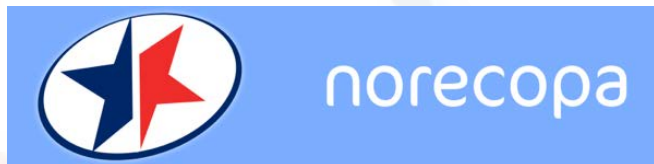


# Design of animal studies: The PREPARE guidelines

[\*norecopa.no/CAAT-1\*](https://norecopa.no/CAAT-1)

Adrian Smith

[\*adrian.smith@norecopa.no\*](mailto:adrian.smith@norecopa.no)

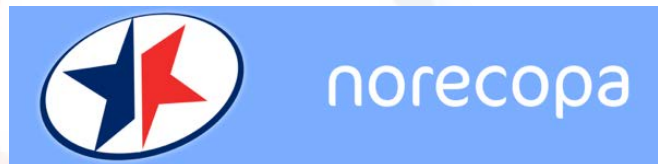


[\*https://norecopa.no\*](https://norecopa.no)

# Norecopa

Norway's National Consensus Platform for the  
Three Rs: Replacement, Reduction and Refinement

and a source of global 3R resources



<https://norecopa.no>

Norecopa: PREPARE for better Science

[norecopa.no](http://norecopa.no)



The screenshot shows the top navigation bar of the norecopa.no website. It features the Norecopa logo (a stylized star) and the text 'norecopa'. To the right, there are language options for 'NORSK' and 'ENGLISH'. A search bar with the text 'Search:' and a magnifying glass icon is circled in red. Below the navigation bar, there is a list of menu items: 'About Norecopa', 'Alternatives', 'Databases & Guidelines', 'Education & training', 'Legislation', 'Meetings', 'News', 'Other resources', 'Species', and 'Feedback'. A secondary list of topics includes 'Anaesthesia and analgesia', 'Animal facilities', 'Animal welfare organisations', 'Blood sampling', 'Email discussion lists', 'Environmental enrichment', 'Ethics', 'Experimental design and statistical analysis', 'Harm-Benefit Assessment', 'Health monitoring', 'Journals', 'Organisations', 'Severity classification', 'Suppliers', and 'Systematic reviews'. Below this, there is a search bar with the text 'Search all Norecopa's databases and webpages simultaneously:' and a magnifying glass icon. To the right of the search bar are social media icons for Facebook, Twitter, Email, and a plus sign. The breadcrumb trail shows 'norecopa.no / Other resources /'.

## 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)

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

9,900 webpages  
350,000 pageviews per year

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**Today's presentation (30 minutes):**

A quick overview of the PREPARE guidelines

**Tomorrow (0830-0930):**

The Refinement Wiki and the International Culture of Care Network  
with more time to explore the Norecopa website

## *Preparing for animal research: my starting point*

- I have supervised animal research, and held courses in lab animal science, since the early 1980's
- I have developed the greatest respect for scientists who are specialists in their field and who plan ground-breaking research
- It becomes clear that one of the greatest challenges to reproducibility lies in the animal material they use and the way they use it
- I suspect that many scientists are unaware of the size of this challenge, or assume that the animal facility is dealing with it

Perspective | Open Access | Published: 10 January 2017

## A manifesto for reproducible science

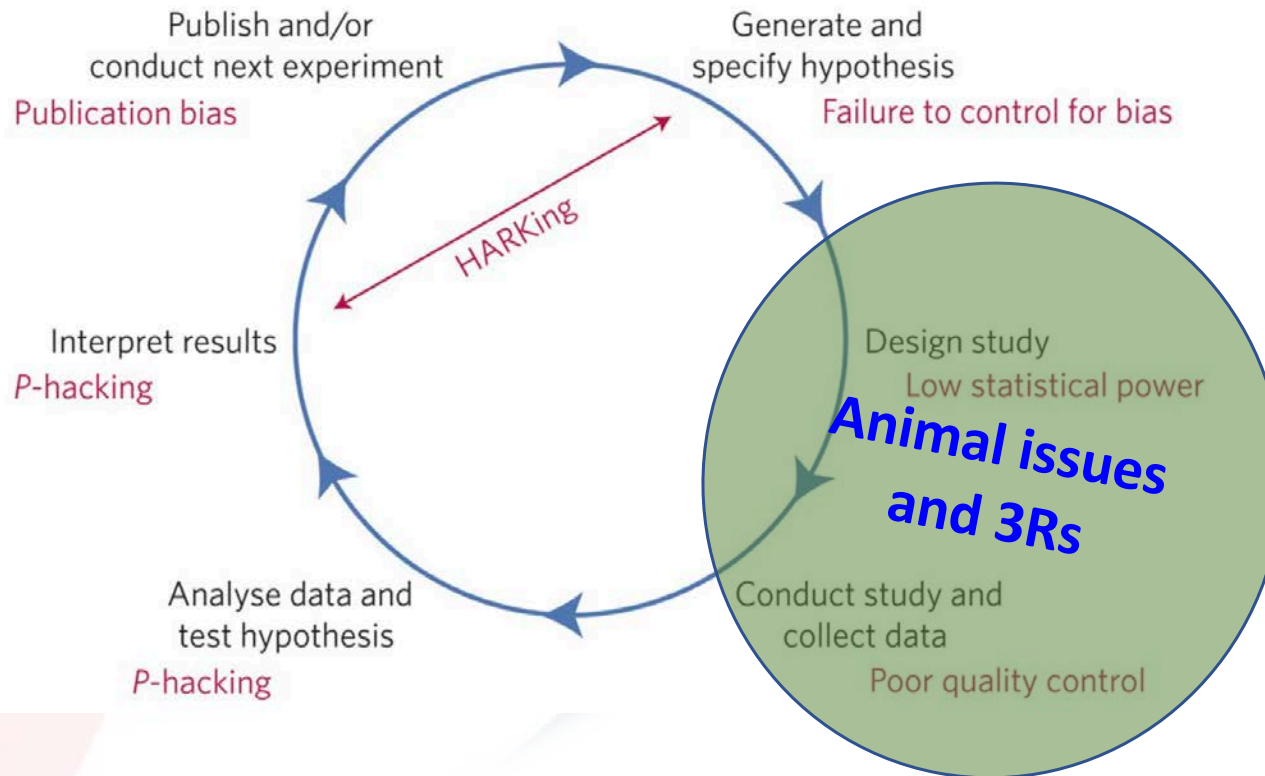
Marcus R. Munafò , Brian A. No-  
Button, Christopher D. Chambers,  
Jan Wagenmakers, Jennifer J. Wa

Nature Human Behaviour 1, Artic

33k Accesses | 518 Citations |

Figure 1: Threats to reproducible science.

From: A manifesto for reproducible science



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Two frustrations:

'We can solve the reproducibility crisis by'

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



[reddit.com](https://www.reddit.com)

## Reporting guidelines are not new...and they have not solved the reproducibility crisis

e.g.

- Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments (GV-SOLAS, 1985)
- Reporting animal use in scientific papers (Jane Smith *et al.*), 1997
- Öbrink & Reh binder: 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 & 2019 (Kilkenny *et al.*; Percie du Sert *et al.*)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals





## 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

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

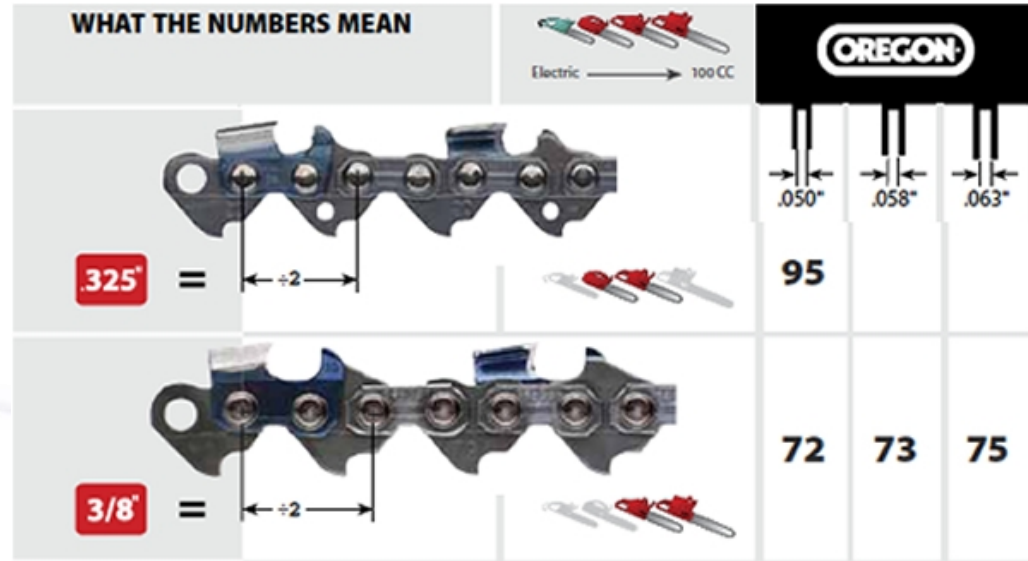


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## The easy parts of design and reporting:



[arborist101.com](http://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:

**'Measure twice, think three times, cut once'**

Luc Noyez *NHJL* 18, 60 (2010) [doi.org/10.1007/BF03091738](https://doi.org/10.1007/BF03091738)

**Measure twice, think three times: prepare**

**Cut once: report**



[leaderonomics.com](http://leaderonomics.com)

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Give me six hours  
to chop down a  
tree and I will  
spend the first  
four sharpening  
the axe.



*Abraham Lincoln*

[www.quote-coyote.com](http://www.quote-coyote.com)



norecopa



Reporting

Planning

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## *How have pilots achieved reproducibility?*



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



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*...and precision in a variable environment?*



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## *10-15 checklists even on short routine flights*



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# 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

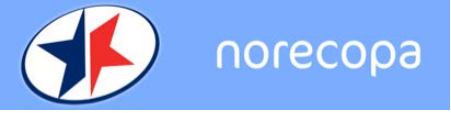
***Too late to read the checklists when you have ARRIVED!***



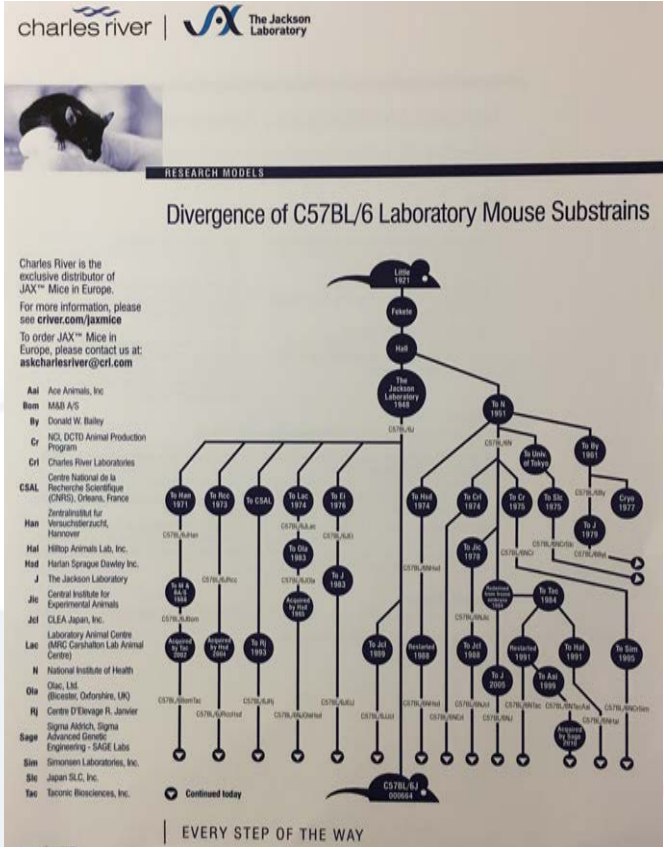
colourbox.com

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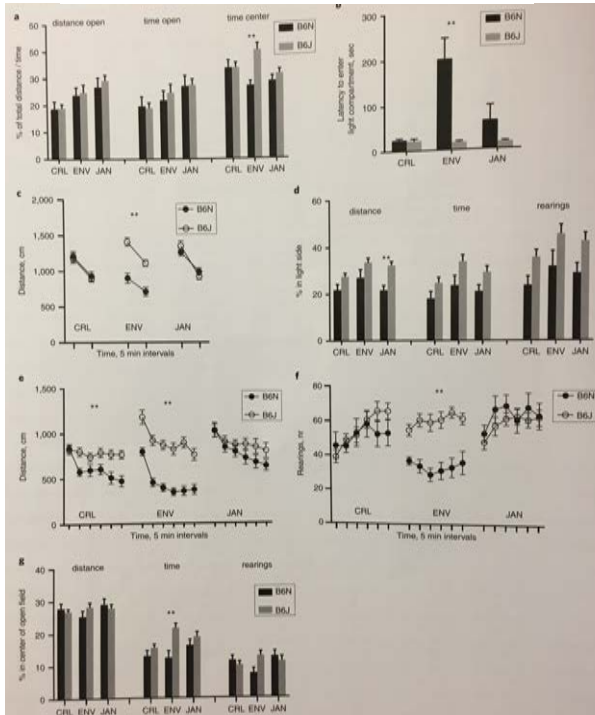


# The C57BL/6 mouse



Åhlgren & Voikar (2019): Behavioural differences between /6J and /6N mice

[nature.com/articles/s41684-019-0288-8](http://nature.com/articles/s41684-019-0288-8)



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we are what we eat...



## Diet-Induced Metabolic Syndrome in Rodent Models

A discussion of how diets made from purified ingredients influence the phenotypes of the MS in commonly used rodent models.

**Angela M. Gajda, MS, Michael A. Pellizzon, Ph.D.,  
Matthew R. Ricci, Ph.D. and Edward A. Ulman, Ph.D.**

Pellizzon and Ricci *Nutrition & Metabolism* (2018) 15:3  
DOI 10.1186/s12986-018-0243-5

Nutrition & Metabolism

PERSPECTIVE

Open Access

The common use of improper control diets in diet-induced metabolic disease research confounds data interpretation: the fiber factor



Michael A. Pellizzon\* and Matthew R. Ricci

Currently no FELASA guidance on nutrition (a working group has been convened)

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3R Symposium, Copenhagen, 12-13 November 2019

## Laboratory Animal Diets: A Critical Part of Your In Vivo Research

Most all of us are aware that certain dietary choices can increase or decrease the likelihood of developing certain diseases. Our diets can also change our metabolism as well the levels of circulating factors (hormones, lipids, etc.) which may be markers for disease risk. What is often overlooked is the fact that these concepts also apply to laboratory animals, making diet a critical part of study design.

**Matthew R. Ricci, Ph.D. and Edward A. Ulman, Ph.D.**

## 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>

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photo: colourbox.com

## *Stress caused by capture and handling*



News > Science

# Scores of scientific studies based on mice thrown into doubt because they were

Mice pick up naturally

Ian Johnston

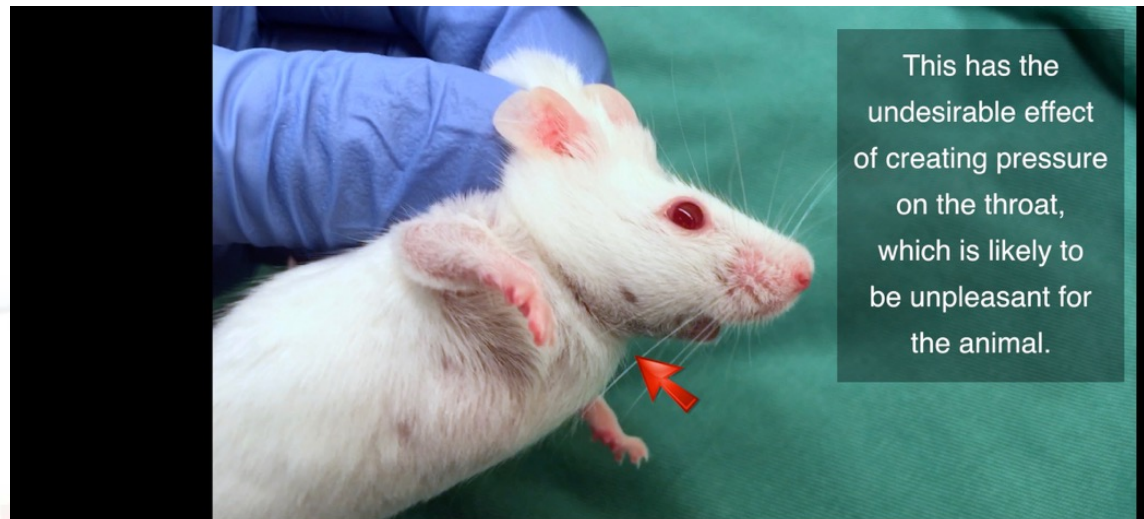


<https://www.nc3rs.org.uk/how-to-pick-up-a-mouse>

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## *Stress caused by capture and handling*



### Three fingers better than two MATURE

5 days ago | More



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Autoplay next video



Three fingers b  
Norecoba

<http://bitly.com/scruff-technique>

Norecoba: PREPARE for better Science

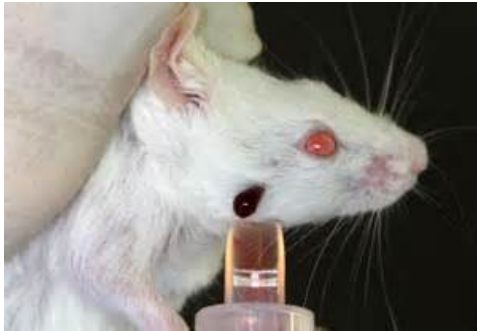
## *Artefacts caused by poor administration techniques*



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' case: a researcher wants a blood sample*



[medipoint.com/html/for\\_use\\_on\\_mice.html](http://medipoint.com/html/for_use_on_mice.html)



[theodora.com/rodent\\_laboratory/blood\\_collection.html](http://theodora.com/rodent_laboratory/blood_collection.html)



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

Carol M. Newton (1925-2014)



National Library of Medicine

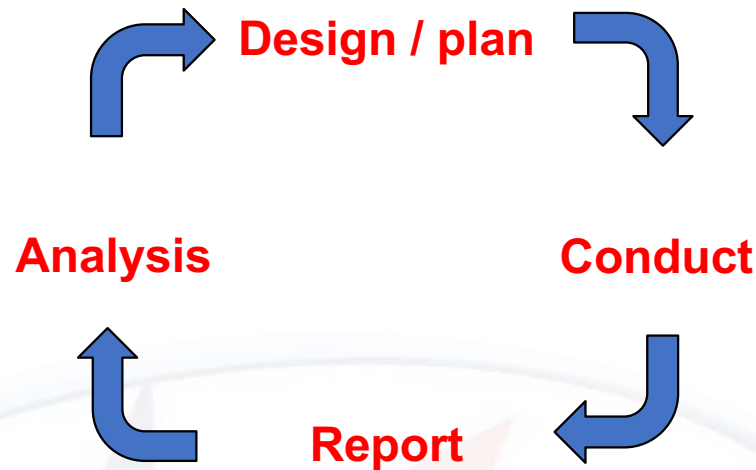
## ***The three S's***

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

<https://norecopa.no/3S>

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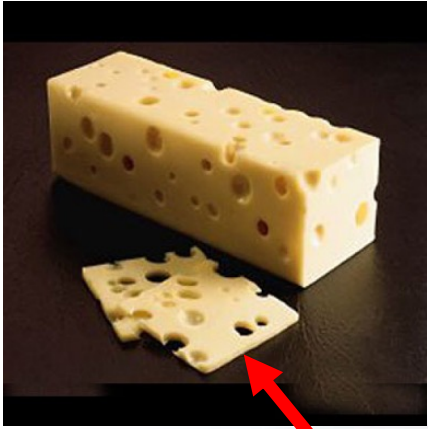
## Preparation and evaluation are part of a continuing learning spiral



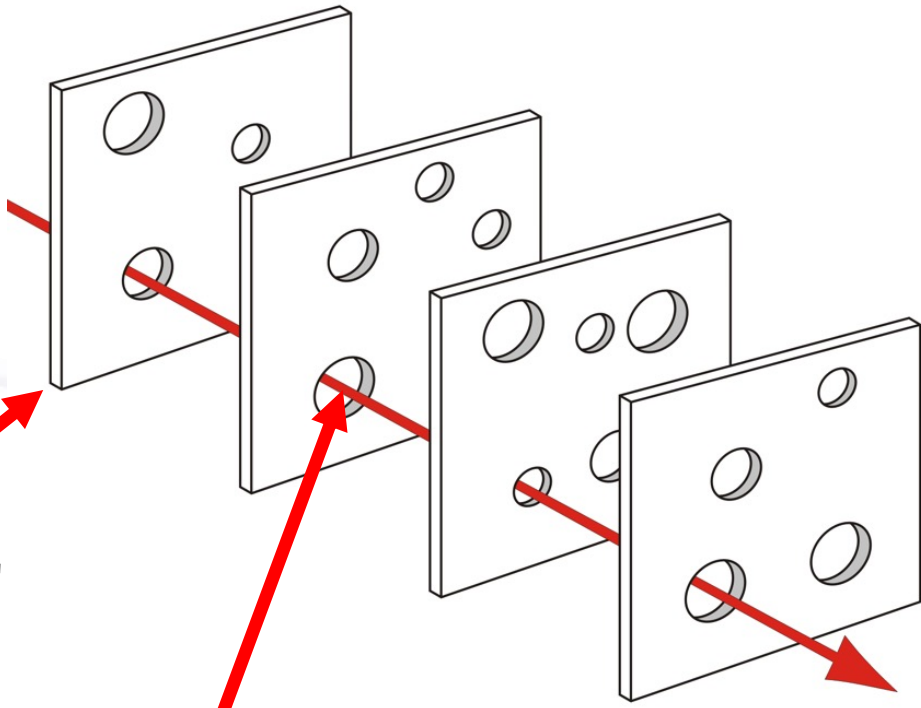
Identify and ensure the quality of (at least) the critical points in the experiment: critical for scientific validity and animal welfare



# Threat and Error Management



[eaugallecheese.com/Swiss-Cheese](http://eaugallecheese.com/Swiss-Cheese)



"Layer of defence"  
or redundancy

Weakness / hazard

**Loss**

[wikipedia.org/wiki/Swiss\\_cheese\\_model](http://wikipedia.org/wiki/Swiss_cheese_model)

## Contingency and redundancy

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

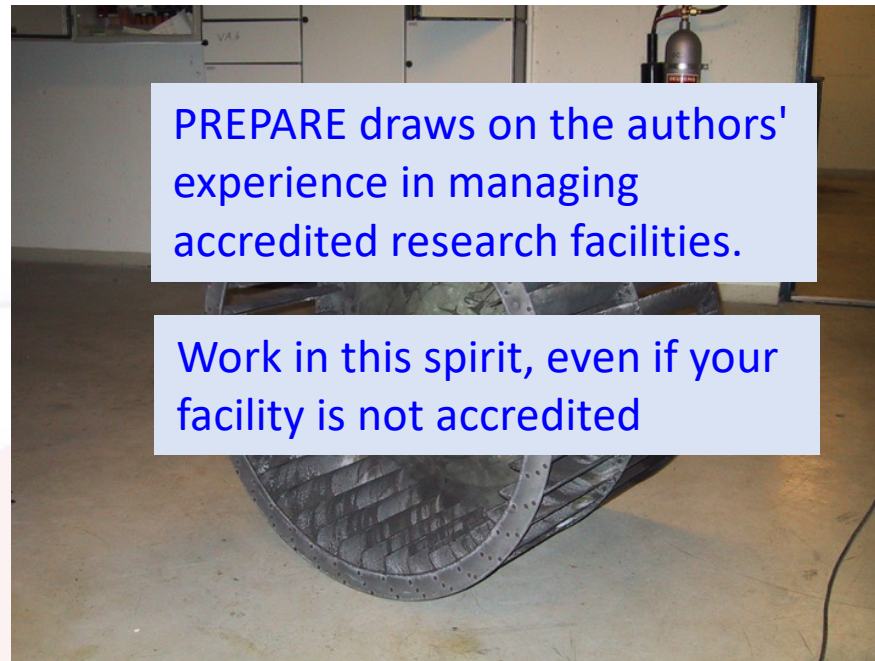


Photo: NMBU



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*

- *Cost-cutting decisions (pushing the safety envelope):*

*"We've got away with it before"*

*"We've managed to publish the experiments before"*

- *A combination of many factors, each of which may be harmless until they occur simultaneously*





Original Article

Laboratory Animals  
0(0) 1-7  
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sagepub.co.uk/journalsPermissions.nav  
DOI: 10.1177/0023677217724823  
journals.sagepub.com/home/lan  
SAGE

**PREPARE: guidelines for planning animal research and testing**

Adrian J Smith<sup>1</sup>, R Eddie Clutton<sup>2</sup>, Elliot Lilley<sup>3</sup>, Kristine E Aa Hansen<sup>4</sup> and Trond Bratteli<sup>5</sup>

**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,<sup>1,2</sup> even after the production and journal endorsement of reporting guidelines.<sup>3</sup> There is also widespread concern about the lack of reproducibility and translatability of laboratory animal research.<sup>4-7</sup> This can, for example, contribute towards the failure of drugs when they enter human trials.<sup>8</sup> 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.<sup>9</sup> This has understandably sparked a demand for reduced waste when planning experiments involving animals.<sup>10-12</sup> 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).<sup>13</sup> 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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<sup>3</sup>Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK  
<sup>4</sup>Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway  
<sup>5</sup>Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

**Corresponding author:**  
Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0104 Oslo, Norway.  
Email: [adrian.smith@norecopa.no](mailto:adrian.smith@norecopa.no)

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 12,000 downloads from the journal website so far

Also downloadable from [norecopa.no/PREPARE](https://norecopa.no/PREPARE)

Norecopa: PREPARE for better Science

## **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



# PREPARE



## The PREPARE Guidelines Checklist

### Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

Adrian J. Smith<sup>1</sup>, R. Eddie Clutton<sup>2</sup>, Elliot Lilley<sup>3</sup>, Kristine E. Aa. Hansen<sup>4</sup> & Trond Brattelid<sup>5</sup>  
<sup>1</sup>Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; <sup>2</sup>Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; <sup>3</sup>Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; <sup>4</sup>Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8146 Dep., 0033 Oslo, Norway; <sup>5</sup>Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

PREPARE consists of planning guidelines which are complementary to reporting guidelines such as ARRIVE<sup>2</sup>. 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 in the checklist can be adapted to meet special needs, such as field studies. PREPARE includes guidance on facilities, since in-house experiments are dependent upon their quality. The full version of the guideline 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
<b>(A) Formulation of the study</b>	
1. Literature searches	<input type="checkbox"/> Form a clear hypothesis, with primary and secondary outcomes. <input type="checkbox"/> Consider the use of systematic reviews. <input type="checkbox"/> <i>Decide upon databases and information specialists to be consulted, and construct search terms.</i> <input type="checkbox"/> <i>Assess the relevance of the species to be used, its biology and suitability to answer the experimental questions with the least suffering and to welfare needs.</i> <input type="checkbox"/> Assess the reproducibility and translatability of the project.
2. Legal issues	<input type="checkbox"/> Consider how the research is affected by relevant legislation for animal research and other areas, e.g. animal transport, occupational health and safety. <input type="checkbox"/> Locate relevant guidance documents (e.g. EU guidance on project evaluation).
3. Ethical issues, harm-benefit assessment and humane endpoints	<input type="checkbox"/> Construct a lay summary. <input type="checkbox"/> In dialogue with ethics committees, consider whether statements about this type of research have already been produced. <input type="checkbox"/> <i>Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities).</i> <input type="checkbox"/> <i>Consider pre-registered and the publication of negative results.</i> <input type="checkbox"/> <i>Perform a harm-benefit assessment and justify any likely animal harm.</i> <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> <i>Allocate a severity classification to the project.</i> <input type="checkbox"/> Define objective, easily measurable and unequivocal humane endpoints. <input type="checkbox"/> Discuss the justification, if any, for death as an end-point.
4. Experimental design and statistical analysis	<input type="checkbox"/> <i>Consider pilot studies, statistical power and significance levels.</i> <input type="checkbox"/> <i>Define the experimental unit and decide upon animal numbers.</i> <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.

Topic	Recommendation
<b>(B) Dialogue between scientists and the animal facility</b>	
5. Objectives and timescale, funding and division of labour	<input type="checkbox"/> Arrange meetings with all relevant staff when early plans for the project exist. <input type="checkbox"/> Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. <input type="checkbox"/> Discuss and disclose all expected and potential costs. <input type="checkbox"/> Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility location	<input type="checkbox"/> Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. <input type="checkbox"/> Discuss staffing levels at times of extra risk.
7. Staffing and training	<input type="checkbox"/> <i>Assess the current competence of staff members and the need for further education or training prior to the study.</i>
8. Risk assessment	<input type="checkbox"/> <i>Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected by the study.</i> <input type="checkbox"/> Assess, and if necessary produce, specific guidance for all stages of the project. <input type="checkbox"/> Discuss means for containment, decontamination, and disposal of all items in the study.
9. Waste disposal and decontamination	<input type="checkbox"/> Assess, and if necessary produce, specific guidance for all stages of the project. <input type="checkbox"/> Discuss means for containment, decontamination, and disposal of all items in the study.
<b>(C) Quality control of the components in the study</b>	
9. Test substances and procedures	<input type="checkbox"/> Provide as much information as possible about test substances. <input type="checkbox"/> Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	<input type="checkbox"/> <i>Decide upon the characteristics of the animals that are essential for the study and for reporting.</i> <input type="checkbox"/> <i>Avoid generation of surplus animals.</i>
11. Quarantine and health monitoring	<input type="checkbox"/> Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	<input type="checkbox"/> <i>Attend to the animals' specific instincts and needs, in collaboration with expert staff.</i> <input type="checkbox"/> <i>Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).</i>
13. Experimental procedures	<input type="checkbox"/> <i>Develop refined procedures for capture, immobilisation, marking, and release or rehoming.</i> <input type="checkbox"/> <i>Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.</i>
14. Humane killing, release, reuse or rehoming	<input type="checkbox"/> <i>Consult relevant legislation and guidelines well in advance of the study.</i> <input type="checkbox"/> <i>Define primary and emergency methods for humane killing.</i> <input type="checkbox"/> <i>Assess the competence of those who may have to perform these tasks.</i>
15. Necropsy	<input type="checkbox"/> 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: 10.1177/0023677217724423.
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](mailto:post@norecopa.no) | [@norecopa](https://twitter.com/norecopa)

# The ARRIVE guidelines 2019: updated guidelines for reporting animal research

[biorxiv.org/content/10.1101/703181v1](https://www.biorxiv.org/content/10.1101/703181v1)

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

Reference to 3R-related issues

## The ARRIVE guidelines 2019: updated guidelines for reporting animal research

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

[biorxiv.org/content/10.1101/703181v1](https://www.biorxiv.org/content/10.1101/703181v1)

Reference to 3R-related issues



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

[norecoba.no/PREPARE](https://norecoba.no/PREPARE)



A screenshot of the norecoba.no website. The header is blue with the Norecoba logo and the word "norecoba" in white. In the top right corner, there are language options for "NORSK" and "ENGLISH", and a search bar with the text "Search: Q". Below the header is a navigation menu with items: "About Norecoba", "Alternatives", "Databases &amp; Guidelines", "Education &amp; training", "Legislation", "Meetings", "More resources", "News", "PREPARE", and "Species". The "PREPARE" item is circled in red. Below the navigation menu is a list of links for the PREPARE Checklist, including: "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", and "Comparison with ARRIVE".

[norecoba.no](https://norecoba.no) / [PREPARE](https://norecoba.no/PREPARE)



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About Norecopa Alternatives Databases & Guidelines Education & training Legislation Meetings More resources News PREPARE Species

- 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

norecopa.no / PREPARE 

### 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

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



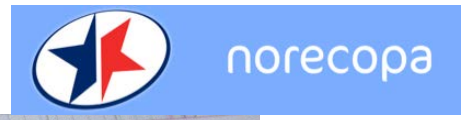
[procedureswithcare.org.uk/intravenous-injection-in-the-mouse](http://procedureswithcare.org.uk/intravenous-injection-in-the-mouse)

[norecopa.no/PREPARE](http://norecopa.no/PREPARE)

PREPARE Checklist | 1-Literature searches | 2-Legal issues |  
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A simple but effective Master Plan



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## A contract between the animal facility and the research group

The division of labour and responsibilities

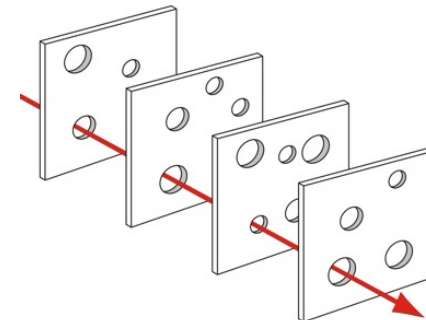
Clarifying all stages of the experiment

Ensuring that all necessary parameters are recorded

	Animal facility	Researcher	Not applicable
<b>Animal:</b>			
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)			
<b>Environment:</b>			
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			
<b>Housing:</b>			
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			

## 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>

# CIRS-LAS Portal

Critical incident reporting system in laboratory animal science

Refine  
Reduce  
Replace



## Operating principles



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Recent incidents

**Injury of the mesentery by vertebral kyphoplasty**

**Mouse neonates exposed to CO2**

**Animal escapes during transportation**

**Kidney damage in mouse after surgery on heating mat**

**Soft tissue implant in rabbit**

***PREPARE encourages scientists to collaborate with animal carers and technicians from Day 1***

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

# Good advice is emerging from the Covid-19 pandemic



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

CATEGORY		CONSIDERATIONS/SUGGESTIONS
<b>PERSONNEL</b>  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).	<b>ANIMAL TECHNICIANS</b>	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
	<b>RESEARCHERS</b>	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 <b>DELIVERIES</b> Avoid this if possible – if you must wear disposable PPE and wipe surfaces of incoming goods <b>VETS</b> Provide veterinary advice via video or phone unless physical presence (e.g. to perform a procedure) is required Use email/ photos/videos to share clinical signs with NACWO, vets and researchers Have a plan for back up in case vet is too ill to work, and plan access arrangements for substitute vet <b>ANIMALS</b> <b>BREEDING</b> 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 <b>REDUCE STOCK</b> 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) 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 Avoid unnecessary movement of animals Prioritise the movement of animals to other facilities or establishments for contingency of valuable lines. <b>ACCESS</b> Check your facility/ies will be open – Provide a list of names requiring access. Check with security how and when essential staff will access <b>SUPPLIES</b> Confirm how essential supplies and waste contractors will service the facility/ies Stock up on diet, bedding, nesting materials, PPE, disinfectants and other essentials, aim for a minimum of 3 months Ensure there will be Liquid nitrogen / dry ice for cryopreserved stocks Have stocks of CO <sub>2</sub> and sodium pentobarbitone and any other drugs as directed by the NVS <b>ESTATES / ENGINEERS</b> 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 <b>RECORDS</b> Record all difficult decisions taken. What/ when /why and any related evidence
<b>ESTABLISHMENT LICENCE HOLDER</b>		
<b>ENGINEERS</b>		

[norecopa.no/be-prepared](http://norecopa.no/be-prepared)

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[lava.uk.net/viewtopic.php?f=3&p=80](http://lava.uk.net/viewtopic.php?f=3&p=80)



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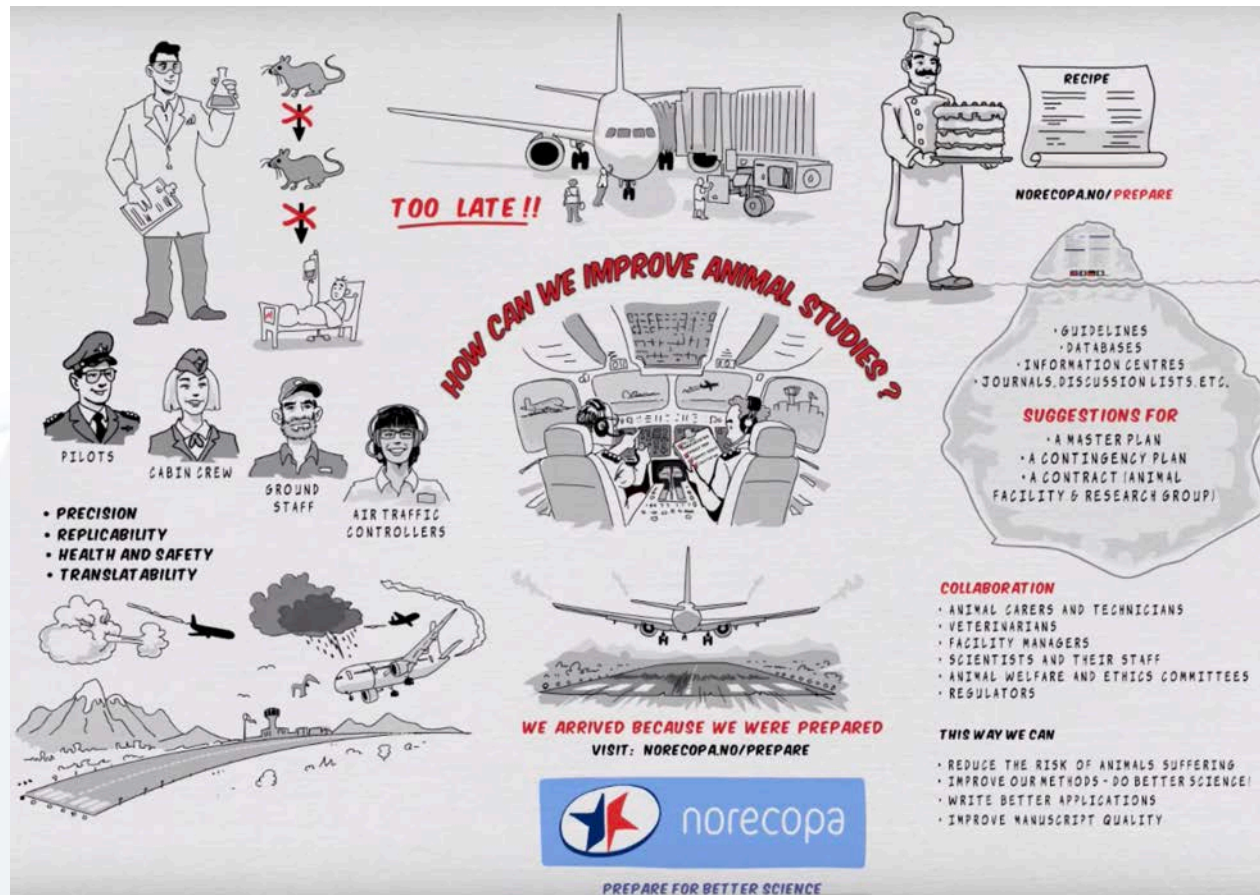
*"We ARRIVED, because we were PREPARED"*

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

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[vimeo.com/358069203](https://vimeo.com/358069203) or [norecopa.no/PREPARE](http://norecopa.no/PREPARE)

3-minute cartoon film



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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!***

**English-language newsletters**

**[post@norecopa.no](mailto:post@norecopa.no)**

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