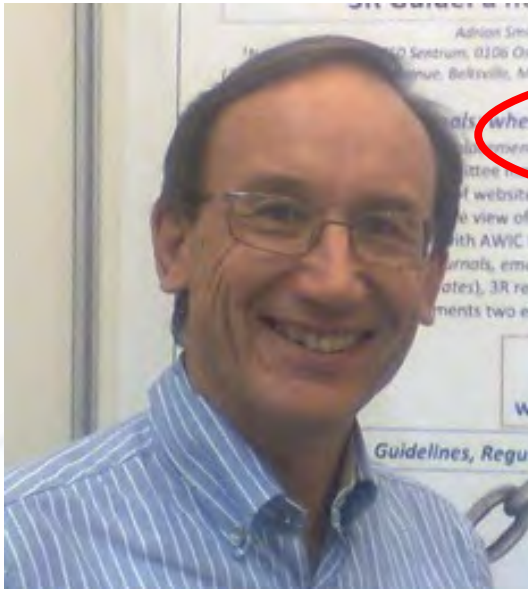


PREPARE before you ARRIVE:
Good reporting relies on good planning



norecopa.no/ESLAV2019

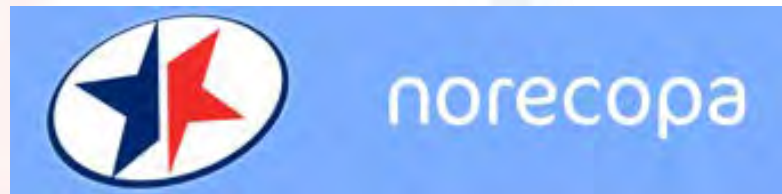
Adrian Smith
adrian.smith@norecopa.no



<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>

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norecopa.no



Organisations of relevance to animal research

Organisations within

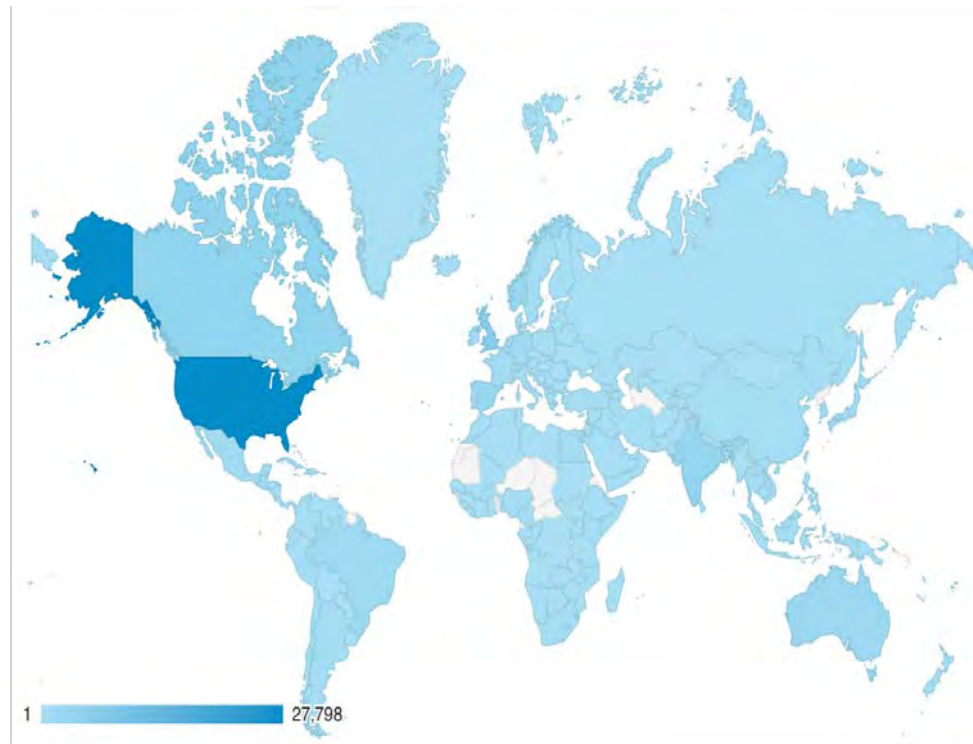
Video presentation of contents:
norecopa.no/info

8,400 webpages
80,000 links

[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)
[ARSAI](#) (Asociația Română pentru Știința Animalelor de Laborator: Romanian Laboratory Animal

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

Averaging about 250,000 page views a year

International consensus meetings

Harmonisation of the Care and Use of:

Fish (2005)

Wildlife (2008)

Fish (2009)

Agricultural animals (2012)

Wildlife (2017)

<https://norecopa.no/meetings>

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





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

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Meetings calendar

([Links to a selection of past meetings can be accessed here](#))

- > [ESLAV/ECLAM Summer School: Experimental and Surgical Techniques, Design and Conduct of Research Programmes and Animal Experiments](#), Stockholm, 24-27 June 2019
- > [Workshop on Surgical Techniques in the Laboratory Mouse](#), Paris, 24-27 June 2019
- > [13th TALAS International Conference](#), Bangkok, 25-30 June 2019
- > [24th Interdisciplinary Toxicology Conference \(TOXCON 2019\)](#), Vyhne, 26-29 June 2019
- > [Therioepistemology – the Study of How Knowledge is Gained from Animal Research](#), Seminar (1 hour), Stockholm, 28 June 2019
- > [Advancing animal welfare science: How do we get there? - Who is it good for?](#) (UFAW International Symposium), Bruges, 3-4 July 2019
- > [Continuing Education Symposium: The Liver](#), Cambridge, 9-11 July 2019
- > [KALAS International Symposium](#), Jeju, 17-20 July 2019
- > [Course in Advanced In Vitro Models](#), Utrecht, 15-19 July 2019



Scientists are becoming increasingly concerned about the validity of animal experiments

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

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

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

selection criteria. Most articles (193/233, 83%) described use of drugs 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 | Audio

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: 26 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.

How do they do it?



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

Aviation and Animal Research: Human Factors



A Pilot's Perspective
By Jake Hannabuss

Accident Rate for commercial flights is
one fatal accident per 16 million flights

Tools – Crew Briefing

- Division of **Responsibilities**
- Planned **Sequence of Events**, including **deviations from normal procedures**
- The **Routine Factors** to be considered
- Actions in the event of an **emergency**
- **Special considerations**, weather, terrain, abnormalities
- Pre take-off and pre-landing **briefings**

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

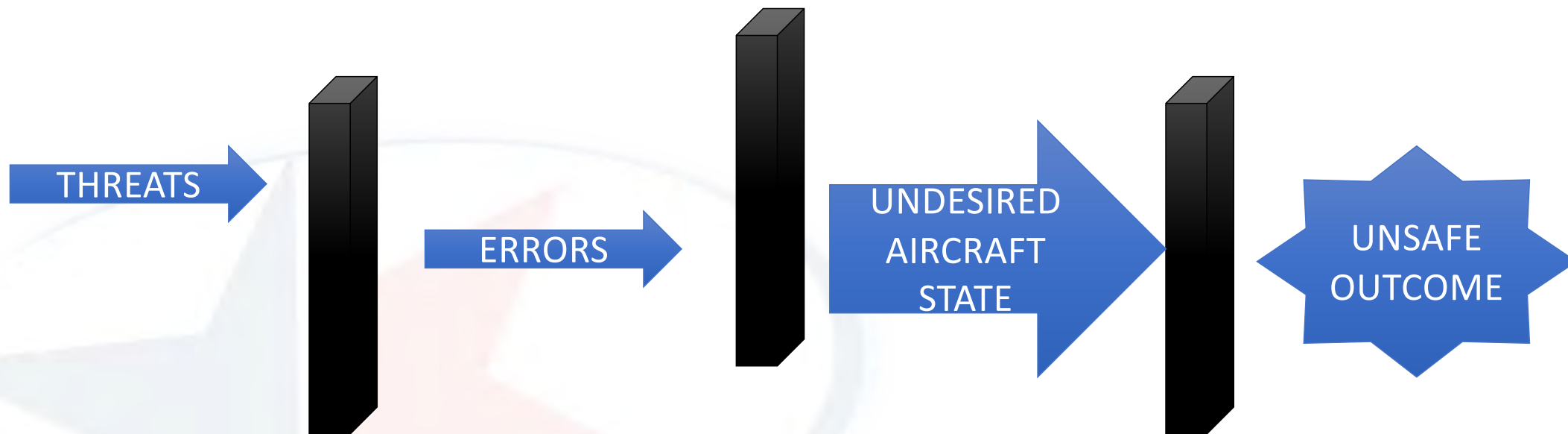
10-15 checklists on short European flights



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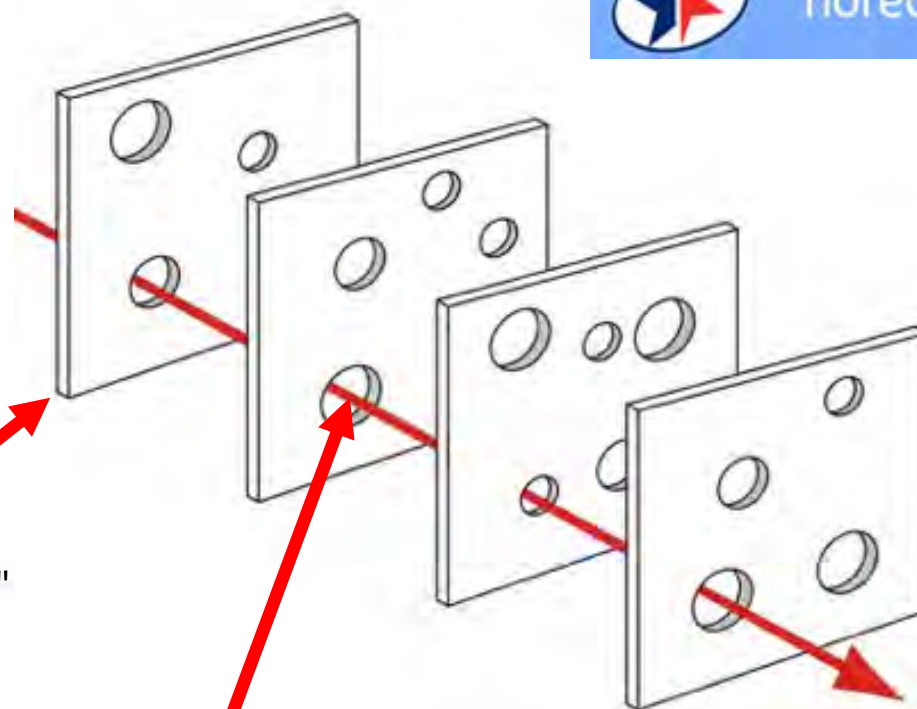
- Threat and Error Management (TEM)
- Identifies a ***chain***, which precedes all ***unsafe outcomes***:



<https://airfactsjournal.com/2012/10/threat-and-error-management-a-primer>



eaugallecheese.com/Swiss-Cheese



"Layer of defence"
or redundancy

Weakness / hazard

Loss

wikipedia.org/wiki/Swiss_cheese_model

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How do we do it...?

Some examples...

Literature searching is so much more than Systematic Reviews...



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norecopa.no/more-resources/literature-searches-and-systematic-reviews

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Identification and elimination of contingent suffering



animalcaresystems.com

(not just the direct suffering caused by the procedure)

Fear, boredom and discomfort

Caused by, for example:

Transport, or changes in housing, husbandry and social groups

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

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



photo: colourbox.com

Stress caused by capture and handling



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

Stress caused by capture and handling



<https://norecopa.no/scruff>

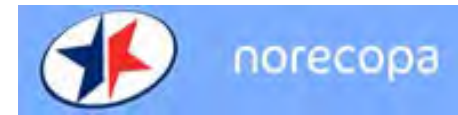
Artefacts caused by poor administration techniques



Photo: NMBU

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

'Simple' blood sampling techniques?



medipoint.com/html/for_use_on_mice.html



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 and
- ✓ not damage the surrounding tissue

Carol M. Newton (1925-2014)



National Library of Medicine

The three S's

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

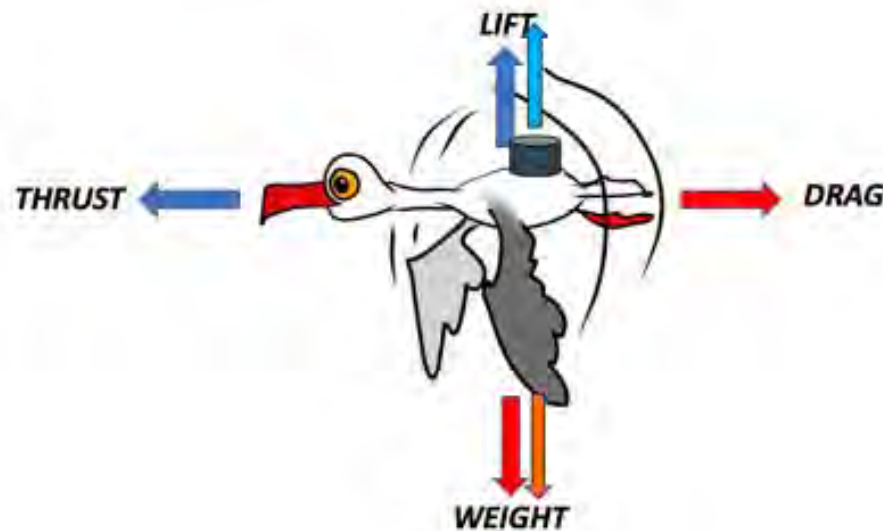
[*norecopa.no/3S*](http://norecopa.no/3S)

Carol M Newton, quoted in 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.

Harmonisation of the Care and Use of Wild and Domestic Mammals and Birds in Field Research
Gardermoen, 26 - 27 October 2017

Primary effects

The increased lift balances the extra force from the tag weight



From Rory Wilson: norecopa.no/media/8018/rory-wilson.pdf

Drag occurs in water as well as in the air...



From Rory Wilson: norecopa.no/media/8018/rory-wilson.pdf

Too late to read the checklists when you have arrived!

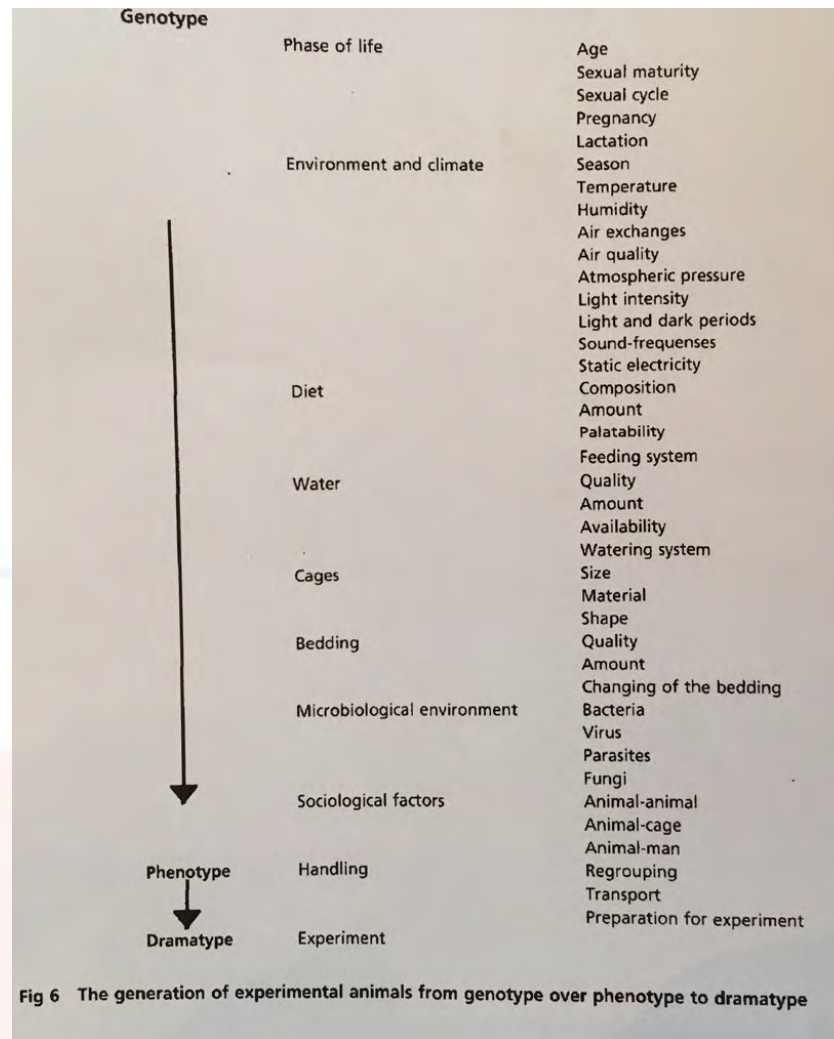


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colourbox.com

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Hurni 1969



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There are many guidelines for *reporting* animal studies

- Öbrink & Waller, 1996
- Reporting animal use in scientific papers (Jane Smith *et al.*), 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals*, 2000
- Guidelines for reporting the results of experiments on fish (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

The ARRIVE Guidelines



	ITEM	RECOMMENDATION
Title	1	Provide an accurate and concise description of the content of the article as possible.
Abstract	2	Provide an accurate summary of the background, research objectives, including details of the species or strain of animal used, key methods, principal findings and conclusions of the study.
INTRODUCTION		
Background	3	a. Include sufficient scientific background (including relevant references to previous work) to understand the motivation and context for the study, and explain the experimental approach and rationale. b. Explain how and why the animal species and model being used can address the scientific objectives and, where appropriate, the study's relevance to human biology.
Objectives	4	Clearly describe the primary and any secondary objectives of the study, or specific hypotheses being tested.
METHODS		
Ethical statement	5	Indicate the nature of the ethical review permissions, relevant licences (e.g. Animal (Scientific Procedures) Act 1986), and national or institutional guidelines for the care and use of animals, that cover the research.
Study design	6	For each experiment, give brief details of the study design including: a. The number of experimental and control groups. b. Any steps taken to minimise the effects of subjective bias when allocating animals to treatment (e.g. randomisation procedure) and when assessing results (e.g. if done, describe who was blinded and when). c. The experimental unit (e.g. a single animal, group or cage of animals). A time-line diagram or flow chart can be useful to illustrate how complex study designs were carried out.
Experimental procedures	7	For each experiment and each experimental group, including controls, provide precise details of all procedures carried out. For example: a. How (e.g. drug formulation and dose, site and route of administration, anaesthesia and analgesia used (including monitoring), surgical procedure, method of euthanasia). Provide details of any specialist equipment used, including supplier(s). b. When (e.g. time of day). c. Where (e.g. home cage, laboratory, water maze). d. Why (e.g. rationale for choice of specific anaesthetic, route of administration, drug dose used).
Experimental animals	8	a. Provide details of the animals used, including species, strain, sex, developmental stage (e.g. mean or median age plus age range) and weight (e.g. mean or median weight plus weight range). b. Provide further relevant information such as the source of animals, international strain nomenclature, genetic modification status (e.g. knock-out or transgenic), genotype, health/immune status, drug or test naïve, previous procedures, etc.

Housing and husbandry	9	Provide details of: a. Housing (type of facility e.g. specific pathogen free (SPF); type of cage or housing; bedding material; number of cage companions; tank shape and material etc. for fish). b. Husbandry conditions (e.g. breeding programme, light/dark cycle, temperature, quality of water etc for fish, type of food, access to food and water, environmental enrichment). c. Welfare-related assessments and interventions that were carried out prior to, during, or after the experiment.
Sample size	10	a. Specify the total number of animals used in each experiment, and the number of animals in each experimental group. b. Explain how the number of animals was arrived at. Provide details of any sample size calculation used. c. Indicate the number of independent replications of each experiment, if relevant.
Allocating animals to experimental groups	11	a. Give full details of how animals were allocated to experimental groups, including randomisation or matching if done. b. Describe the order in which the animals in the different experimental groups were treated and assessed.
Experimental outcomes	12	Clearly define the primary and secondary experimental outcomes assessed (e.g. cell death, molecular markers, behavioural changes).
Statistical methods	13	a. Provide details of the statistical methods used for each analysis. b. Specify the unit of analysis for each dataset (e.g. single animal, group of animals, single neuron). c. Describe any methods used to assess whether the data met the assumptions of the statistical approach.
RESULTS		
Baseline data	14	For each experimental group, report relevant characteristics and health status of animals (e.g. weight, microbiological status, and drug or test naïve) prior to treatment or testing (this information can often be tabulated).
Numbers analyzed	15	a. Report the number of animals in each group included in each analysis. Report absolute numbers (e.g. 10/20, not 50%). b. If any animals or data were not included in the analysis, explain why.
Outcomes and estimation	16	Report the results for each analysis carried out, with a measure of precision (e.g. standard error or confidence interval).
Adverse events	17	a. Give details of all important adverse events in each experimental group. b. Describe any modifications to the experimental protocols made to reduce adverse events.
DISCUSSION		
Interpretation/scientific implications	18	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including any potential sources of bias, any limitations of the animal model, and the imprecision associated with the results. c. Describe any implications of your experimental methods or findings for the use of animals in research. Findings of this study are likely to translate to any relevance to human biology. Grant number(s) and the role of the funders.



The ARRIVE Guidelines

<https://www.nc3rs.org.uk/arrive-guidelines>

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The ARRIVE guidelines

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 **improve**

- **study quality**
- **animal welfare**
- **and therefore reproducibility**
- **and also the safety of humans and animals** affected directly or indirectly by the work



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ARRIVE

PREPARE

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

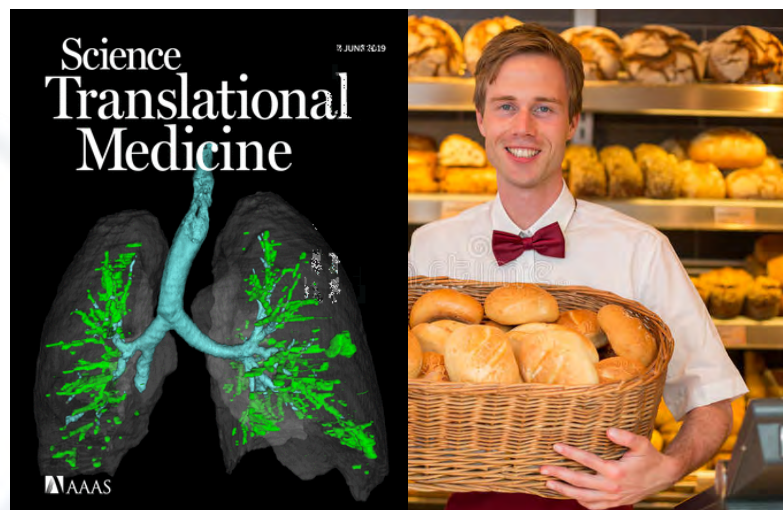


<https://www.bls.gov/ooh/images/3077.jpg>



PREPARE *from day 1*

ARRIVE



<https://www.dreamstime.com>

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ESLAV/ECLAM Summer School, 24-27 June 2019



Original Article

PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Lilley³,
Kristine E Aa Hansen⁴ and Trond Bratteli⁵

Laboratory Animals
0(0) 1-7
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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 Norecoba website, with links to guidelines for animal research and testing, at <https://norecoba.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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⁴Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway

⁵Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

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

<https://doi.org/10.1177/0023677217724823>



Over 8,000 downloads from the
journal website so far

Also downloadable from
norecoba.no/PREPARE

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ESLAV/ECLAM Summer School, 24-27 June 2019

A downloadable checklist



PREPARE



The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith¹, R. Eddie Clutton², Elliot Lilley³, Kristine E. Aa. Hansen⁴ & Trond Brattolid⁵

¹Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; ²Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; ³Research Animals Department, Science Group, RSPCA, Woburn, Bedfordshire, MK43 0NF, U.K.; ⁴Section 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; ⁵Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE¹. 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 transatability 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.

Topic	Recommendation
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding and division of labour	☐ Arrange meetings with all relevant staff when early plans for the project exist. ☐ Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. ☐ Discuss and disclose all expected and potential costs. ☐ Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility 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 & Brattolid T. PREPARE: Guidelines for Planning Animal Research and Testing. *Laboratory Animals*, 2017; DOI: 10.1177/0023677217734823.
2. Kilkenny C, Brown 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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PREPARE:

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

The PREPARE Checklist

Planning and preparation

1. Define the research objectives and aims of the study.
2. Identify the research questions and hypotheses.
3. Review the literature and identify the key concepts and theories.
4. Identify the research methods and procedures.
5. Identify the research participants and sample.
6. Identify the research ethics and safety issues.
7. Identify the research funding and resources.
8. Identify the research timeline and milestones.
9. Identify the research communication and dissemination plan.
10. Identify the research evaluation and impact plan.

ARRIVE

ARRIVE Checklist

Abstract

1. Title
2. Background
3. Objectives
4. Methods
5. Results
6. Conclusions
7. Funding
8. Acknowledgements
9. References
10. Supplementary material

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ARRIVE

ARRIVE Checklist

Abstract

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7. Funding
8. Acknowledgements
9. References
10. Supplementary material



Day 1 of planning

Experiment and data analysis

Manuscript Submission



PREPARE

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ARRIVE

ESLAV/ECLAM Summer School, 24-27 June 2019

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

norecopa.no/PREPARE





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Harm-Benefit Assessment

[Harm-Benefit assessment](#), an evaluation of the likely sources and level of suffering of a planned procedure, followed by an assessment of the potential benefits of the research weighed against these harms, lies at the heart of [legislation in the EU](#) and elsewhere. [A framework for severity assessment and severity classification](#) must be established and justified. The likely adverse effects of each procedure should be described, along with their likely incidence and methods of recognising them, with indications of how these effects can be mitigated by implementing refinement. This necessitates the involvement of personnel with the relevant expertise to recognise, assess and reduce animal suffering, especially severe suffering. [Guidance on this is available on the RSPCA website](#). Specific justification of all unavoidable animal suffering must be provided. An estimate must be made of the maximum amount of pain, distress or lasting harm to which an individual can be

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

Contract between the animal facility and the research group

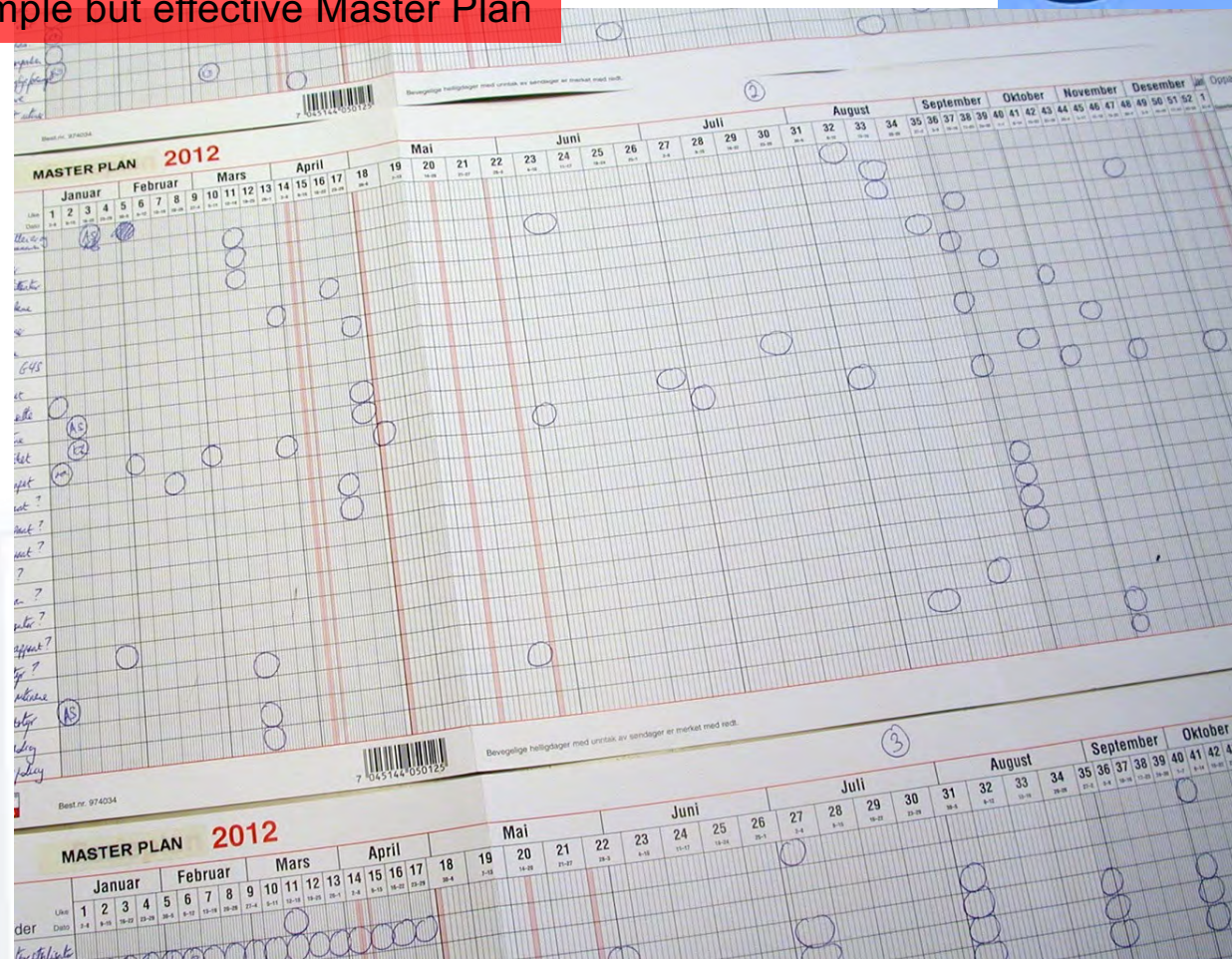
The division of labour and responsibilities

Clarifying all stages of the experiment

Ensuring that all necessary parameters are recorded

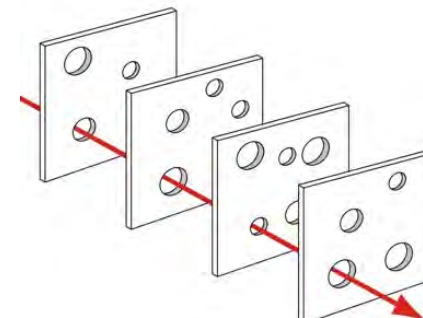
	Animal facility	Researcher	Not applicable
Animal:			
Arrival date			
Species			
Strain/stock and substrain			
Supplier (full name and address) or bred on the premises			
Number and sex			
Age, weight, stage of life cycle on arrival			
Pre-treatment (surgical or medical) from supplier			
Quality (e.g. 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 $\pm$ variation)			
Light schedule			
Relative humidity (mean $\pm$ 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			

A simple but effective Master Plan



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
 - allergic and anaphylactic reactions
 - burns
 - head injuries
 - bites
 - 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



Temporary staff at weekends and holidays

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

Consult the 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

An International Culture of Care Network

norecopa.no/CoC

Before you speak....

THINK!

T - is it true?
h - is it helpful?
i - is it inspiring?
n - is it necessary?
k - is it kind?

FREE YOUR MIND and THINK



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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.

"because we've always done it that way»

«as often as necessary»



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

An example: i.v. injection of a radioactive isotope:



procedureswithcare.org.uk/intravenous-injection-in-the-mouse

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PREPARE Checklist

1-Literature searches	2-Legal issues
3-Ethical issues, Harm-Benefit Assessment and humane endpoints	4-Experimental design and statistical analysis
5-Objectives and timescale, funding and division of labour	6-Facility evaluation
7-Education and training	8-Health risks, waste disposal and decontamination
9-Test substances and procedures	10-Experimental animals
11-Quarantine and health monitoring	12-Housing and husbandry
13-Experimental procedures	14-Humane killing, release, re-use or re-homing
15-Necropsy	Comparison with ARRIVE

Thanks to Norecoba's main sponsors:

- Standing Committee on Business Affairs, Norwegian Parliament
- Norwegian Ministries of Agriculture and Fisheries
- Research Council of Norway
- Laboratory Animals Ltd.
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Society for Animal Protection
- Novo Nordisk
- Scottish Accreditation Board
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture



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Interactive map of European 3R Centres



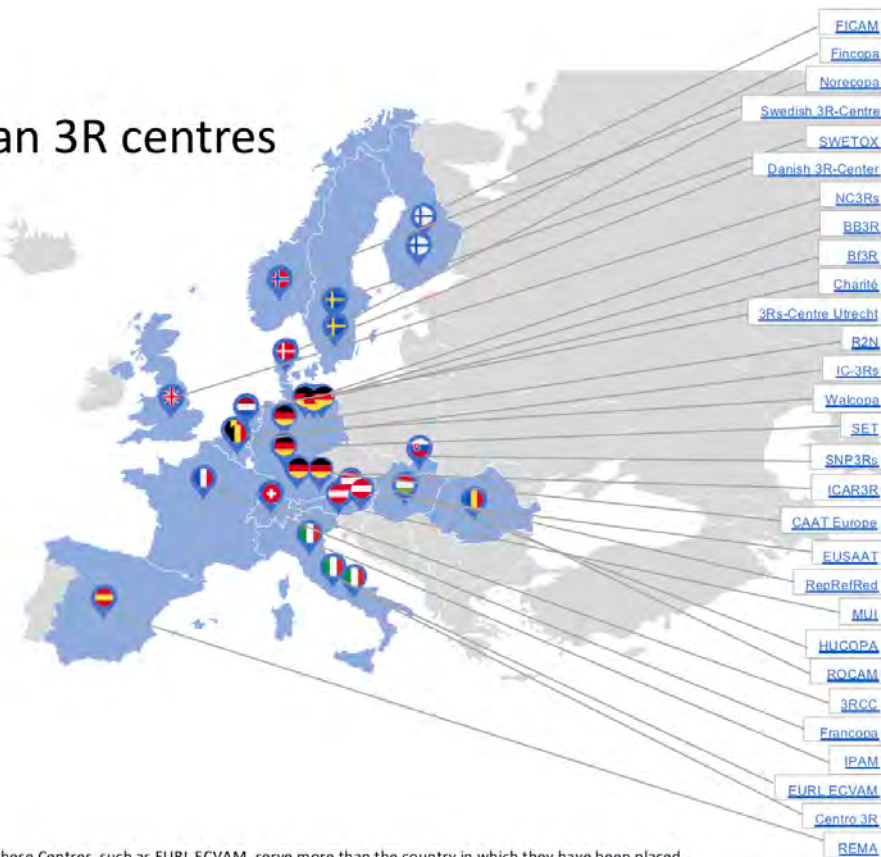
European 3R centres

Map:

norecopa.no/3REuropeOverview

List of centres:

norecopa.no/3REurope



Please note that some of these Centres, such as EURL ECVAM, serve more than the country in which they have been placed.

This overview has been compiled by Norecopa. Please report any errors or send suggestions for additions to post@norecopa.no

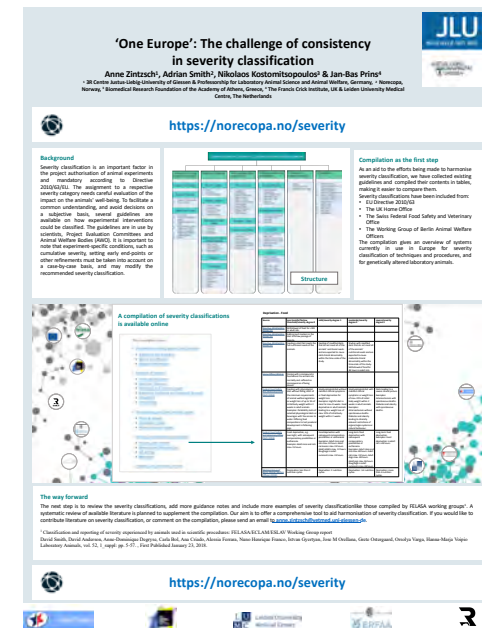
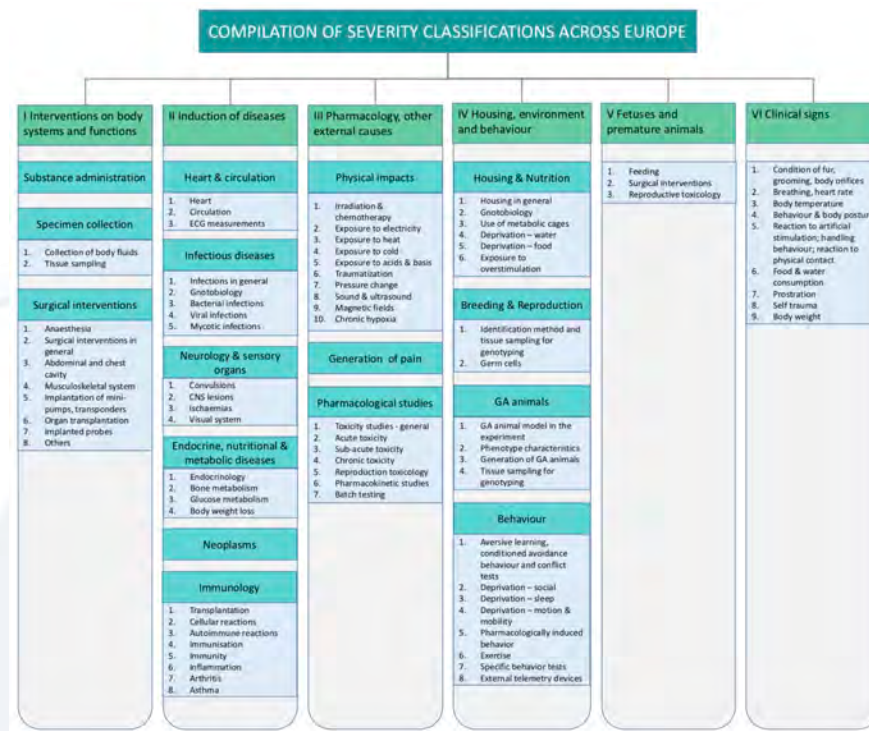
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Mild, Moderate or Severe? A compilation of severity classification



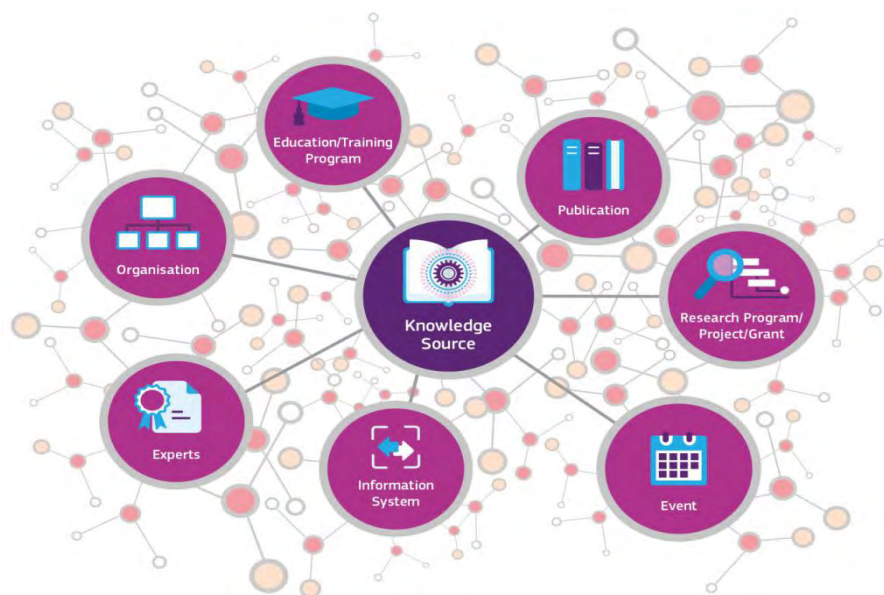
norecopa.no/severity

Anne Zintzsch, Nikolaos Kostomitsopoulos
& Jan-Bas Prins



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Which knowledge resources are there?
How are they being shared?
Where are the gaps or missed opportunities?

norecopa.no/3RInventory

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protective ingredients of consumer products by means of alternative methods in vitro, instruments and clinical studies with the aim of public health protection and promotion. EU-NETVAL member

In Silico Pharmacology

European Commission Inventory of 3Rs Knowledge Sources/97746

In Silico Pharmacology provides a forum for research articles conceiving the interface between computational and experimental work in pharmacology and toxicology. Primarily, interdisciplinary papers are published that address computational approaches in drug-design and multi-scale analysis of bioactive substances from the cellular up to behavioral level. The journal especially encourages deterministic and stochastic modeling of biological (e.g., biochemical, biophysical and immunological) processes leading to therapeutic advancements as well as mathematical methods characterizing the pharmacology of substances within the living organism. Papers investigating substance- or material-induced morphological and genetic alterations are also welcome. It is anticipated that all computational and experimental approaches are represented within In Silico Pharmacology.

CAAT Academy Hands-on training in toxicology

European Commission Inventory of 3Rs Knowledge Sources/97501

CAAT Academy is an extension of a joint venture of Johns Hopkins University Center for Alternatives to Animal Testing (CAAT) and CAAT-Europe (University of Konstanz). CAAT Academy is not-for profit and connects experts from Europe and the U.S. to provide hands-on-training in human-relevant alternative methods and technologies for toxicologists of all levels of experience, from entry level technician (BS) to laboratory or department manager (MS/PhD).

In Vitro and Alternative Methods - SOT Specialty Section

European Commission Inventory of 3Rs Knowledge Sources/97796

The In Vitro and Alternative Methods Specialty Section (IVAM) is a specialty group within the Society of Toxicology whose members have expertise in the application of in vitro techniques to problems of cellular toxicity, with a special emphasis on product safety evaluation. The interests of IVAM include studies of the basic cellular processes involved in the induction of adverse outcomes.

Category	+
Owner/Developer	+
Owner (abbr.)	+
Country	+
Language	+
Channel	+
Audience	+
Potential Audience	+
User access	+
Update frequency	+
3R Relevance	+
Purpose	+
Legislation framework	+
Technology / Tools	+

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English-language newsletters

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"We ARRIVED, because we were PREPARED"

norecopa.no/prepareFELASA

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