How to plan animal experiments:

PREPARE before you ARRIVE

norecopa.no/PREPARE

Adrian Smith, Eddie Clutton, Elliot Lilley, Kristine Hansen & Trond Brattelid

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norecopa.no

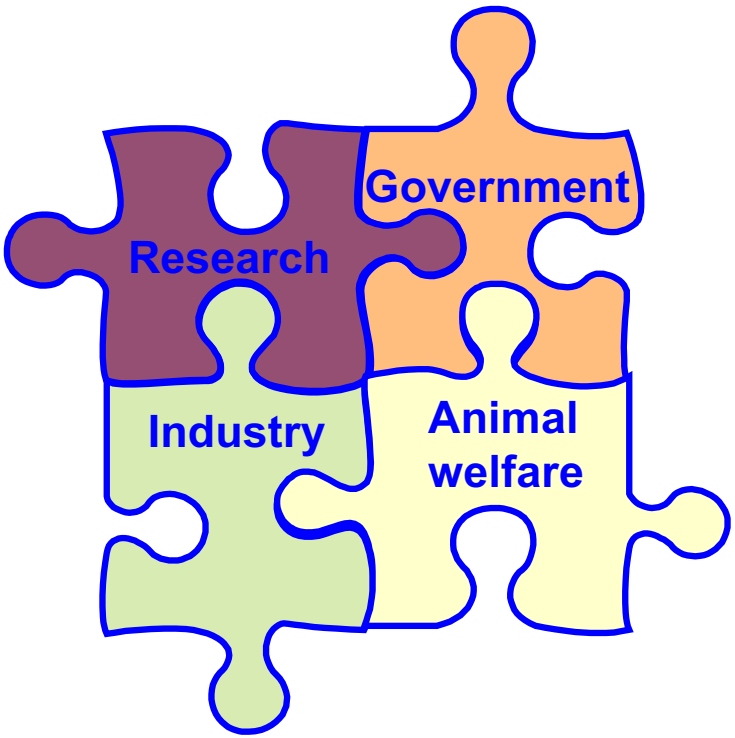
Norecopa

National Consensus Platform for the Replacement, Reduction and Refinement of Animal Experiments

European Consensus-Platform for Alternatives

ecopa.eu

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



International consensus meetings

Harmonisation of the Care and Use of:

Fish (2005)
Wildlife (2008)
Fish (2009)
Agricultural animals (2012)
Wildlife 26-27 October 2017

norecopa.no/meetings

All presentations and consensus statements are on the internet: ***a lasting resource***

Published online on 9 May 2011 Lab Anim, doi: 10.1258/la.2011.010181

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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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

Guidance on the severity classification of procedures involving fish

Report from a Working Group
convened by Norecopa

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

norecopa.no

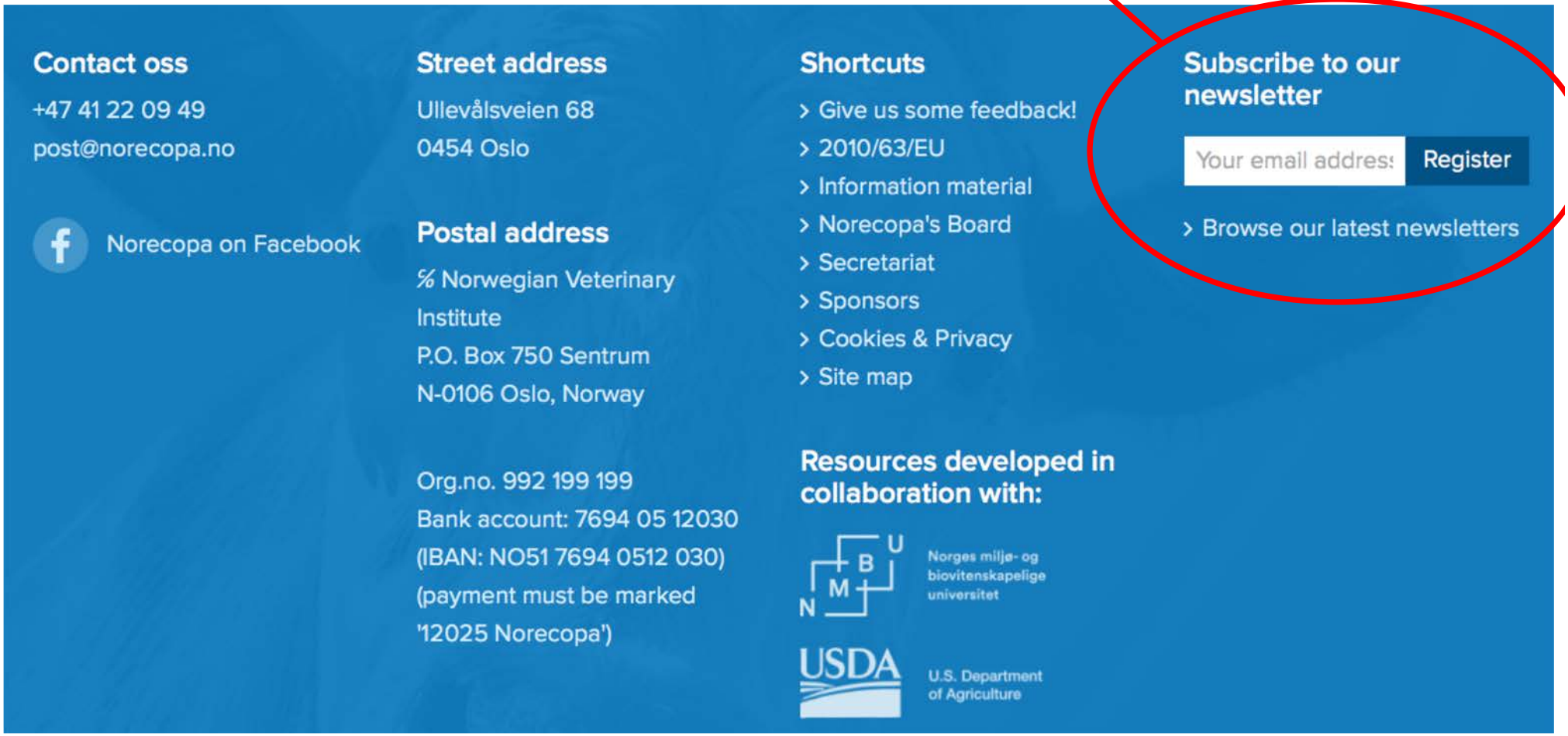
Organisations of relevance to animal research

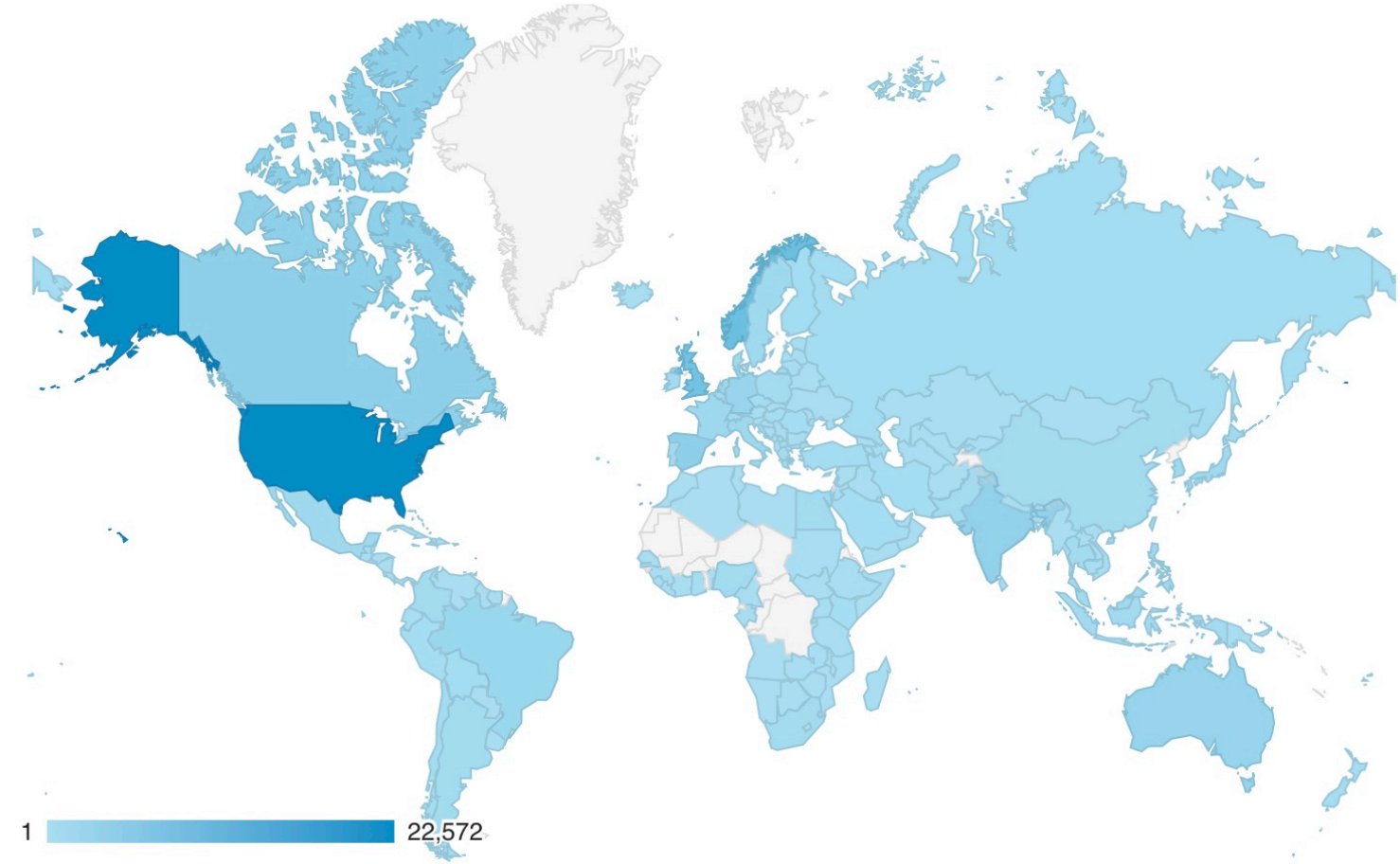
Organisations within Laboratory Animal Science

AAALAC International (Association for Assessment and Accreditation of Laboratory Animal Care International)
AALAS (American Association for Laboratory Animal Science)
ACLAM (American College of Laboratory Animal Medicine)
AniMatch (an online sharing platform for the exchange of organs and tissues)
ARSAL (Asociatia Româna pentru Stiinta Animalelor de Laborator; Romanian Laboratory Animal Science Association)
ASLAP (American Society of Laboratory Animal Practitioners)

6,000 webpages
80,000 links
22,000 unique links
<3.5% dead links

English-language newsletters





1. United States
2. Norway
3. United Kingdom
4. Spain
5. Canada
6. India
7. Australia
8. Germany
9. Brazil
10. France

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Original Article

Laboratory Animals
2018, Vol. 52(2) 135–141

DOI: 10.1177/0023677217724823
journals.sagepub.com/home/lan
SAGE

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]

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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UFAW

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

Published in the April 2018 issue of Laboratory Animals

http://journals.sagepub.com/doi/full/10.1177/0023677217724823

A brief history of reporting...

Berti & Cima 1955, quoted in Öbrink and Rehbinder

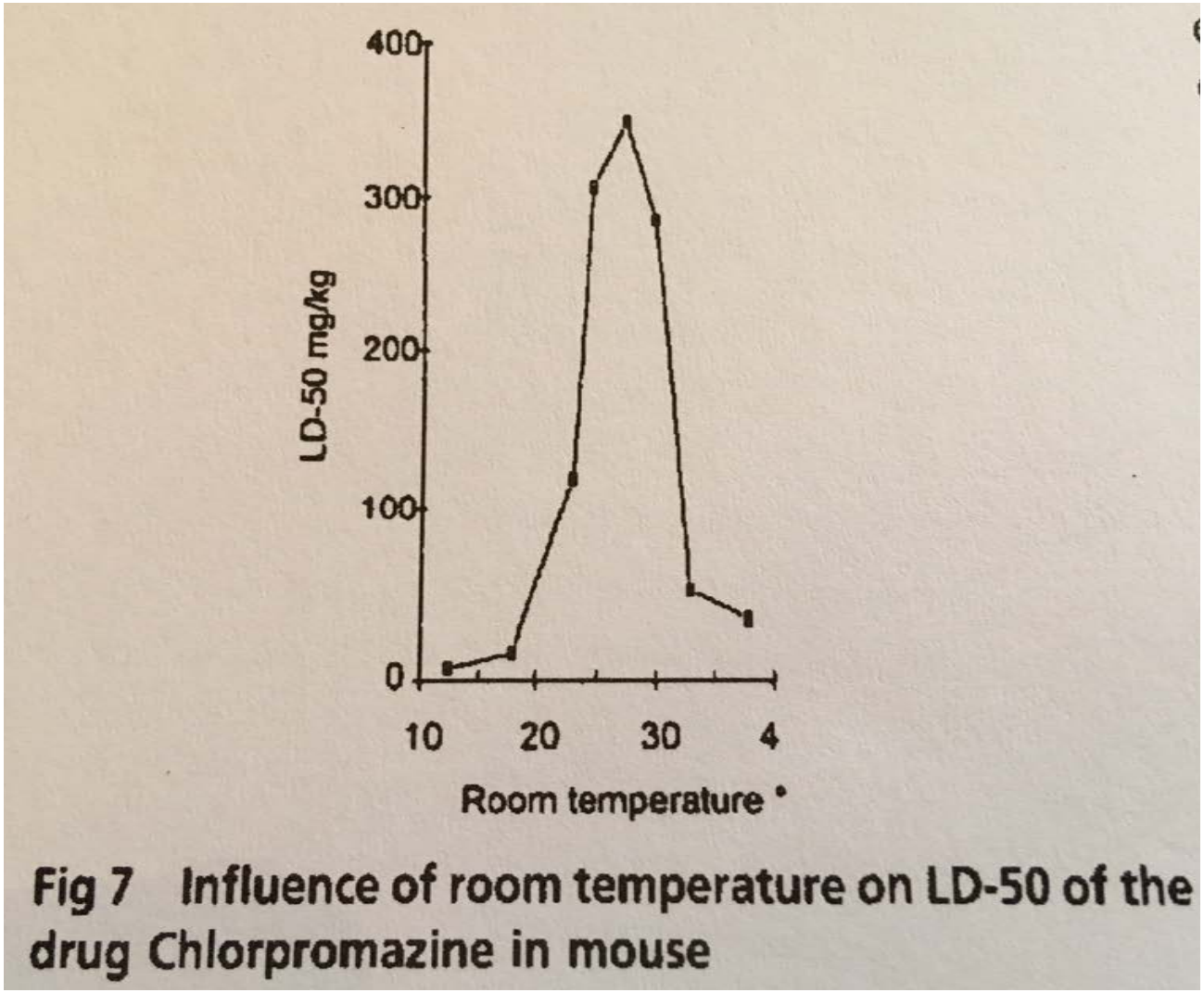

Fig 7 Influence of room temperature on LD-50 of the drug Chlorpromazine in mouse

A brief history of reporting...

Hurni 1969, quoted in Öbrink and Rehbinder

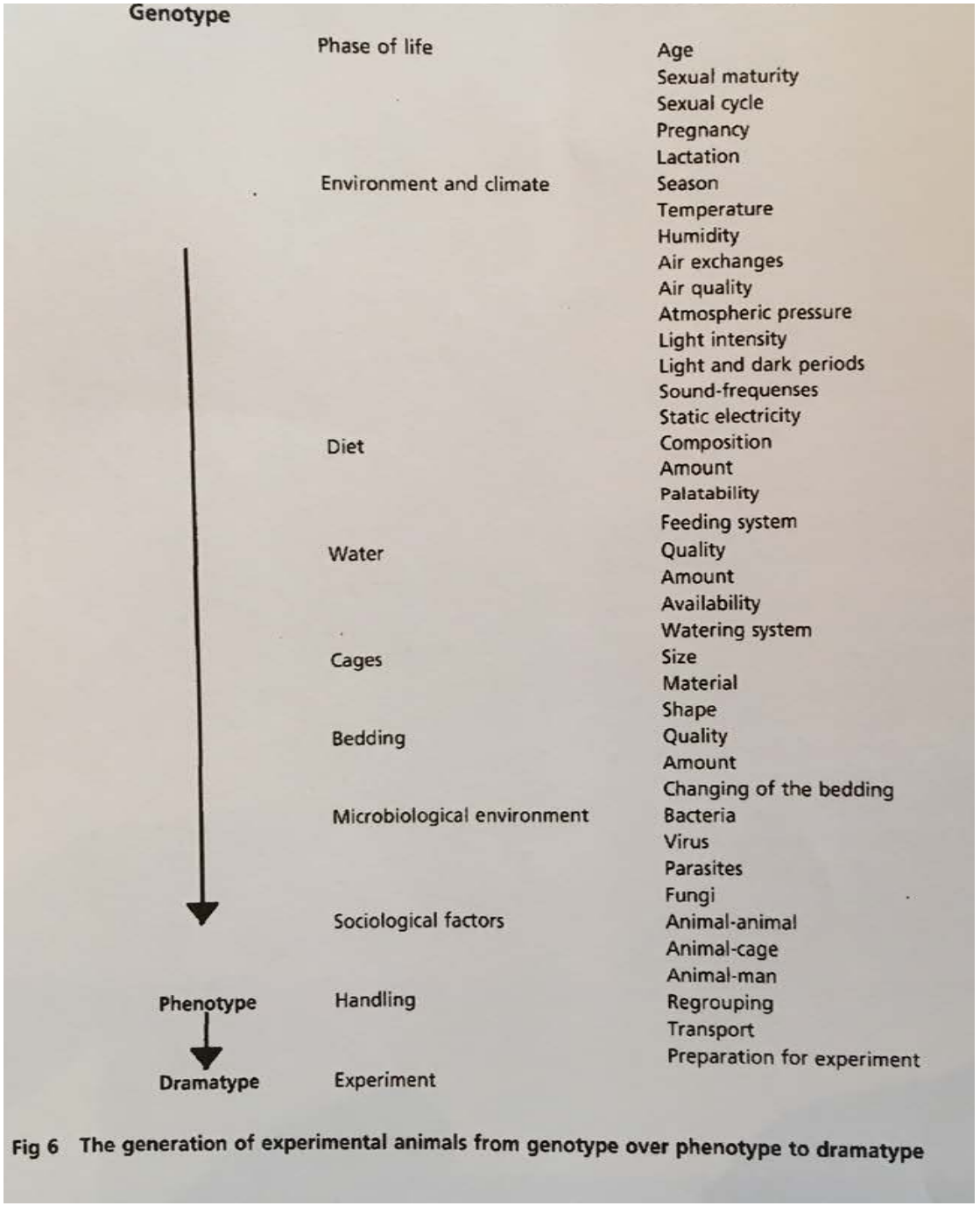

Fig 6 The generation of experimental animals from genotype over phenotype to dramatype

GV-SOLAS committee, chaired by AW Ellery (1985)

Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments

Jørgen Carstensen, Scand-LAS, one of the committee members

Cites Michael Festing's papers from 1972 and 1973 on standardised nomenclature for inbred strains and outbred stocks

'The minimum information which should be reported'

Two worked examples of approx. 150 words each

JA Smith, L Birke & D Sadler (1997)

149 scientific papers in 8 journals from 1990-1

Percentages of papers that did **NOT** mention:

sex	28%	room temperature	72%
age	52%	relative humidity	89%
weight	71%	photoperiod	72%
source	53%	no. animals/cage	73%

30% of the papers didn't mention how many animals were used!

45% of the papers where animals were killed said nothing about how the animals were killed.

Many papers «toned down» what happened to animals that died or developed problems during the experiment.

TOXLET 02240

Effect of ethanol on fatal carbon monoxide poisoning in awake rats

Masafumi Tomita[1], Toshiko Okuyama[1], Kazuaki Shimosato[1], Yoshiro Kondo[2] and Iwao Ijiri[3]

[1]Department of Legal Medicine and [2]Department of Physics, Kawasaki Medical School, Kurashiki and [3]Department of Legal Medicine, Kagawa Medical School, Miki-cho (Japan)

(Received 15 October 1988)
(Accepted 23 July 1989)

Key words: Forensic toxicology; Acute CO fatal poisoning; Ethanol; CO-Hb saturation level

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SUMMARY

The effect of ethanol on fatal carbon monoxide (CO) poisoning was investigated in mice injected intraperitoneally with ethanol. Ethanol (1.5 and 3.0 g/kg) was injected 15 min prior to exposure to gas containing 6.6% CO. The survival period was significantly lengthened with ethanol in proportion to the doses injected, although the carboxyhemoglobin (CO-Hb) saturation level in postmortem blood was almost the same in all groups. On the other hand, the CO-Hb level in the blood of mice injected with ethanol was

MATERIALS AND METHODS

Twenty-one male Sprague-Dawley rats weighing 180–210 g at the beginning of the study were randomly divided into two groups of 15 comprising a DAS-treated group and a control group. The animals were housed in wire-mesh cages and had free access to food pellets and tap water. Temperature and light–dark cycle were permanently controlled. A suspension of DAS in corn oil was administered every morning by oe-

nature International weekly journal of science

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News & Comment > News > 2017 > May > Article

NATURE | NEWS

Swiss survey highlights potential flaws in animal studies

Poor experimental design and statistical analysis could contribute to widespread problems in reproducing preclinical animal experiments.

Ramin Skibba

20 December 2016

Pain management in pigs undergoing experimental surgery; a literature review (2012–4) FREE

A. G. Bradbury, M. Eddleston, R. E. Clutton

Br J Anaesth (2016) 116 (1): 37-45. **DOI:** https://doi.org/10.1093/bja/aev301

Published: 03 October 2015

with analgesic properties, but only 87/233 (37%) described postoperative analgesia. No article provided justification for the analgesic chosen, despite the lack of guidelines for analgesia in porcine surgical models and the lack of formal studies on this subject. Postoperative pain assessment was reported in only 23/233 (10%) articles. It was found that the reporting of postoperative pain management in the studies was remarkably low, reflecting either under-reporting or under-use. Analgesic description, when given, was frequently too limited to enable reproducibility. Development of a

nature International weekly journal of science

Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audi

Archive > Volume 533 > Issue 7604 > News Feature > Article

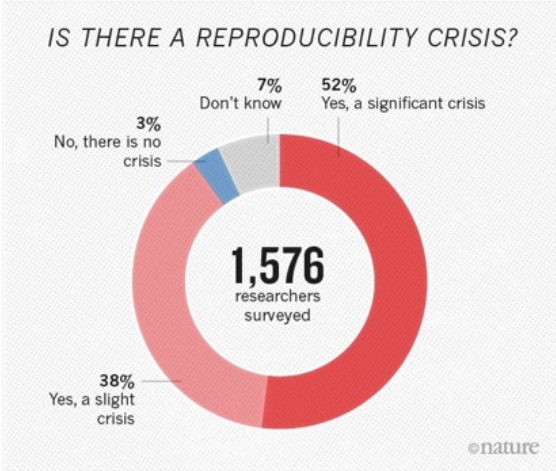
NATURE | NEWS FEATURE

1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

25 May 2016 | Corrected: 28 July 2016



More than 70% of researchers have tried and failed to reproduce another scientist's experiments, and more than half have failed to reproduce their own experiments. Those are some of the telling figures that emerged from *Nature*'s survey of 1,576 researchers who took a brief online questionnaire on reproducibility in research.

There are many guidelines for *reporting* animal studies

- Öbrink & Waller, 1996
- Jane Smith *et al.*, 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals,* 2000
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*, NC3Rs)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals

  e.g. Nature's Reporting Checklist

and more species- and situation- specific guidance is needed

Guidelines for reporting the results of experiments on fish

Trond Brattelid & Adrian J. Smith

Laboratory Animal Unit, The Norwegian School of Veterinary Science, PO Box 8146 Dep., 0033 Oslo, Norway

Summary

A detailed account of experimental design, including an accurate description of the animals used, is an essential part of good research practice. Without these details, the reader will be unable not only to form an opinion on the significance of the findings but also to repeat the experiment in another laboratory. This paper presents suggested guidelines for reporting experimental studies using fish.

Keywords Fish; experiment; study; report; refinement

Laboratory Animals, 2000

The ARRIVE guidelines have been endorsed by over 1,000 journals...

However,

Thomas Reichlin, Lucile Vogt and Hanno Würbel, 2016:

Survey sent to all scientists in Switzerland performing animal experiments
Of the 302 who returned fully completed questionnaires:

51% of the scientists publishing in journals which have endorsed the ARRIVE guidelines, had not even heard of them...

So why do we need PREPARE when we have ARRIVE?

The ARRIVE guidelines claim that they 'provide a logical checklist with all the things that need to be considered when designing an experiment' *

In our experience when planning animal research, **a number of additional points need to be addressed at the planning stage**.

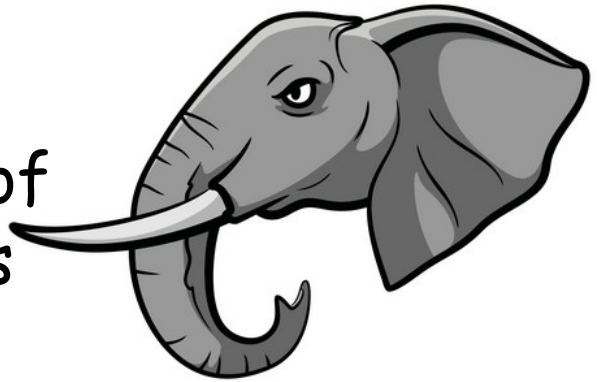
These items not only improve study quality and animal welfare (and therefore reproducibility), but also the safety of humans and animals affected directly or indirectly by the work.

*http://www.nc3rs.org.uk/sites/default/files/documents/Guidelines/ARRIVE%20Guidelines%20Speaker%20Notes.pdf

The elephants in the room…

reddit.com

…the largest of them all is the lack of focus on planning animal experiments



Rory Wilson, Swansea University

ohiobirdsanctuary.com

The stress of capture and restraint!

”Simple” identification methods?
Do they affect the animal?

Photo: T. Poppe, NMBU

Tags can collect seaweed and shellfish, which dramatically reduce the fish’s ability to swim efficiently

http://blogs.discovermagazine.com/notrocketscience/2011/01/12/flipper-bands-impair-penguin-survival-and-breeding-success/#.VLU6_8Y7_wo

Flipper bands can reduce the penguin’s ability to swim efficiently

Photo: colourbox.com

Many animals can be identified by non-invasive biometric methods, like photographing the pattern of stripes on the zebra

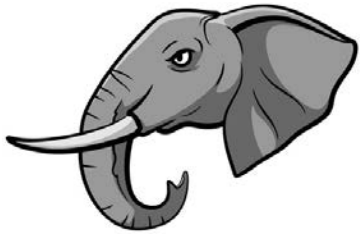


photo: NMBU

Identify and eliminate causes of **contingent suffering**

(not just direct suffering caused by the procedure)
e.g. fear, boredom, discomfort

which may caused by

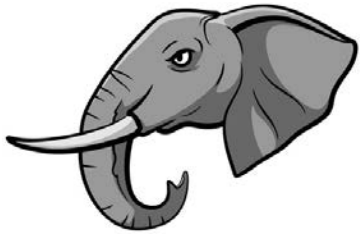
e.g. transport, housing, husbandry, social hierarchy

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

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

photo: colourbox.com

INDEPENDENT



Scores of scientific studies based on mice thrown into doubt because they were picked up by the tail

Mice picked up by the tail – standard practice in labs – are stressed and anxious so don't act naturally in some experiments, new study finds

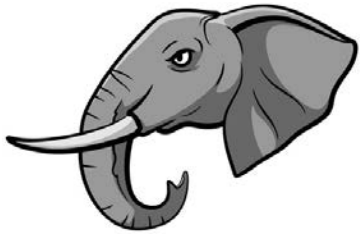
Ian Johnston Science Correspondent | @montaukian | Tuesday 21 March 2017 10:58 GMT | 3 comments

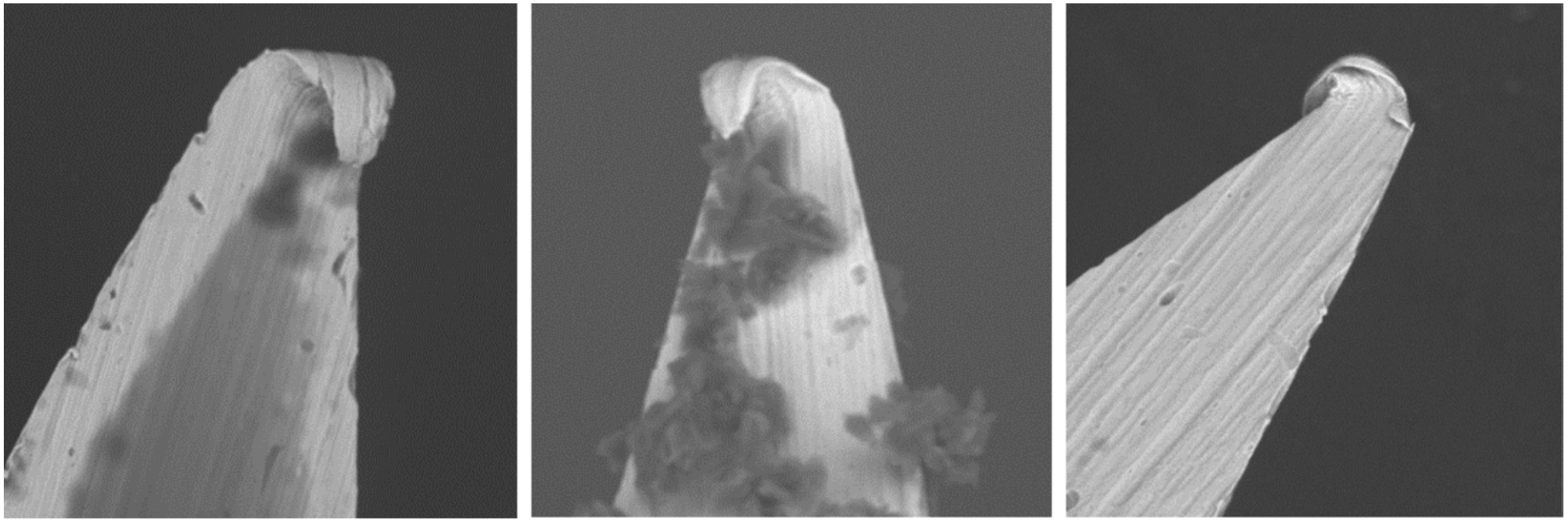
"Simple" techniques?

Photo: NMBU

- *Are you sure that your injection ends up in the same place each time?*
- *Are the injections painful?*
- *Are they feasible? e.g. intramuscular injections in small animals*

Disposable needles are designed to be used only once!

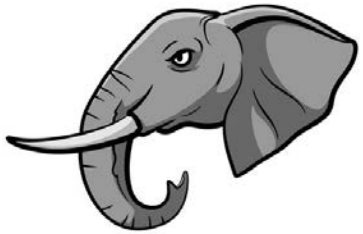




Lucy Whitfield, RVC and Sally Robinson, AstraZeneca
Photo: AstraZeneca

https://www.nc3rs.org.uk/news/re-use-needles-indicator-culture-care

Consider the effects on the animal of the treatment

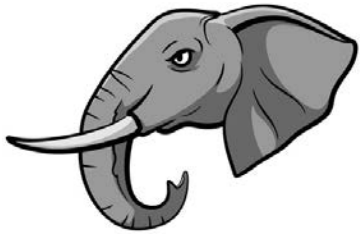


'the drug was administered by gavage in 3 daily doses'

photo: NMBU

"How much ethanol do I need to give a mouse to be the equivalent of 2 glasses of red wine in the evening?"
Carefully consider the dose, use of allometric scaling, and the method of administration

‘Simple’ blood sampling techniques?



At the doctor:

I think I’ll take a blood sample from you tomorrow.

I take my blood samples by sticking a knife into your neck, without anaesthesia.

But don’t worry, I’ll inject 2 litres of liquid into your abdomen first so you don’t die from fluid loss.

medipoint.com/html/for_use_on_mice.html

The best blood sampling techniques are those where you can (1) see the blood vessel, (2) control the amount of blood you remove, (3) stop the bleeding easily and (4) not damage surrounding tissue.

norecopa.no/3S

Carol M. Newton (1925-2014)

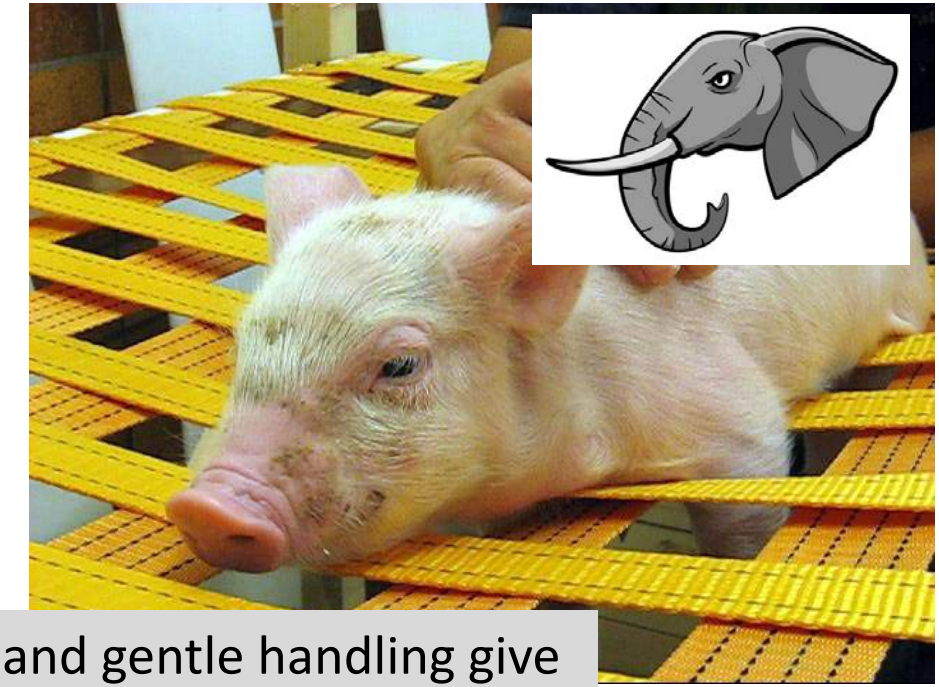
National Library of Medicine

The three S's

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

Rowsell HC (1977): The Ethics of Biomedical Experimentation, in *The Future of Animals, Cells, Models, and Systems in Research, Development, Education, and Testing* pp. 267-281, National Academy of Sciences, Washington, D.C., ISBN 0-309-02603-2.

Smith AJ & Hawkins P (2016): Good Science, Good Sense and Good Sensibilities: The Three Ss of Carol Newton. *Animals*, 6(11), 70, doi:10.3390/ani6110070



Good housing conditions and gentle handling give good animal welfare and better science

photos: NMBU

photo: NMBU

"Happy animals make good science", Trevor Poole

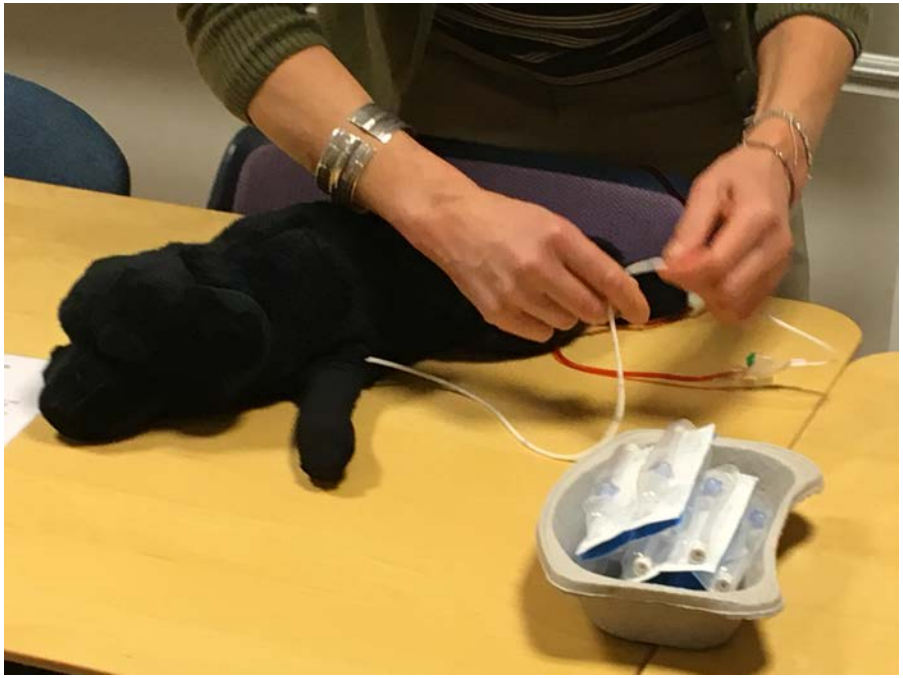
journals.sagepub.com/doi/pdf/10.1258/002367797780600198

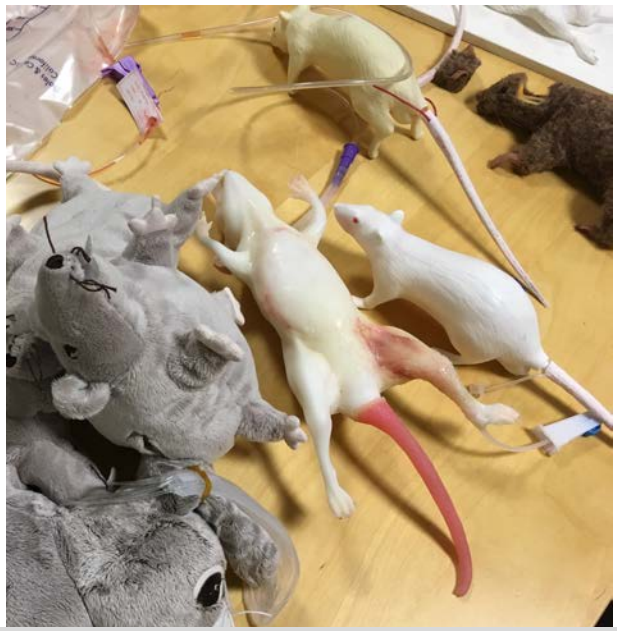
The use of animals in education and training

frame.org.uk

’We may need the animals, as it were, on the night; but the machines will do very well at rehearsals’

norecopa.no/education-training/homemade-educational-materials





Workshop 11 April in Oslo

norecopa.no/education-training/homemade-educational-materials

How to construct a literature search

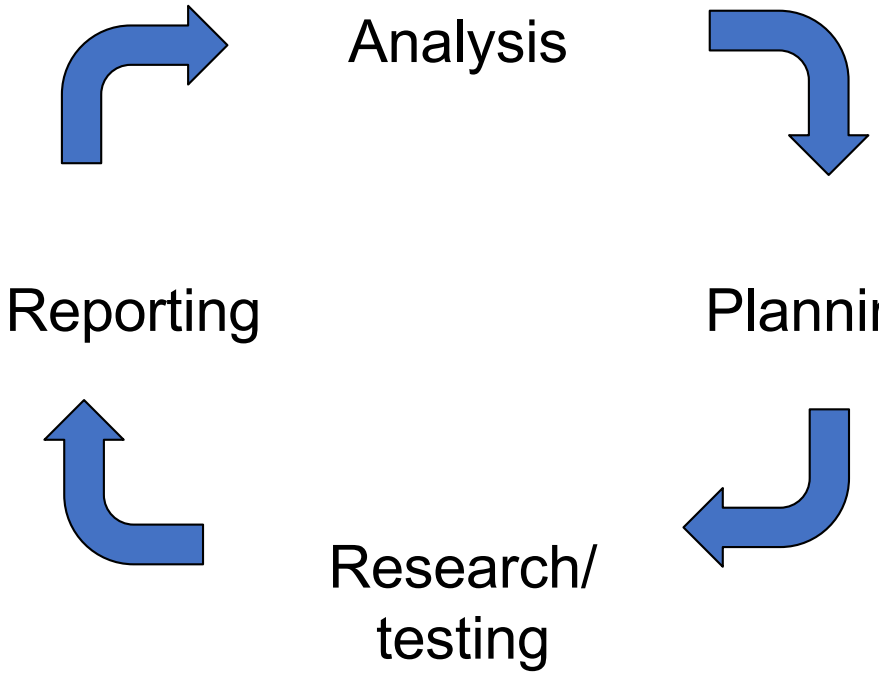
Alice Tillema, Medical Library, Nijmegen

http://libguides.ru.nl/norecopa

Radboud University

Radboudumc
university medical center

Reporting is only one part of quality-controlled science...

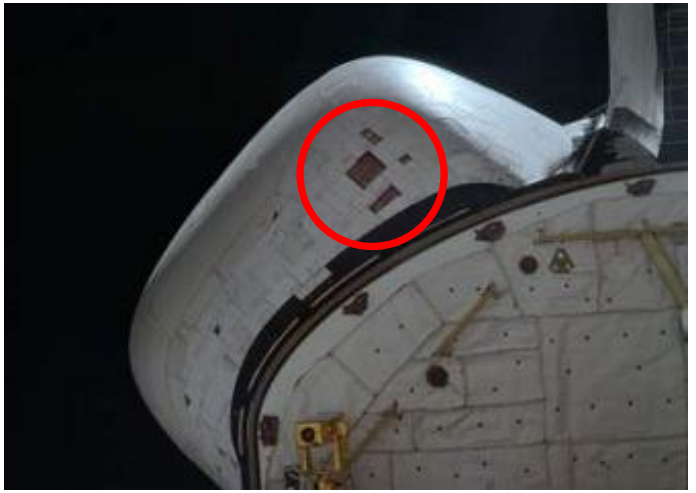


Space Shuttle, NASA

Identify and ensure the quality of (at least) the **critical points** in the experiment: critical for animal welfare and scientific value

1) Columbia

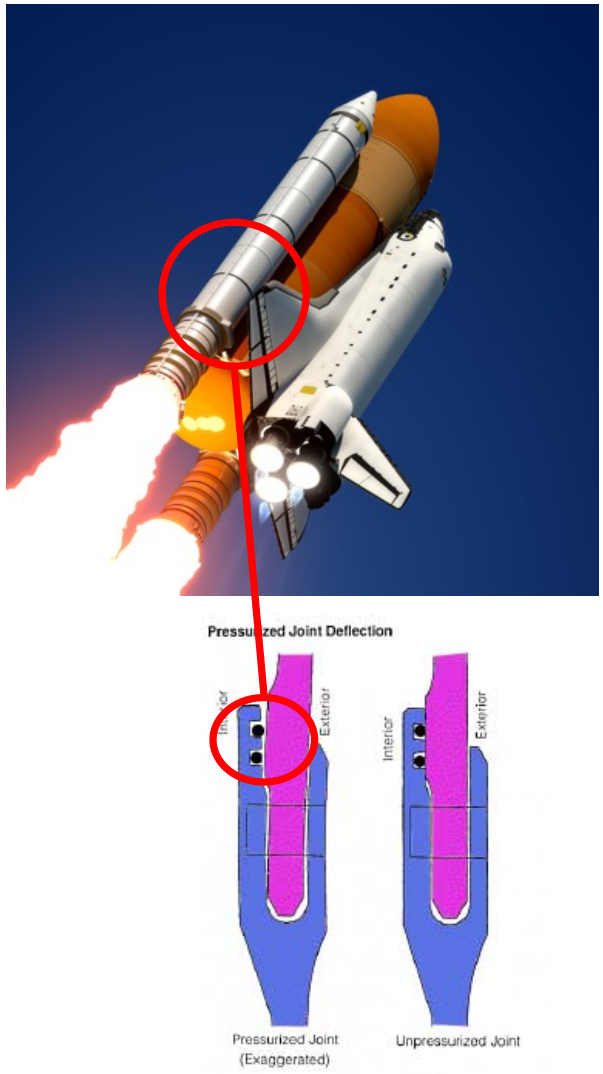
Photo: gettyimages.no



First shuttle flight, Columbia, in April 1981
Photo: nasaspaceflight.com

Columbia burnt up in 2003, killing all 7 crew members
Photo: cbsnews.com

2) Challenger



www.mahal.org

Challenger disintegrated in January 1986 killing all 7 crew members

Photo: no.wikipedia.org

Details are important!!

EXPLODING RATS ROCK LABORATORY

A UNIVERSITY research lab at a top hospital has been rocked by ... exploding RATS.

The explosion, at Glasgow University's building at Yorkhill Hospital, blew up a fridge.

It smashed four windows and damaged fittings and equipment.

And two women scientists – who normally work in the lab – escaped because they were in the room next door.

By MARK McGIVERN

Glasgow University has launched an inquiry into how the blast at its "Animal House" took place.

A spokesman said the blast had been caused after 15 rats had been soaked in anaesthetic ether to kill them humanely.

INJURED

But, while they were stored in a special fridge, a thermostat gave off a tiny spark, which ignited the volatile ether. The spokesman admitted that the two researchers – a genetics postgraduate and a researcher – could have been seriously injured.

"If people had been in the room there could have been serious consequences," he added.

"We have suspended these kind of experiments until our inquiry is complete."

Good planning is critical!

- Complex machines (animals) create *known or unknown unknowns* (interactions between parts that are impossible to foresee until you “fly”)

- Possible design weaknesses must be discussed (damage from foam, and susceptibility to low temperature, *which the engineers knew about!)*

- Avoid “pressure to launch” (political, media). = Publish or perish.

- Don’t make bad management decisions (pushing the safety envelope):
  “We’ve got away with it before”
  = ”We’ve managed to publish the experiments before”

- Often a combination of many factors, each of which may be harmless until they occur simultaneously
  Don’t ignore “insignificant” issues!
  Pay Attention to Detail

Reporting guidelines like ARRIVE describe the experiment. Guidelines like PREPARE are used to plan the experiment (choose the «ingredients» and «baking time»)

marksandspencer.com

https://www.bls.gov/ooh/images/3077.jpg

PREPARE

ARRIVE

https://www.dreamstime.com

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 highlighted in ARRIVE

PREPARE

norecopa

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

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PREPARE[1] consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE[2].
PREPARE covers the three broad areas which determine the quality of the preparation for animal studies:

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

The topics will not always be addressed in the order in which they are presented here, and some topics overlap. The PREPARE checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on the management of animal facilities, since in-house experiments are dependent upon their quality. The full version of the guidelines is available on the Norecopa website, with links to global resources, at **https://norecopa.no/PREPARE**.
The PREPARE guidelines are a dynamic set which will evolve as more species- and situation-specific guidelines are produced, and as best practice within Laboratory Animal Science progresses.

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*

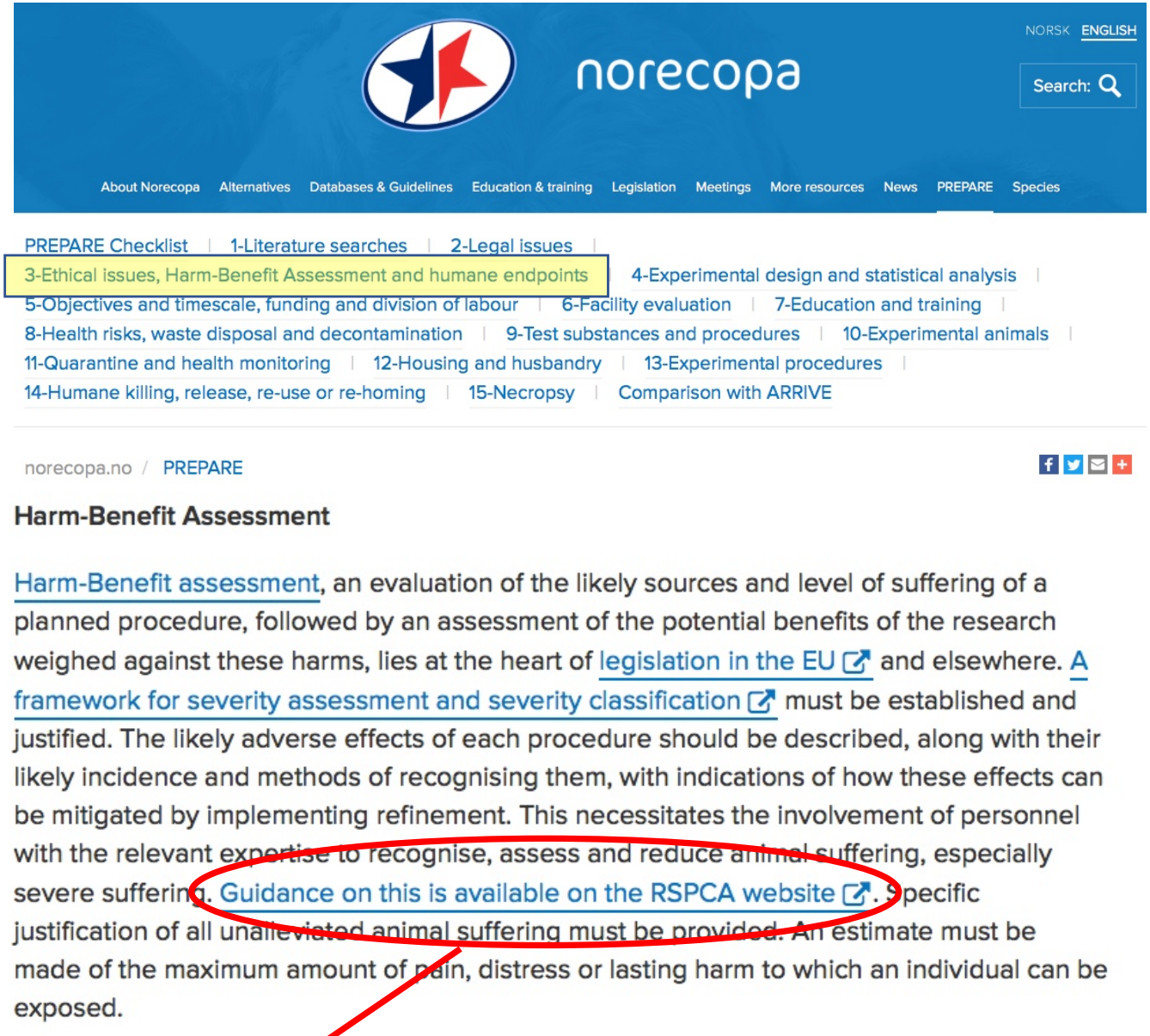
https://norecopa.no/prepare/prepare-checklist

Two pages, translated into 13 languages so far

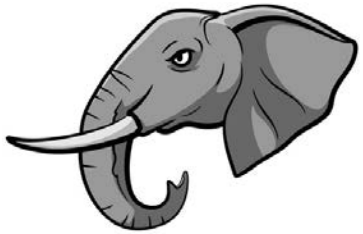
In addition to the checklist, much more information is available on:

norecopa.no/PREPARE

norecopa.no/PREPARE



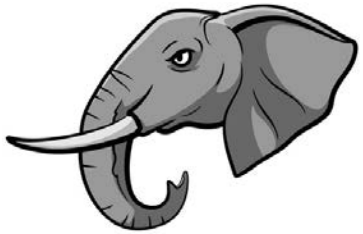
Links to quality guidelines worldwide on e.g. blood sampling, injection volumes, housing and husbandry, analgesia, humane endpoints, experimental design



Health risks: there are many people to think about

People engaged in animal capture, transport and breeding
Animal carers and technologists
Security personnel
Administrative personnel with occasional access to the animal facility
Students
Sales representatives and those delivering supplies or equipment
Craftsmen carrying out facility repairs
Other visitors, including inspectors, journalists and students
Cleaning staff
Waste disposal personnel
Those who re-home research animals

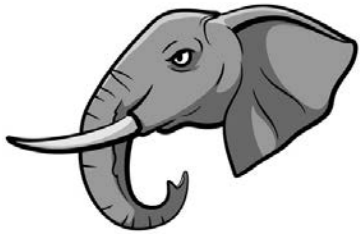
Many of these people often possess a number of features which increase their health risks



They may:

- enter the facility **outside normal working hours**, when advice on hazards may not be readily available
- **not understand** messages left in the facility, especially if scientific jargon is used. Special consideration should be paid to employees with other native languages.
- **have little knowledge** of animal research, scientific method and the need for controlled experiments
- **have no intrinsic concern** of potential health hazards unless these are pointed out to them. Ironically, the cleaner and tidier an animal facility appears to be, the less likely they are to be fearful of such hazards.
- **have not been health-screened** before entering the facility. Those predisposed for allergy or asthma are particularly at risk when working with animals.
- **be planning a family**. Early embryonic development and spermatogenesis are known to be at risk upon exposure to ionising radiation and chemicals, including volatile anaesthetics.

Are we prepared for equipment failure?



Anything that can go wrong, will go wrong (Murphy's Law)

Photo: NMBU

Are the animals ready for the experiment?

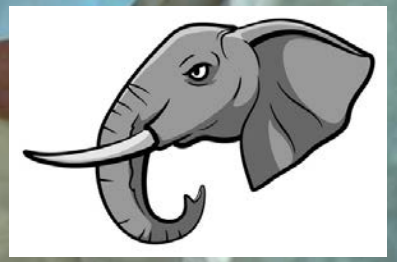
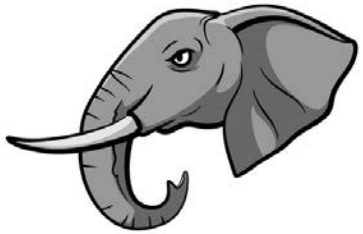


Photo: NMBU

norecopa.no/farm-animals

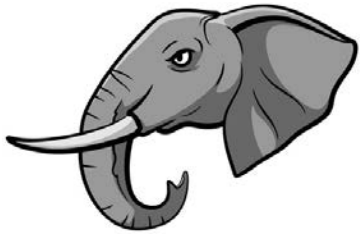


We strongly recommend the PREPARE checklist and its associated webpages with more detailed recommendations. Some, but by no means all, of the challenges include:

- health status, acquisition, transport and acclimation to new buildings
- quarantine and adaptation to new feeding regimes
- establishment of new social groups
- provision of sufficient space for exercise, sampling, anaesthesia and necropsy
- ventilation issues
- the differences in practices between traditional farm work and those used in controlled studies in a laboratory environment
- health, safety and general hygiene
- waste disposal (e.g. contaminated carcases)
- containment of pathogens
- identification of sufficient numbers of staff who are familiar with, and competent to handle, farm animal species

Many of these issues are exacerbated by the sheer size of the animals.

A simple but effective Master Plan



Contract between the animal facility and the research group

The division of **labour**, **responsibilities** and **costs** between the two parties, with the aim of clarifying all stages of the experiment and ensuring that all necessary parameters 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			

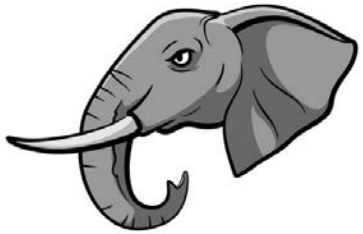
Quality assurance and a culture of care at all levels of the animal facility

- SOPs describing good techniques, carried out by competent operators
- Checklist ("contract") between researcher and the facility
- The AAALAC Program Description template* as an overall performance checklist
  - Institutional policies on animal care and use
  - Animal environment, housing and management
  - Veterinary care
  - Physical plant
- A Master Plan as a weekly checklist for the whole facility during the year

+ the necessary literature/resources/finances/support to implement these

*https://www.aaalac.org/programdesc/index.cfm

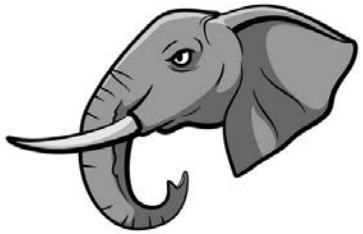
Think ”3R-Alternatives” at all stages



- Breeding
- Transport
- Acclimation
- Procedures, e.g. choice of
  - dose
  - method of administration
  - methods of data collection (blood sampling, body temperature, heart rate, blood pressure etc.)
- Pilot studies

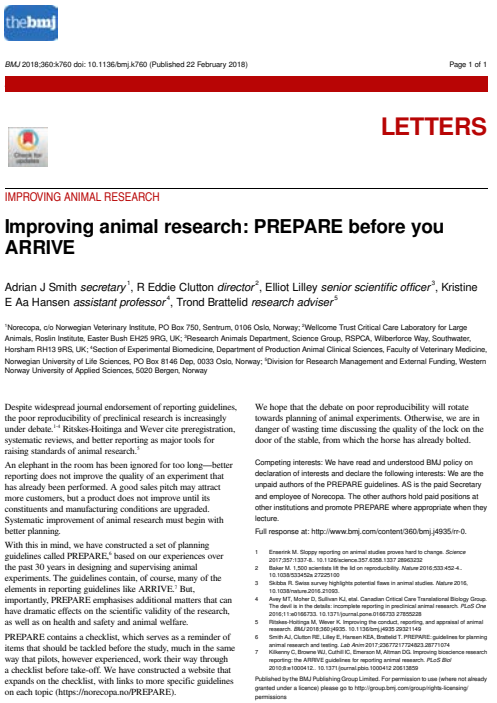
Consult the technicians from Day 1:

- 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



www.pixcove.com

Are we wasting time discussing the quality of the lock on the door of the stable from which the horse has already bolted?



thebmj

BMJ 2018;360:k760 doi: 10.1136/bmj.k760 (Published 22 February 2018)

LETTERS

IMPROVING ANIMAL RESEARCH

Improving animal research: PREPARE before you ARRIVE

Adrian J Smith *secretary*[1], R Eddie Clutton *director*[2], Elliot Lilley *senior scientific officer*[3], Kristine E Aa Hansen *assistant professor*[4], Trond Brattelid *research adviser*[5]

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Despite widespread journal endorsement of reporting guidelines, the poor reproducibility of preclinical research is increasingly under debate.[1-4] Ritskes-Hoitinga and Wever cite preregistration, systematic reviews, and better reporting as major tools for raising standards of animal research.[1]

An elephant in the room has been ignored for too long—better reporting does not improve the quality of an experiment that has already been performed. A good sales pitch may attract more customers, but a product does not improve until its constituents and manufacturing conditions are upgraded. Systematic improvement of animal research must begin with better planning.

With this in mind, we have constructed a set of planning guidelines called PREPARE,[4] based on our experiences over the past 30 years in designing and supervising animal experiments. The guidelines contain, of course, many of the elements in reporting guidelines like ARRIVE.[5] But, importantly, PREPARE emphasises additional matters that can have dramatic effects on the scientific validity of the research, as well as on health and safety and animal welfare.

PREPARE contains a checklist, which serves as a reminder of items that should be tackled before the study, much in the same way that pilots, however experienced, work their way through a checklist before take-off. We have constructed a website that expands on the checklist, with links to more specific guidelines on each topic (https://norecopa.no/PREPARE).

We hope that the debate on poor reproducibility will rotate towards planning of animal experiments. Otherwise, we are in danger of wasting time discussing the quality of the lock on the door of the stable, from which the horse has already bolted.

Competing interests: We have read and understood BMJ policy on declaration of interests and declare the following interests: We are the unpaid authors of the PREPARE guidelines. AS is the paid Secretary and employee of Norecopa. The other authors hold paid positions at other institutions and promote PREPARE where appropriate when they lecture.

Full response at: http://www.bmj.com/content/360/bmj.j4935/rr-0.

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bmj.com/content/bmj/360/bmj.k760.full.pdf

Even experienced pilots use checklists as an aide memoire...

wikipedia.org

Søren Kirkegaard (1813-1855)

It is perfectly true, as philosophers say, that life must be understood backwards. Reporting!

But they forget the other proposition, that it must be lived forwards. PREPARE!

Thanks to our main sponsors:

- Standing Committee on Business Affairs, Norwegian Parliament
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- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture, Animal Welfare Information Center (AWIC)

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