PREPARING, CARING, SHARING and FLAGGING:

tools for animal care staff

norecopa.no/IAT

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norecopa

https://norecopa.no

Norecopa

Norway's National Consensus Platform for the

Three Rs: Replacement, Reduction and Refinement

and a source of global 3R resources

https://norecopa.no

The views expressed in this presentation are my own and not necessarily those of Norecopa

Norecopa: PREPARE for better Science

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

approx. 9,000 webpages
300,000 hits annually

7-8 detailed newsletters per year

Norecopa: PREPARE for better Science

norecopa.no/meetings/meetings-calendar

+ webpages for past meetings and recorded meetings

norecopa.no/global3R

Centres

- Replacement
- Reduction
- Refinement
- ecopa

Associations

- AFLAS (includes South Korea)
- Culture of Care Network
- EU3Rnet
- FELASA
- FESSACAL
- Scand-LAS

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Databases & Guidelines

Published lists of resources are difficult to search and quickly become outdated. Lists on a website are easier to search, but do not enable the use of filters or intelligent search engines.
Norecopa has therefore constructed four databases, which together with all the text on this website can be searched simultaneously using the search field at the top of every page.

- 3R Guide: a global overview of **databases, guidelines, information centres, journals, email lists, regulations and policies** which may be of use when planning experiments which might include animals. A quick overview of all the guidelines can be accessed here. Norecopa has written several of these, including the PREPARE guidelines for planning animal research and testing.
- NORINA: a global overview of audiovisual aids and other items which may be used as **alternatives or supplements to animals in education and training** at all levels from junior school to University, including dissection alternatives and surgical simulators.
- TextBase: a global overview of **textbooks and other literature within laboratory animal science** and related topics.
- Classic AVs: a subset of NORINA covering **audiovisual aids that are based on older technology**.

These databases are updated regularly. Please give us feedback if you discover errors or omissions.

The Norecopa website also includes four other collections:

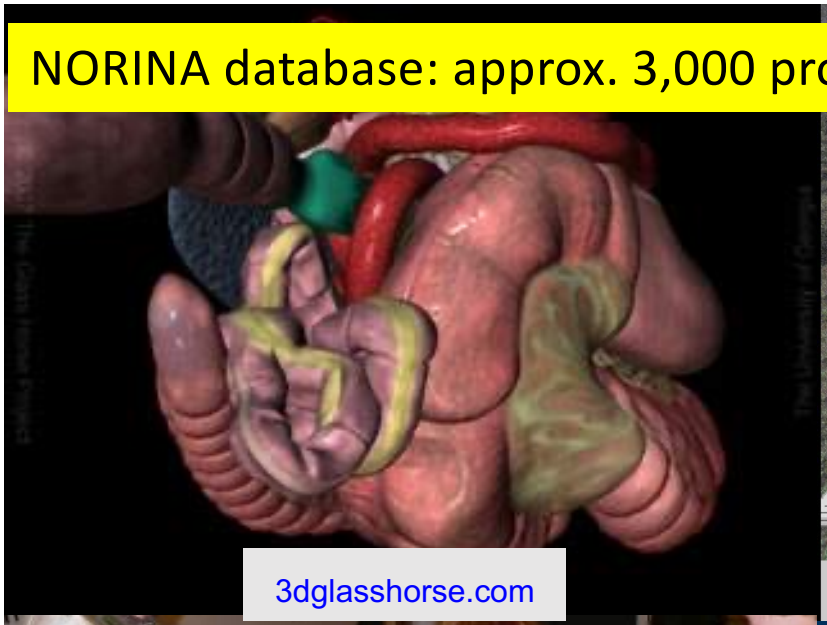
- NAL: a collection of literature references relating to the 3Rs from the US National Agricultural Library
- European Commission datasets:
  - 3Rs Knowledge Sources: over 800 resources collected by the Commission in 2016
  - 3Rs Education and Training Resources, over 560 items collected in 2018
  - Non-animal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

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

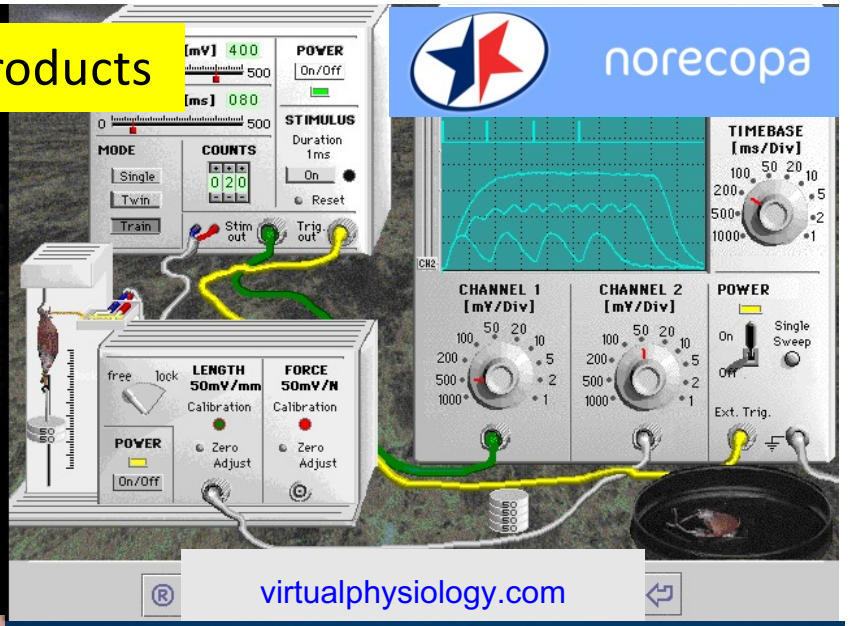
norecopa.no/databases-guidelines

links to over 70 other databases

NORINA database: approx. 3,000 products

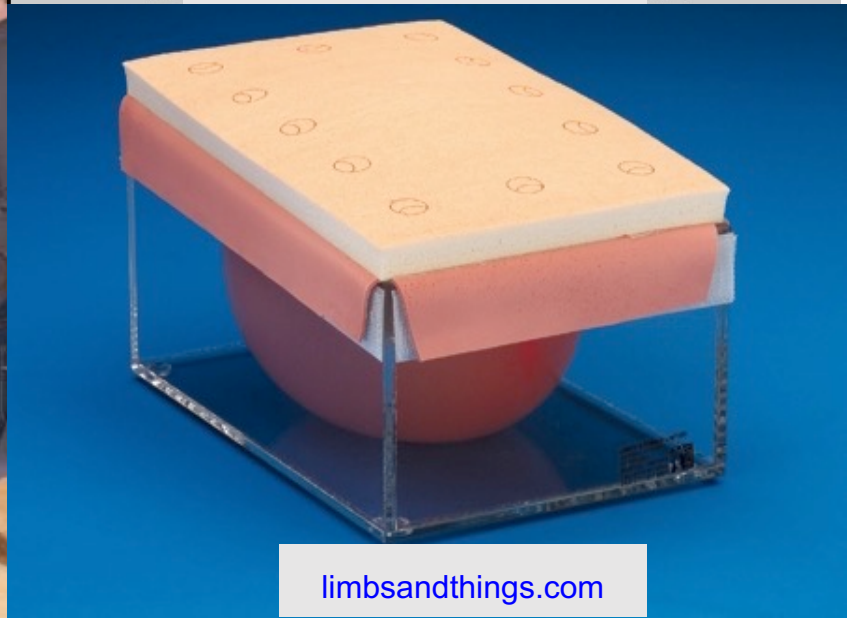


3dglasshorse.com



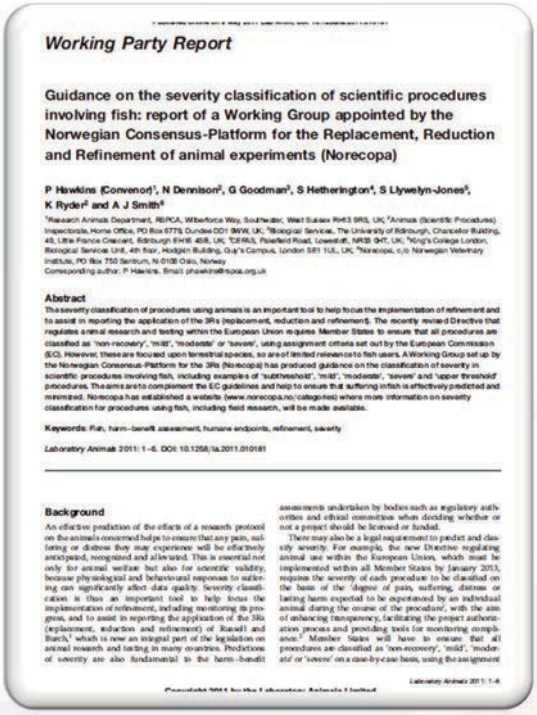
virtualphysiology.com

rescuecritters.com



limbsandthings.com

From **3R-Guide** (380 guidelines for animal research and testing)
norecopa.no/3r-guide



Working Party Report

Guidance on the severity classification of scientific procedures involving fish: report of a Working Group appointed by the Norwegian Consensus-Platform for the Replacement, Reduction and Refinement of animal experiments (Norecopa)

P Hawkins (Convenor)[1], N Dennison[2], G Goodman[3], S Hetherington[4], S Llywelyn-Jones[5], K Ryder[2] and A J Smith[6]

[1]Research Animals Department, RSPCA, Wilberforce Way, Southwater, West Sussex RH13 9RS, UK; [2]Animals (Scientific Procedures) Inspectorate, Home Office, PO Box 6779, Dundee DD1 9WW, UK; [3]Biological Services, The University of Edinburgh, Chancellor Building, 49, Little France Crescent, Edinburgh EH16 4SB, UK; [4]SFIRS, Pitsfield Road, Lowestoft, NR33 0HT, UK; [5]King's College London, Biological Services Unit, 4th floor, Hodgkin Building, Guy's Campus, London SE1 1UL, UK; [6]Norecopa, c/o Norwegian Veterinary Institute, PO Box 750 Sentrum, N-0106 Oslo, Norway
Corresponding author: P Hawkins. Email: phawkins@rspca.org.uk

Abstract

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 aims are to complement the EC guidelines and help to ensure that suffering in fish is effectively predicted and minimized. Norecopa has established a website (www.norecopa.no/categories) where more information on severity classification for procedures using fish, including field research, will be made available.

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

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

Background

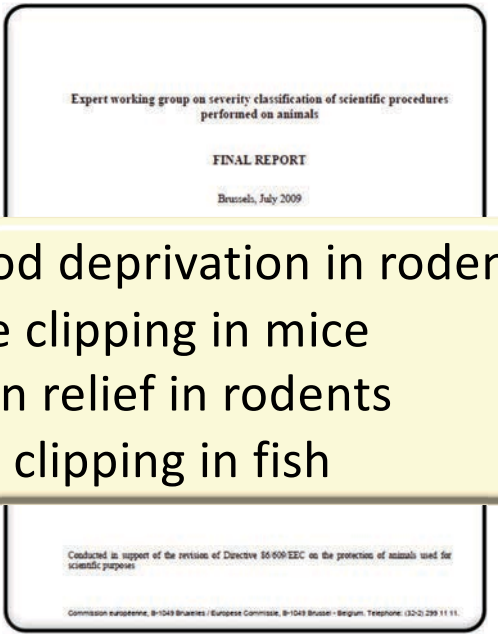
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because physiological and behavioural responses to suffering can significantly affect data quality. Severity classification is thus an important tool to help focus the implementation of refinement, including monitoring its progress, and to assist in reporting the application of the 3Rs (replacement, reduction and refinement) of Russell and Burch,[1] which is now an integral part of the legislation on animal research and testing in many countries. Predictions of severity are also fundamental to the harm–benefit assessments undertaken by bodies such as regulatory authorities and ethical committees when deciding whether or not a project should be licensed or funded.

There may also be a legal requirement to predict and classify severity. For example, the new Directive regulating animal use within the European Union, which must be implemented within all Member States by January 2013, requires the severity of each procedure to be classified on the basis of the 'degree of pain, suffering, distress or lasting harm expected to be experienced by an individual animal during the course of the procedure', with the aim of enhancing transparency, facilitating the project authorization process and providing tools for monitoring compliance.[2] Member States will have to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe' on a case-by-case basis, using the assignment

Laboratory Animals 2011; 1–6

Guidance on the severity classification of procedures involving fish

Report from a Working Group
convened by Norecopa



Expert working group on severity classification of scientific procedures performed on animals

FINAL REPORT

Brussels, July 2009

Conducted in support of the revision of Directive 86/609/EEC on the protection of animals used for scientific purposes

Commission européenne, B-1049 Bruxelles / Europese Commissie, B-1049 Brussel - Belgium. Telephone: (32-2) 299 11 11.

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

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

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

Laboratory Animals, 45: 219-224, 2011

norecopa.no/categories

My reasons for offering to present at IAT congress

- I have planned, conducted and supervised animal research, and held courses in Laboratory Animal Science, since the early 1980's
- I have developed the greatest respect for scientists who are specialists in their field
- But is clear that one of the greatest challenges to validity and reproducibility lies in the animals they use and the way they use them
- I suspect that many scientists are unaware of the size of this challenge, or they assume that the animal facility is dealing with it
- **The animal carers and technologists are therefore some of the most important people they should be consulting, from day 1**

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nature human behaviour

Perspective | Open Access | Published: 10 January 2017

A manifesto for reproducible science

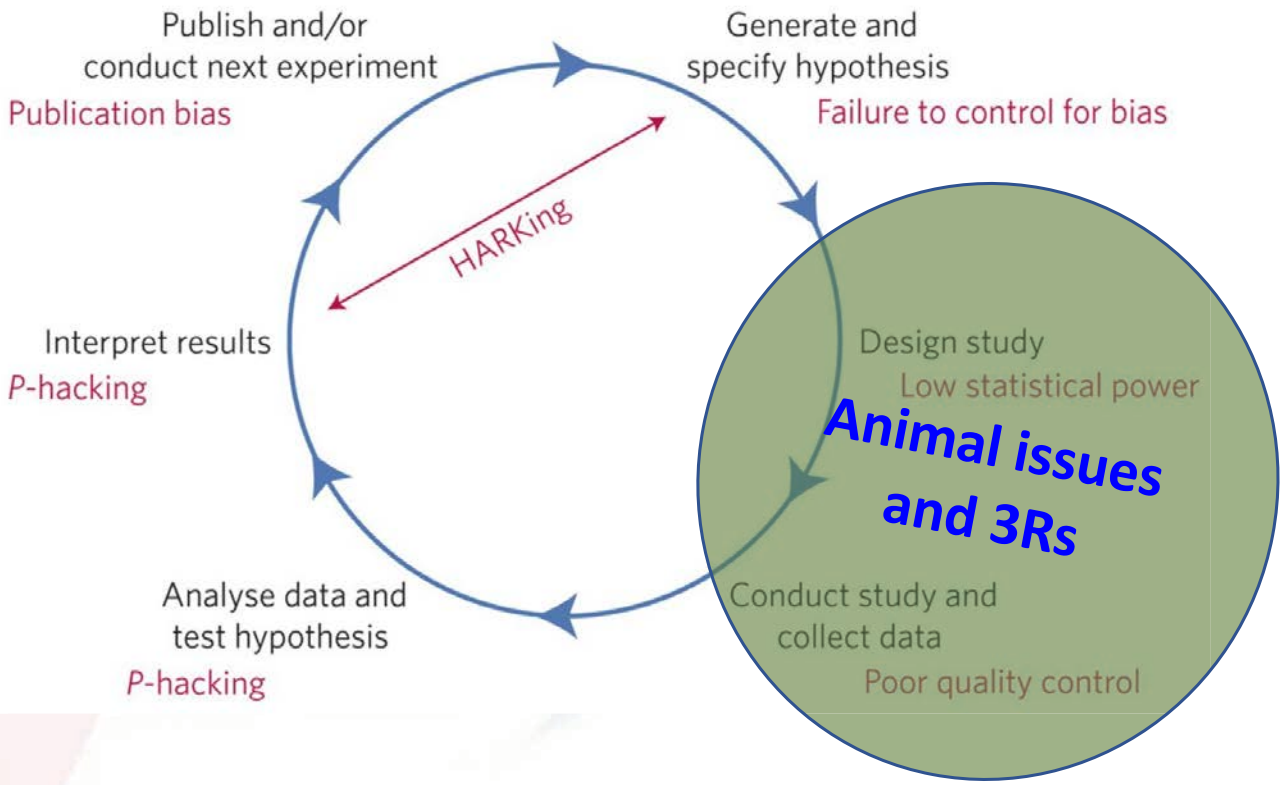
Marcus R. Munafò, Brian A. No
Button, Christopher D. Chambers,
Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



Collaboration on the road to better preclinical research

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

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

Encourage scientists to collaborate with animal carers and technicians from Day 1

- you have a right to know and will be more motivated
- you know the possibilities (and limitations) in the animal facility
- you possess a large range of practical skills and are good at lateral thinking
- you know the animals best
- the animals know you best
- lack of involvement creates anxiety, depression and opposition to animal research, as well as limiting creativity which might improve the experiments

Reporting

Planning

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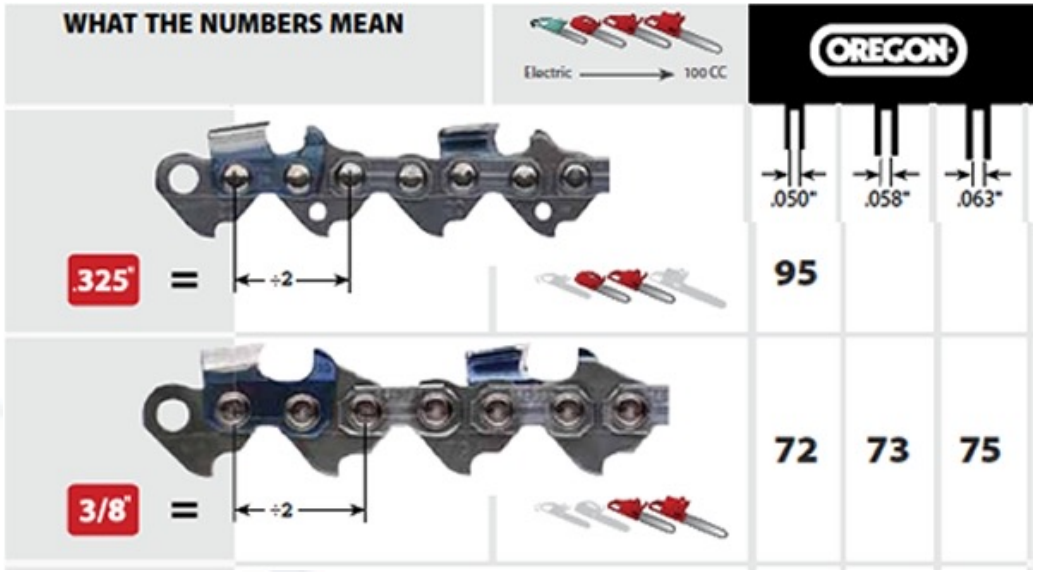
The easy parts of design and reporting:



arborist101.com

- Chainsaw
  - Blade characteristics
  - Sparkplug type
  - Petrol/oil mixture
  - Service history
- Angle of cut in tree
- Length of tree logs

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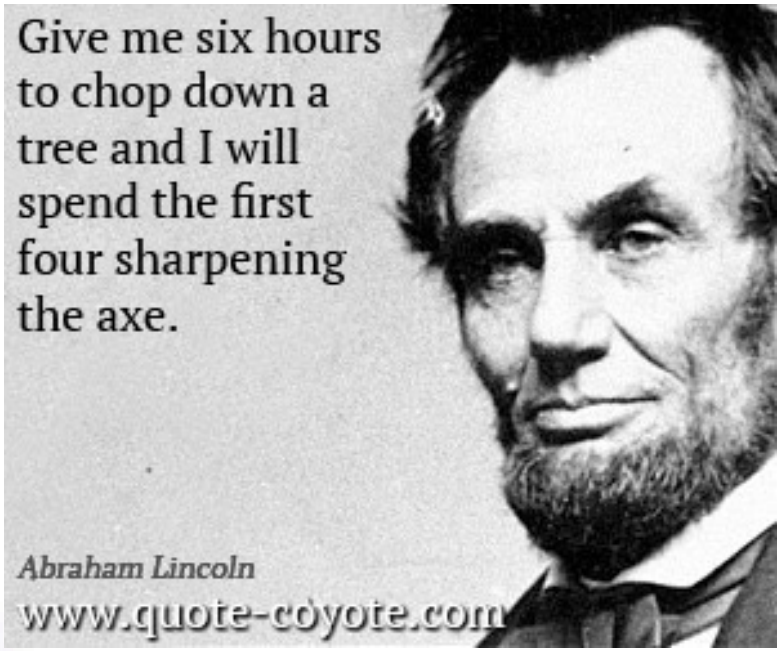
Critical issues behind the scenes that may not get reported:

- Experience of the workers
- Inspection for signs of rot and to decide felling direction
- Additional equipment (winch, chains, straps, wedges)
- Routines and equipment for sharpening the chain
- Clearing-up and transport of logs
- Health and safety precautions – clothing, onlookers
- **Division of labour and costs**

Starts long before the actual work.

leaderonomics.com



Norecopa: PREPARE for better Science

editorial | Published: February 2010

Measure twice, think three times, cut once

L. Noyez

Netherlands Heart Journal **18**, 60(2010) | Cite this article

doi.org/10.1007/BF03091738

Abstract

When I was a child, my father taught me how to fix a punctured tyre. He stressed the importance of checking the whole tyre, even if I had already found a puncture, because there could always be more. In addition, he made me check the outer tyre for sharp pieces that could again damage the inside tyre.

Two frustrations:

'We can solve the reproducibility crisis by'

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

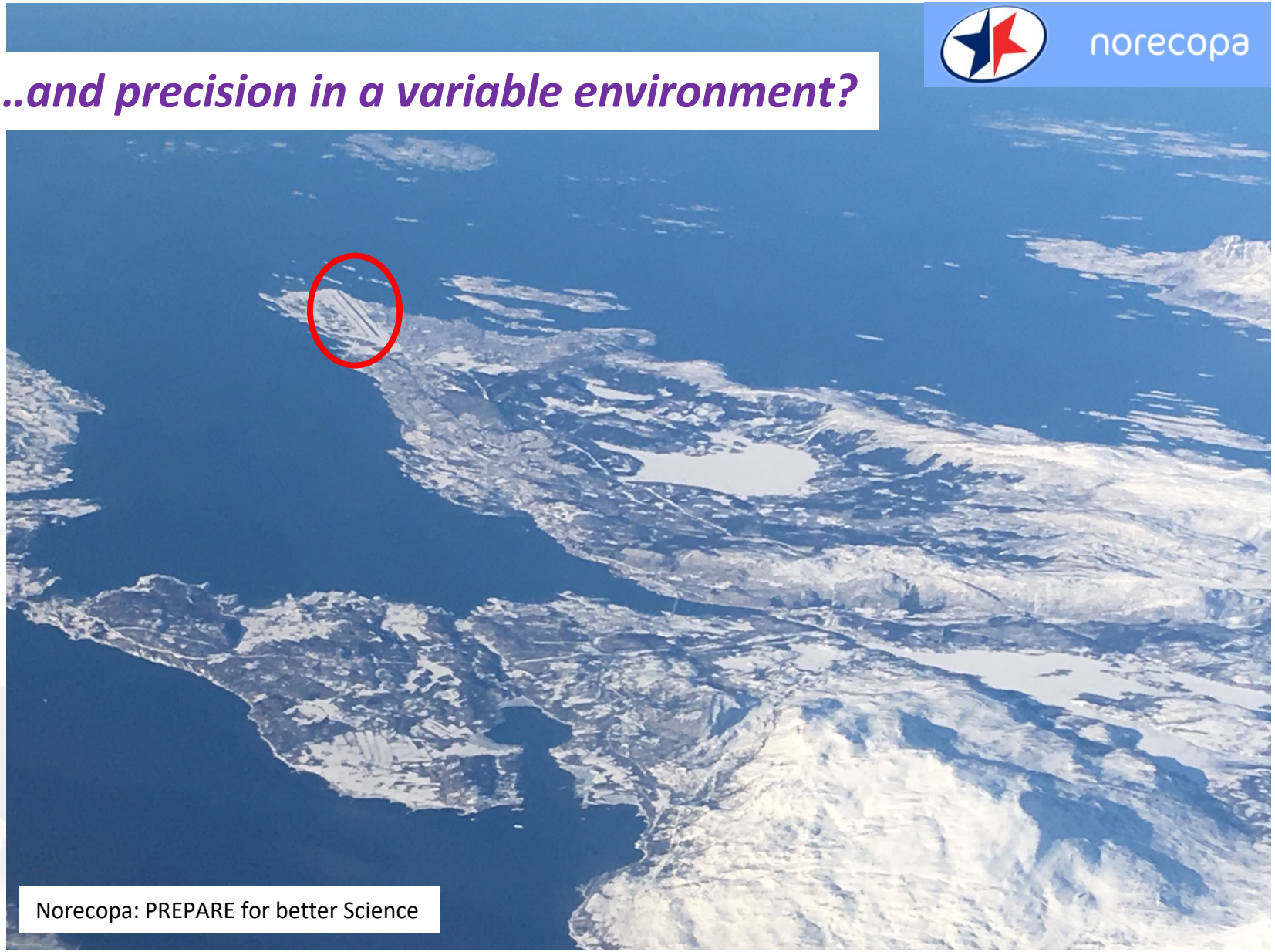
- **better reporting**

reddit.com

How do other professionals achieve reproducibility?

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

…and precision in a variable environment?



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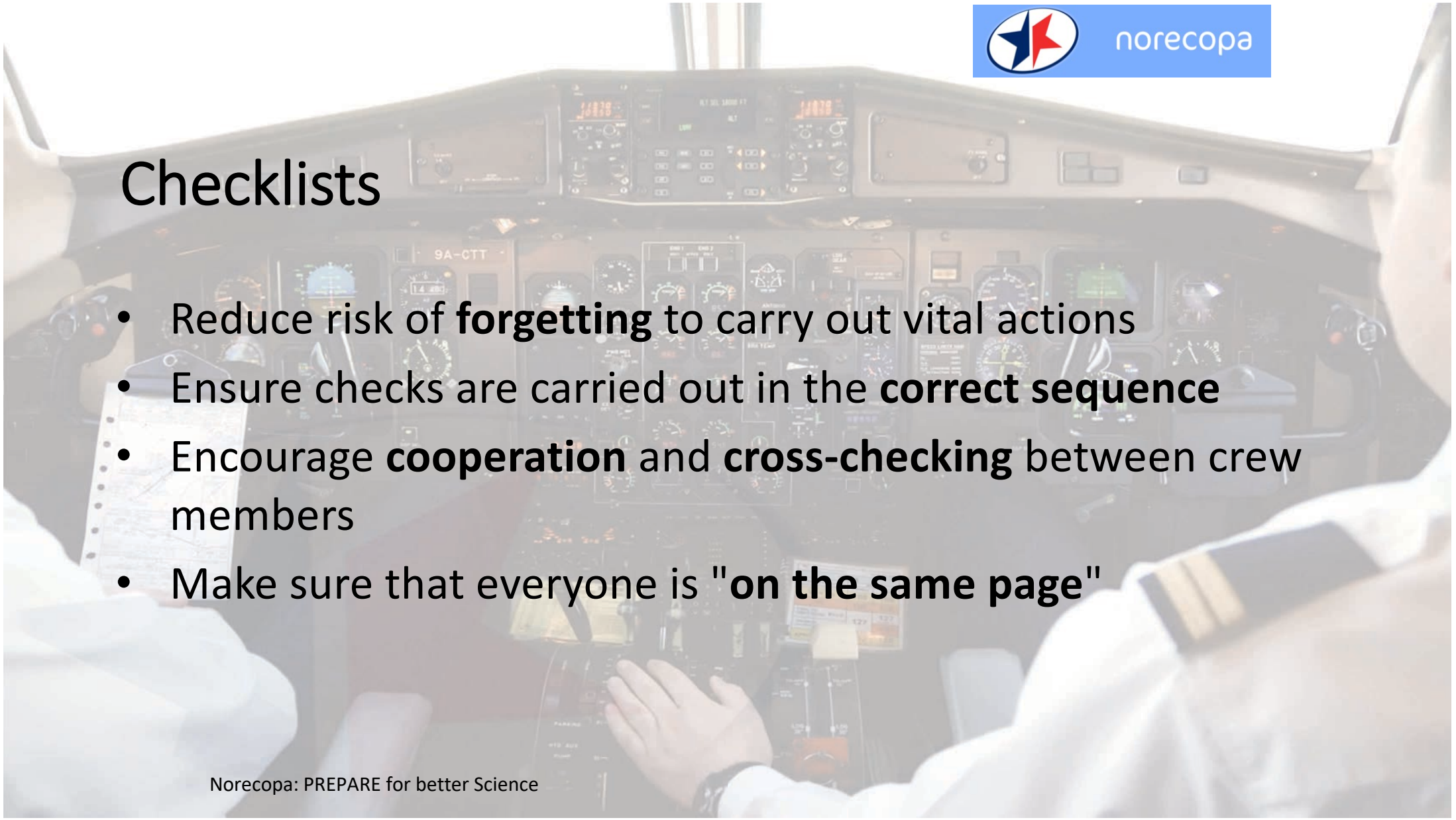
10-15 checklists even on short routine flights



Checklists

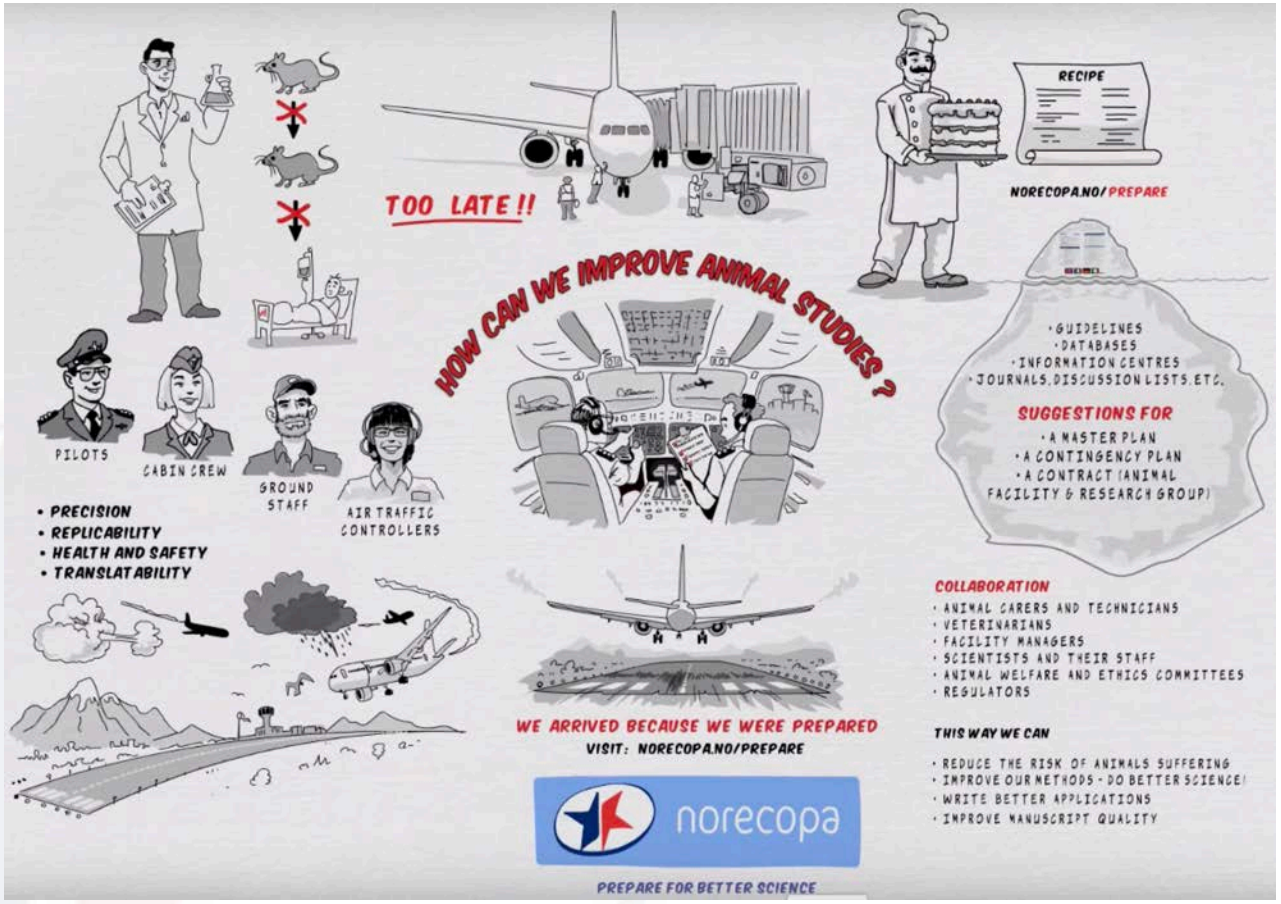
- Reduce risk of **forgetting** to carry out vital actions
- Ensure checks are carried out in the **correct sequence**
- Encourage **cooperation** and **cross-checking** between crew members
- Make sure that everyone is "**on the same page**"

Too late to read the checklists when you have ARRIVEd!

colourbox.com

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

3-minute cartoon film



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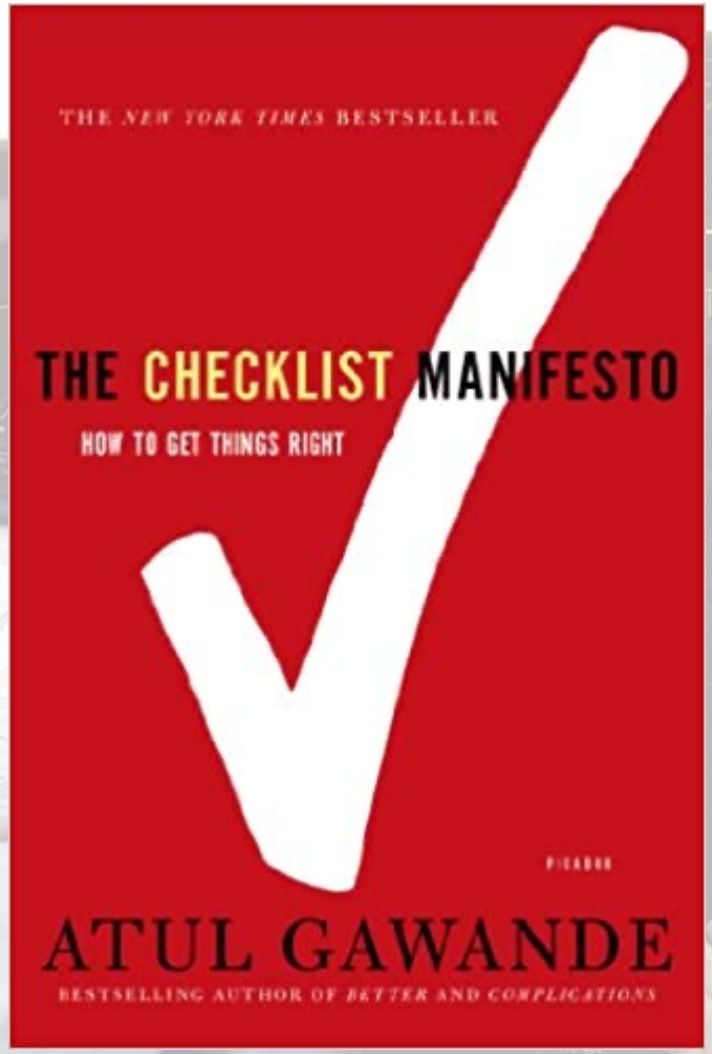

Surgical Safety Checklist

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

Before induction of anaesthesia (with at least nurse and anaesthetist)	Before skin incision (with nurse, anaesthetist and surgeon)	Before patient leaves operating room (with nurse, anaesthetist and surgeon)
Has the patient confirmed his/her identity, site, procedure, and consent? ☐ Yes	☐ **Confirm all team members have introduced themselves by name and role.**	**Nurse Verbally Confirms:** ☐ The name of the procedure
Is the site marked? ☐ Yes ☐ Not applicable	☐ **Confirm the patient's name, procedure, and where the incision will be made.**	☐ Completion of instrument, sponge and needle counts
Is the anaesthesia machine and medication check complete? ☐ Yes	**Has antibiotic prophylaxis been given within the last 60 minutes?** ☐ Yes ☐ Not applicable	☐ Specimen labelling (read specimen labels aloud, including patient name)
Is the pulse oximeter on the patient and functioning? ☐ Yes	**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?	☐ Whether there are any equipment problems to be addressed
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	**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	**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

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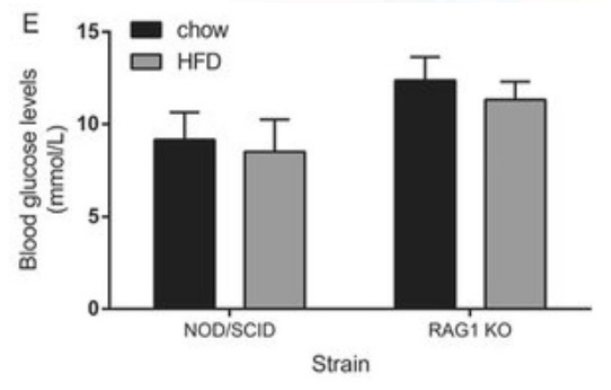
amazon.com/gp/product/0312430000

The scientist



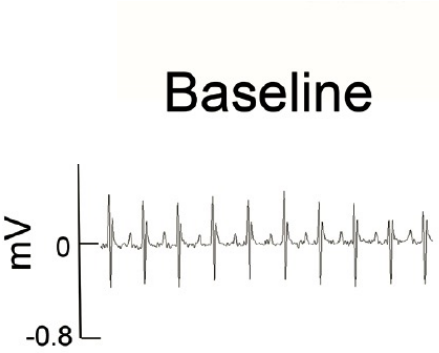
The mouse

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

One example: scruffing mice

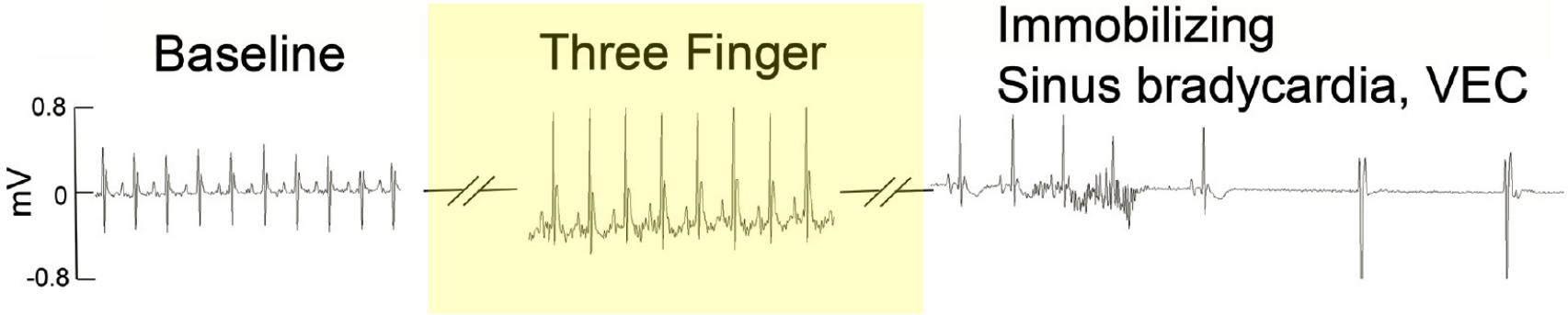


Sinus bradycardia
ventricular escape complexes

Labitt *et al.*, 26 February 2021

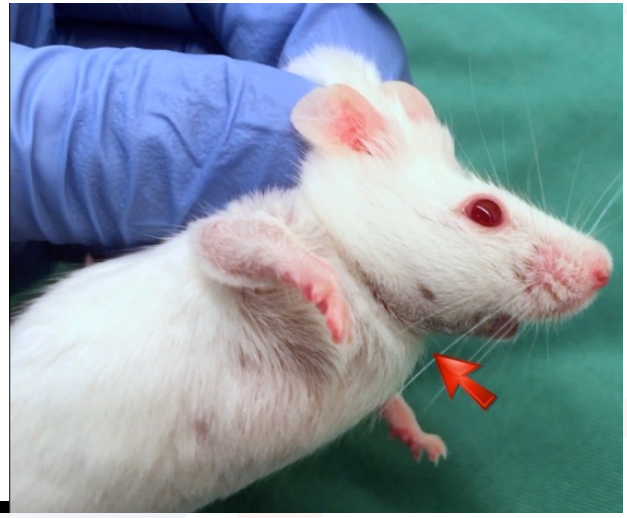
Both sexes and 4 strains of mice, 3 experienced handlers

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



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

norecopa.no/scruff



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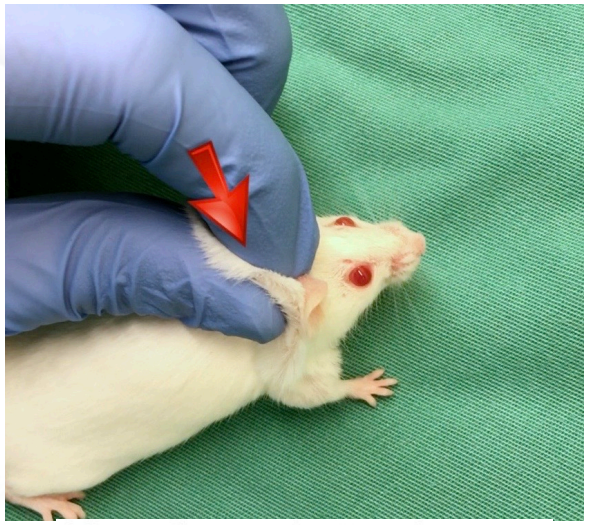


Three fingers better than two

Artefacts caused by poor administration techniques

Photo: NMBU

- *Do injections always end up in the same place?*
- *Are the injections painful?*
- *Are they realistic? (intramuscular injections in small animals)*

'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

If scientists ask for the scientific evidence...

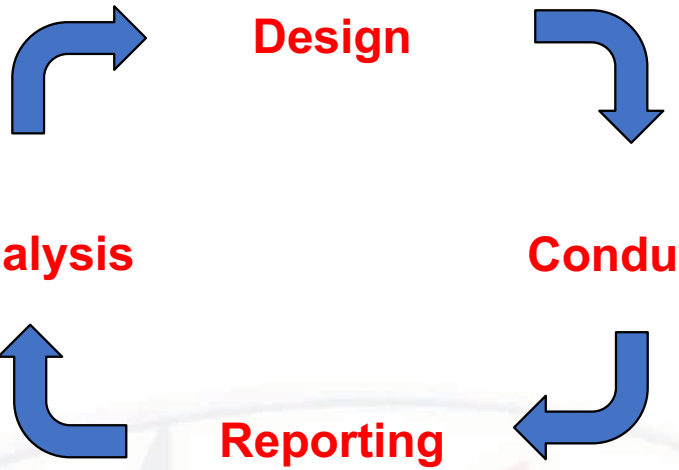
Carol M. Newton (1925-2014)

National Library of Medicine

The three S's

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

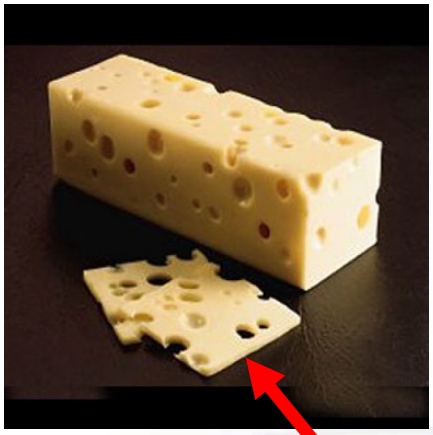
https://norecopa.no/3S



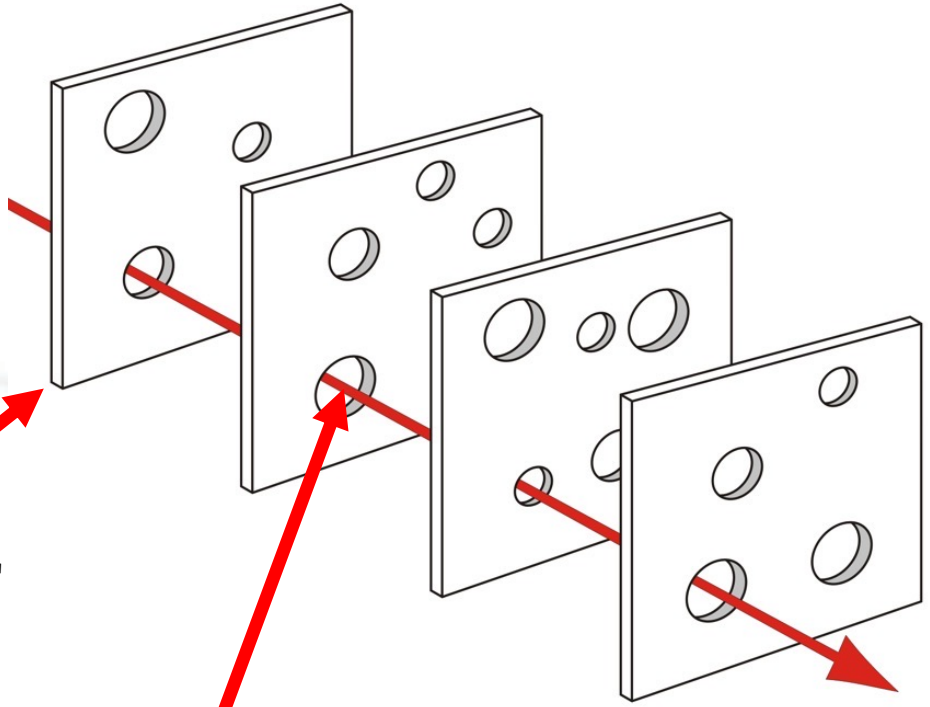
Identify and ensure the quality of (at least) the critical points in the experiment:

for scientific output and animal welfare

Threat and Error Management



eaugallecheese.com/Swiss-Cheese



"Layer of defence"
or redundancy

Weakness / hazard

Loss

wikipedia.org/wiki/Swiss_cheese_model

A simple but effective Master Plan

Norecopa: PREPARE for better Science

Contingency and redundancy

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

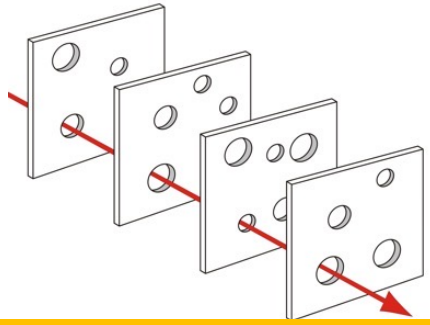
Photo: NMBU

A Contingency Plan, based upon risk assessment

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

These need to be revised or supplemented in the light of Covid-19

norecopa.no/be-prepared



Temporary staff at weekends and holidays

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

Good advice is emerging from the Covid-19 pandemic

norecopa

Suggested considerations for establishment working under ASPA during the COVID19 lock-down

CATEGORY		CONSIDERATIONS/SUGGESTIONS	
PERSONNEL Provide 'essential worker' letter to show authorities, include home address. Consider whether company/ photo i.d. would be helpful All personnel must prioritise their health and the health of others by wearing suitable PPE and by observing social distancing as advised by the government Support mental health Consider mindfulness apps, Convert empty animal room into a relaxation/yoga room (online yoga classes).	ANIMAL TECHNICIANS	Run 2 or more teams if possible to lower the risk of transmission(**each team is treated as 'household'**) to the wider team. Examples of how onsite teams might be run include alternate days, 2days on 2days off and utilising an early shift / a late shift to reduce contact and total staff in an area at any one time. If people are in isolation or have caring responsibilities they may (if well enough) be able to work offsite as part of a "virtual office" team	
		Where teams can't be separated use full PPE/ RPE and have staggered entry/break/exit times or other means of avoiding people not in PPE. Physically segregate in unit if possible	
		Review teams regularly – this may need to be daily in some situations	
		Introduce regular and frequent routines for surface decontamination, paying particular attention to door handle/ door plates, taps and work surfaces. Clean with detergent / 70% isopropyl alcohol or similar	
		Limit reliance on public transport methods. Accommodate parking where possible to allow individuals to travel by car	
			Ensure all alarm systems are checked regularly and are functional. Monitor, record and act on all alarms
			Review contingencies for critical system failure (e.g. HVAC) and have an action plan. Make sure all backup systems are fully functional and that sufficient spare parts are available and accessible
		DELIVERIES	
		VETS	equired
	RESEARCHERS	ANIMALS	BREEDING	Ensure all non-replaceable lines are cryopreserved
				Consider stopping breeding of lines that are frozen down and have been on "tick over"
				Breed only for colony management, i.e. minimum number of breeding pairs to maintain the health of the colony
				Avoid breeding animals with phenotype – maintain animals where homozygotes may be phenotypic as wild type x heterozygote crosses to avoid generation of homozygotes
				Genotype promptly in order to identify animals required for ongoing breeding and cull animals not required ASAP
				Consider outsourcing genotyping if internal facilities are closed
			REDUCE STOCK	Do not start new work unless absolutely essential/ internal review has been performed that confirms that the work can be properly serviced
				Essential research work may continue if staffing levels allow it. A local decision making process which records decision making as to which projects may remain ongoing should be in place. Examples of what may be reasonable are COVID-19 work, aged animal work and work to complete studies
				There may be reasons for prioritising ongoing work with some species (e.g. NHPs)
	ESTABLISHMENT LICENCE HOLDER			If the facilities allow, consolidate animals to one area, check light cycle, room temps & designation first
				Spread work evenly / reduce cleaning of cages – but not to extent that welfare could be compromised
				Re-assess stock levels /staff levels at least once per week
				Cull animals that are not going to be needed for colony management and cannot otherwise be used
	ENGINEERS			Avoid unnecessary movement of animals
				Prioritise the movement of animals to other facilities or establishments for contingency of valuable lines.
		ACCESS		Check your facility/ies will be open – Provide a list of names requiring access. Check with security how and when essential staff will access
				Confirm how essential supplies and waste contractors will service the facility/ies
		SUPPLIES		Stock up on diet, bedding, nesting materials, PPE, disinfectants and other essentials, aim for a minimum of 3 months
				Ensure there will there be Liquid nitrogen / dry ice for cryopreserved stocks
				Have stocks of CO_2 and sodium pentobarbitone and any other drugs as directed by the NVS
		ESTATES / ENGINEERS		Check your contractors are working and get emergency contacts. Maintain a list of mobile numbers, available to everyone
				Consider if essential equipment will require servicing or repair. Ensure that you have a plan to enable this
				Will waste be being removed from site? – prepare an area for on-site storage if necessary
		RECORDS		**Record all difficult decisions taken. What/ when /why and any related evidence**

norecopa.no/be-prepared

lava.uk.net/viewtopic.php?f=3&p=80

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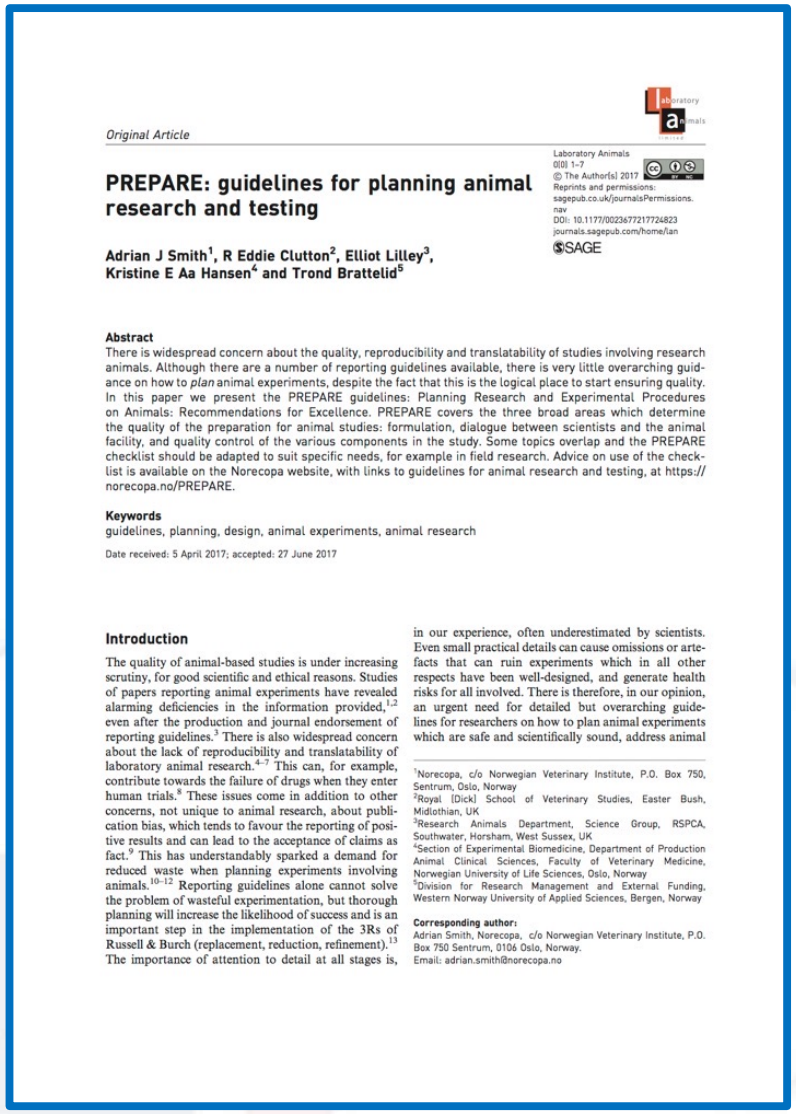
A contract between the animal facility and the research group

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			



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

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SAGE

Abstract

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

Keywords

guidelines, planning, design, animal experiments, animal research

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

Introduction

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

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Over 18,000 downloads from the journal website so far

Also downloadable from norecopa.no/PREPARE

PREPARE:

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

PREPARE covers 15 topics:

Formulation of the study

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

Dialogue between scientists and the animal facility

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

Methods

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

Items in pink are not typically highlighted in reporting guidelines

norecopa.no/PREPARE/prepare-checklist

PREPARE

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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 S[illegible]; [d]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; [e]Division for Research Management, Faculty of Medicine, University of Bergen, Sciences, 5020 Bergen, Norway.

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

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

The topics will not always be addressed in the order in which they checklist can be adapted to meet special needs, such as field stud facilities, since in-house experiments are dependent upon their qu[illegible] the management of animal [illegible]rsion 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.

Three Rs

Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	☐ Form a clear hypothesis, with primary and secondary outcomes. ☐ Consider the use of systematic reviews. ☐ Decide upon databases and information specialists to be consulted, and construct search terms. ☐ Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering, and its welfare needs. ☐ Assess the reproducibility and translatability of the project.
2. Legal issues	☐ Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. ☐ Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	☐ Construct a lay summary. ☐ In dialogue with ethics committees, consider whether statements about this type of research have already been produced. ☐ Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities). ☐ Consider pre-registration and the publication of negative results. ☐ Perform a harm-benefit assessment and justify any likely animal harm. ☐ Discuss the learning objectives, if the animal use is for educational or training purposes. ☐ Allocate a severity classification to the project. ☐ Define objective, easily measurable and unequivocal humane endpoints. ☐ Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	☐ Consider pilot studies, statistical power and significance levels. ☐ Define the experimental unit and decide upon animal numbers. ☐ Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding and division of labour	☐ Arrange meetings with all relevant staff when early plans for the project exist. ☐ Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. ☐ Discuss and disclose all expected and potential costs. ☐ Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility evaluation	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
7. Education and training	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health risks, waste disposal and decontamination	☐ Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. ☐ Assess, and if necessary produce, specific guidance for all stages of the project. ☐ Discuss means for containment, decontamination, and disposal of all items in the study.
(C) Quality control of the components in the study	
9. Test substances and procedures	☐ Provide as much information as possible about test substances. ☐ Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	☐ Decide upon the characteristics of the animals that are essential for the study and for reporting. ☐ Avoid generation of surplus animals.
11. Quarantine and health monitoring	☐ Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	☐ Attend to the animals' specific instincts and needs, in collaboration with expert staff. ☐ Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).
13. Experimental procedures	☐ Develop refined procedures for capture, immobilisation, marking, and release or rehoming. ☐ Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	☐ Consult relevant legislation and guidelines well in advance of the study. ☐ Define primary and emergency methods for humane killing. ☐ Assess the competence of those who may have to perform these tasks.
15. Necropsy	☐ Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

References

1. Smith AJ, Clutton RE, Lilley E, Hansen KEA & Brattelid T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017, DOI: 10.1177/0023677217724823.
2. Kilkenny C, Browne WJ, Cuthill IC *et al.* Improving Bioscience Research Reporting: The ARRIVE Guidelines for Reporting Animal Research. *PloS Biology*, 2010; DOI: 10.1371/journal.pbio.1000412.

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

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

norecopa.no/PREPARE

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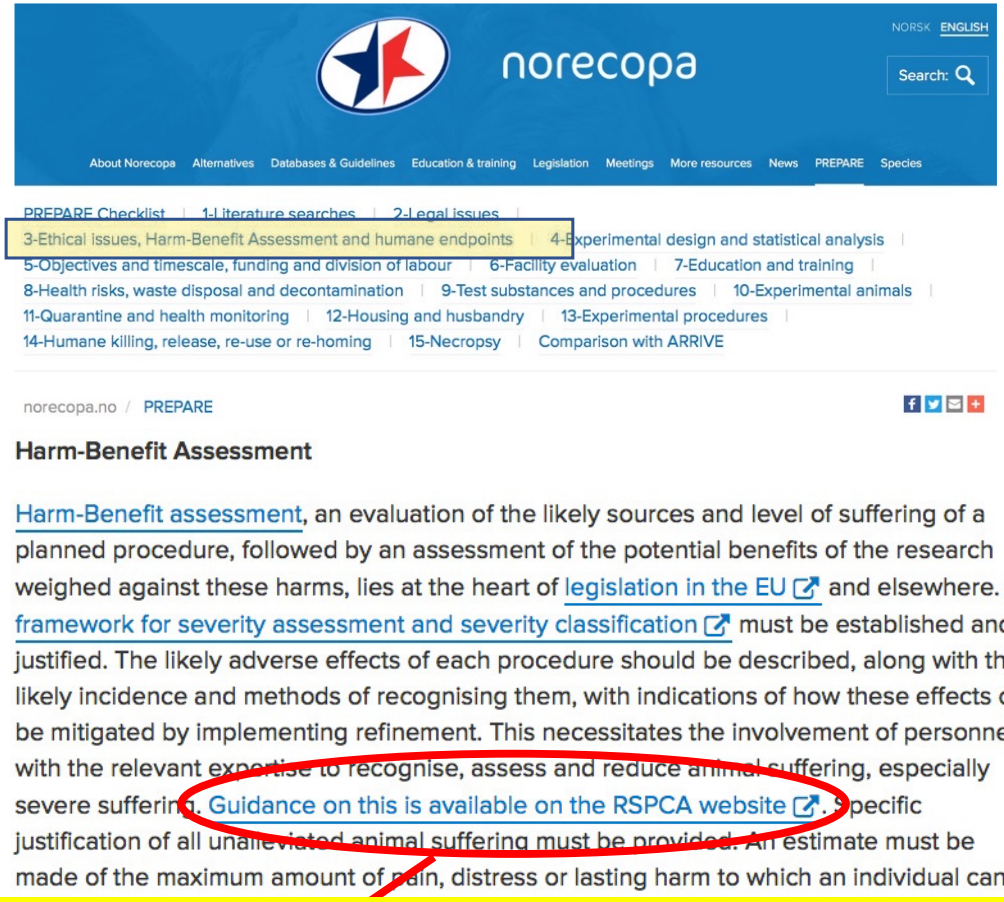
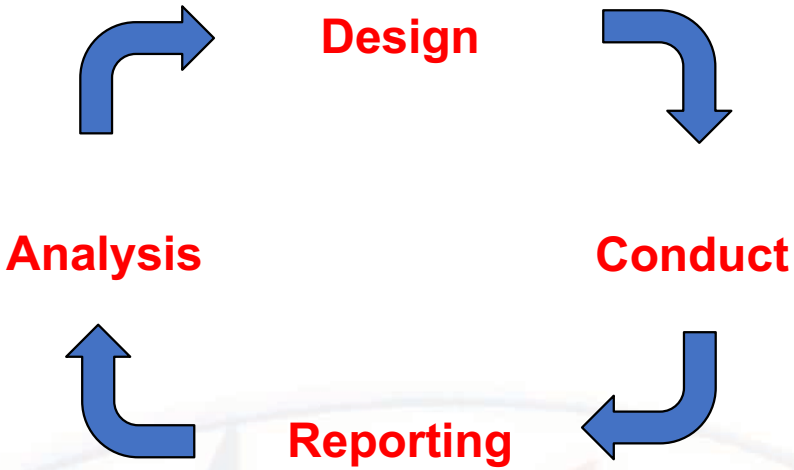
norecopa.no/PREPARE



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



Space Shuttle, NASA

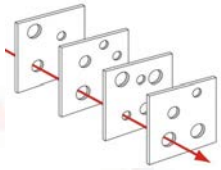
NASA

cbsnews.com

no.wikipedia.org

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

We need a Culture of Care!



A Culture of Care

A demonstrable commitment, throughout the establishment, to improving:

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

It goes beyond simply complying with the law!

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The International Culture of Care Network

A Quick Start Guide and more resources

norecopa.no/CoC

"because we've always done it that way"

"as often as necessary"

"there are no alternatives"

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

Look for the acceptable, rather than choosing the accepted

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

Why is 3R literature hard to find?

- Bibliographic databases are often not used adequately (poor overlapping between the databases)
- Too few scientists are aware of the specialist 3R-databases
- Scientists rarely use ”3R” words when they write titles/abstracts/keywords for their papers
- Databases rarely flag 3R-papers with explicit thesaurus terms
- We have no single ”Journal of Alternatives”

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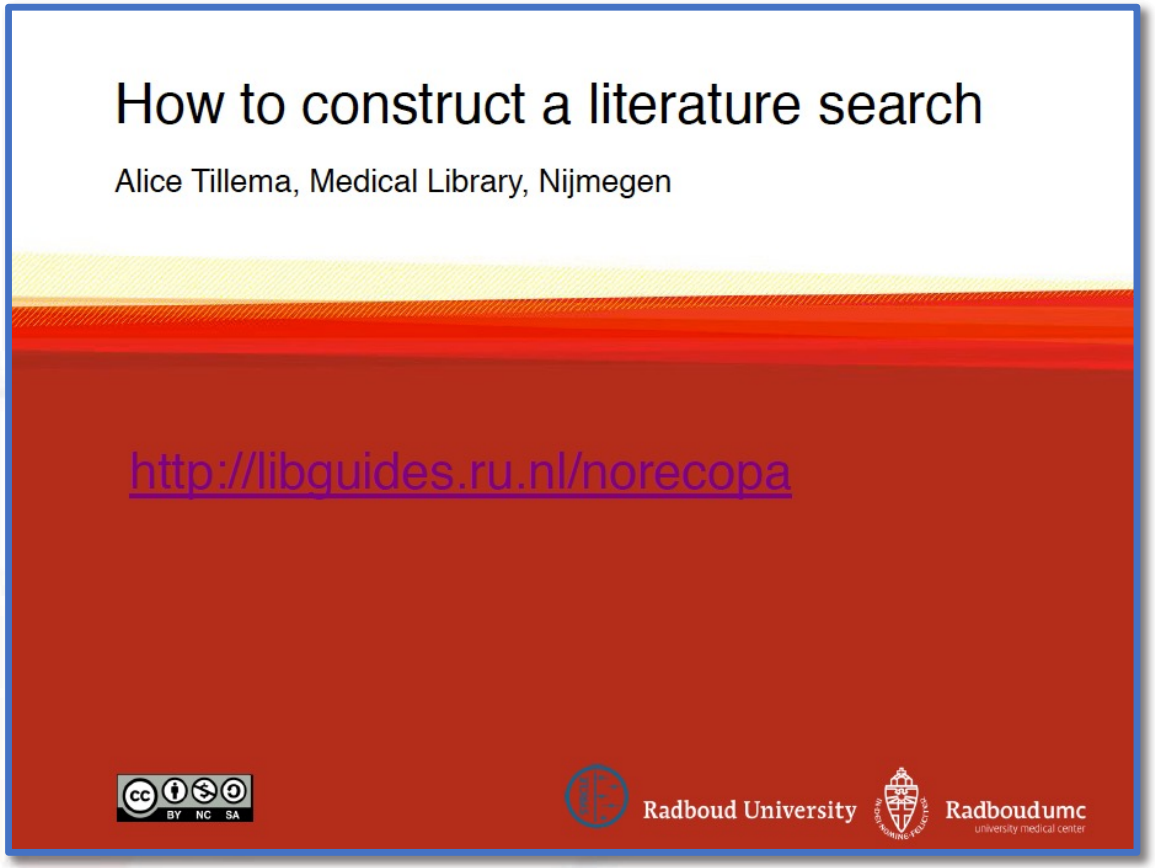
norecopa.no/prepare/1-literature-searches



Refinement Wiki

wiki.norecopa.no

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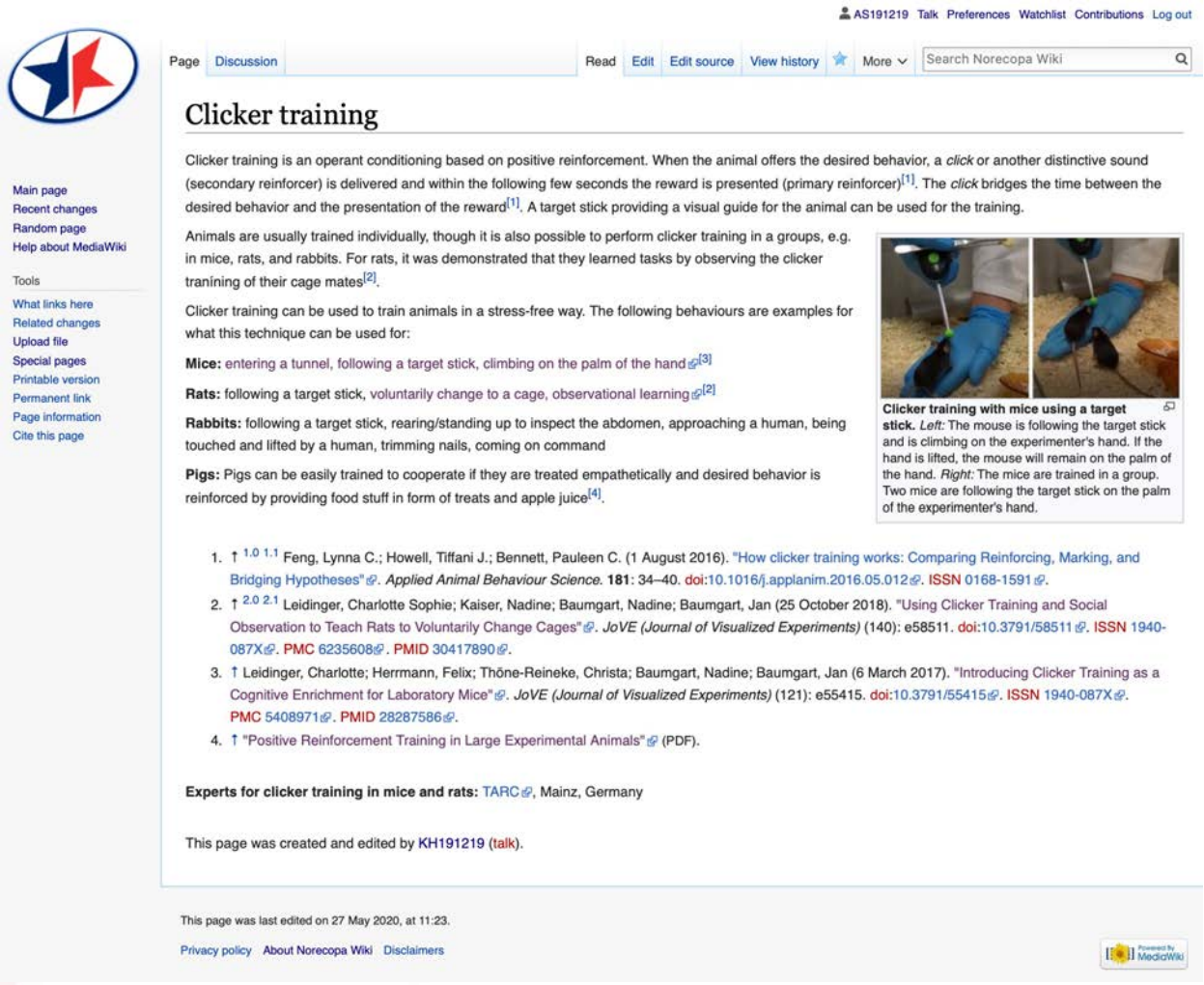

wiki.norecopa.no

Pages created as of today

- Acclimatisation
- Adrian Smith
- Anaesthesia in neonates
- Analgesia
- Blood sampling of hamsters
- Blood sampling of rainbow trout
- Clicker training
- Contingency plans
- Detecting early onset of clinical signs in the mouse model of Covid-19
- Detection of pain and distress in mice
- Experimental Autoimmune Encephalomyeltis (EAE)
- Facial expression analysis
- General discusson on use of analgesics
- Hot Bead Sterilisers
- Housing research fish
- Humane endpoints
- Intraperitoneal injection
- Ketamine and alpha-2 agonist combinations
- Lumpfish
- Main Page
- Metabolic cages
- Mouse Grimace Scale
- Mouse handling
- Nest building material
- Rotarod Test
- TTEAM and TTouch
- Tail vein injection
- Tumour cell implant into mammary fat pad
- Ulcerative Dermatitis in Mice
- Water quality

3R improvements are often not highlighted in the scientific literature

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

photo:NMBU

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

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

Annelise Hem[1], Adrian J. Smith[2] & Per Solberg[1]

[1]Laboratory Animal Unit, National Institute of Public Health, PO Box 4404 Torshov, N-0403 Oslo and [2]Laboratory Animal Unit, Norwegian School of Veterinary Science, PO Box 8146 Dep., N-0033 Oslo, Norway

© Laboratory Animals Ltd. *Laboratory Animals* (1998) **32**, 364–368

Summary

A method is described for blood collection from the lateral saphenous vein. This enables rapid sampling, which if necessary can be repeated from the same site without a need for new puncture wounds. The method is a humane and practical alternative to cardiac and retro-orbital puncture, in species where venepuncture has traditionally been regarded as problematic.

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

Not necessarily a high-impact journal

Thanks to Norecopa's main sponsors:

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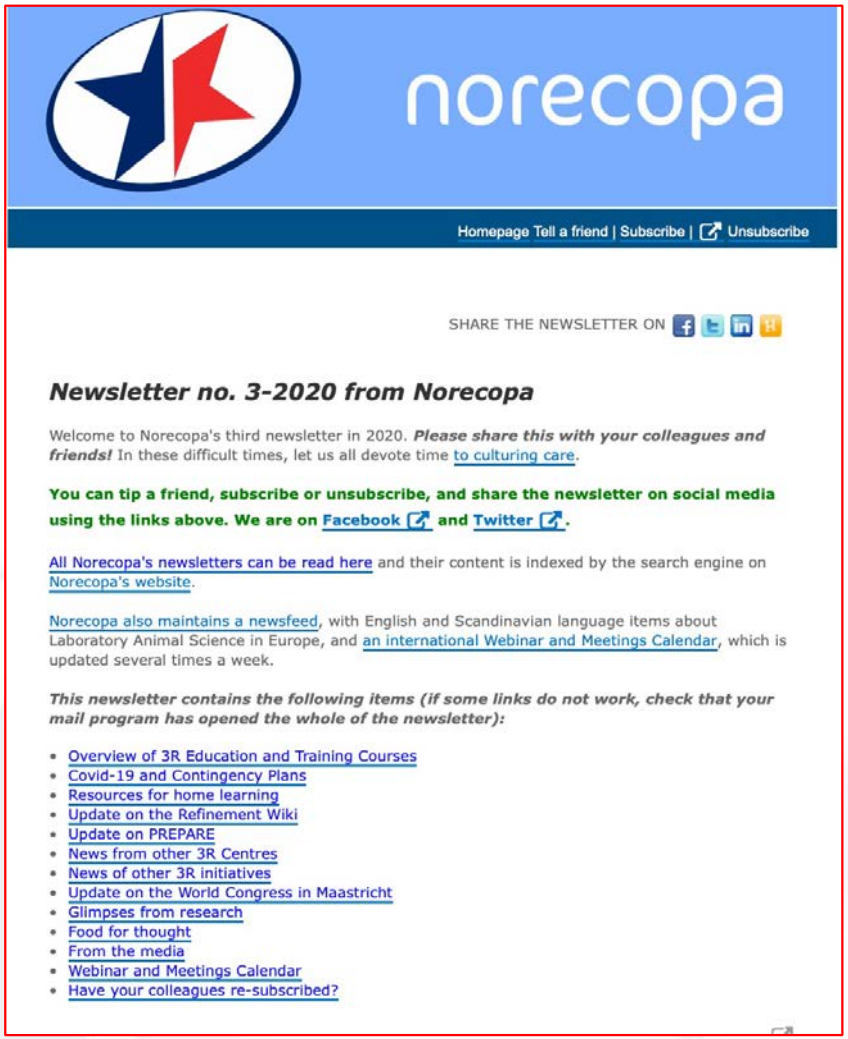
- Laboratory Animals Ltd.
- Architect Finn Rahn's Legacy
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Society for Animal Protection (Dyrebeskyttelsen Norge)
- Norwegian Animal Protection Alliance (Dyrevernalliansen)
- Novo Nordisk
- Sanofi
- Scottish Accreditation Board (SAB)
- Stiansen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

Graphics: colourbox.com



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