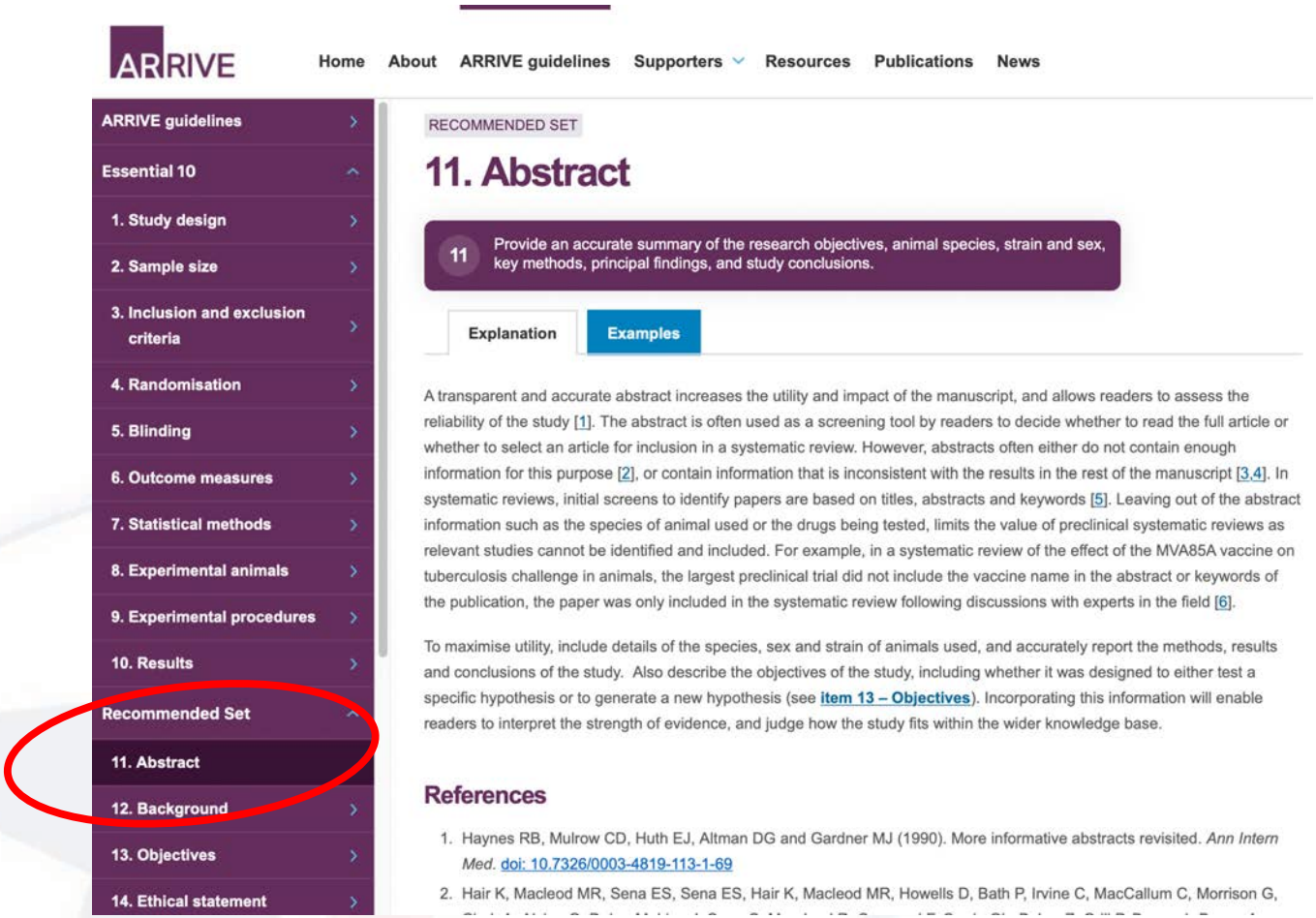
These ten items are the basic minimum that must be included in any manuscript describing animal research. Without this information readers and reviewers cannot assess the reliability of the findings.

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.

Norecopa: PREPARE for better Science

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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"We ARRIVED, because we were PREPARED"

- ✓ *Better Science*
- ✓ *Improved animal welfare*
- ✓ *Advancement of the 3Rs*
- ✓ *Safer working environment*

Norecopa: PREPARE for better Science

English-language newsletters

norecopa.no/news/newsletters 1,300 international subscribers

7-8 times a year

- Norecopa's Annual Meeting and 3R Prize
- Updates about Norecopa
- Nordic Zebrafish Network and course
- News of PREPARE
- News of other 3R Centres and activities
- Harmonisation of education and training
- New forum for behavioural research
- New textbook on anaesthesia
- Fish research
- Glimpses from research
- Food for thought
- For Norwegian readers
- From the media
- Webinars and Meetings Calendar
- Have your colleagues subscribed?

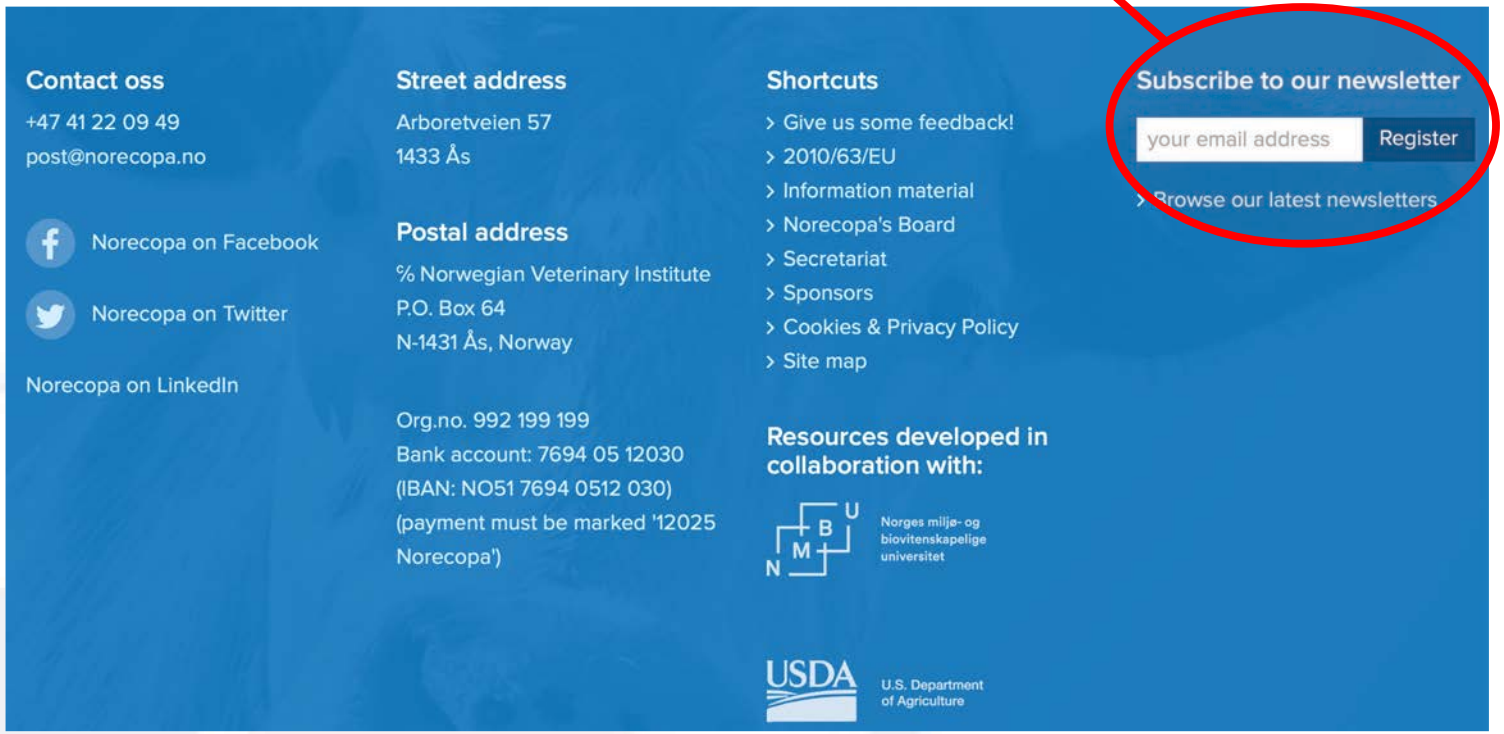
Thanks to Norecopa's main sponsors:

- 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 Animal Protection Alliance's Research Fund
- Norwegian Society for the Protection of Animals
- Novo Nordisk
- Scanbur
- Scottish Accreditation Board
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture

Graphics: colourbox.com

norecopa.no/Albania

English-language newsletters



Thank you for listening!