

**Norecopa:**  
**Working to advance harmonisation and dissemination of  
best practice in animal research and testing**

***[norecopa.no/Linz2019](https://norecopa.no/Linz2019)***

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*<https://norecopa.no>*

✓ **Coming together is a beginning**

✓ **Keeping together is progress**

**Working together is success**

Edward Everett Hale



# Norecopa:

Norway's consensus  
platform for the 3Rs

founded 10.10.2007

<https://norecopa.no/about-norecopa/the-first-10-years>

Norecopa: PREPARE for better Science



EUSAAT Congress, Linz, 10-13 October 2019

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

The screenshot shows the top section of the norecopa.no website. It features a blue header with the norecopa logo (a stylized star) and the text 'norecopa'. In the top right corner, there are language options for 'NORSK' and 'ENGLISH', and a search bar with a magnifying glass icon. Below the header is a navigation menu with links for 'About Norecopa', 'Alternatives', 'Databases & Guidelines', 'Education & training', 'Legislation', 'Meetings', 'News', 'Other resources', 'Species', and 'Feedback'. A secondary menu lists various topics such as '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'. A red circle highlights the search bar, and a red arrow points from it to a search box below.

norecopa.no / Other resources /

Search all Norecopa's databases and webpages simultaneously:

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## 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

8,400 webpages  
80,000 links

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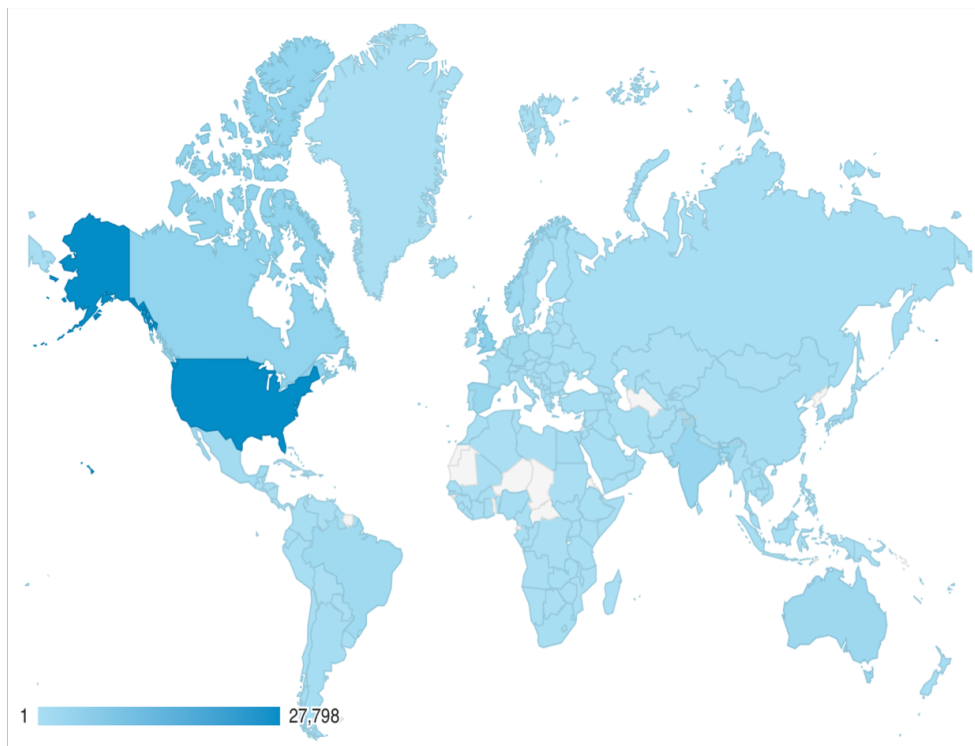
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**If you think it's expensive to hire a professional to do the job, wait until you hire an amateur.**



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[Welcome to Norecopa, Norway's 3R centre!](#)

[\\*The PREPARE Guidelines for Planning Animal Research and Testing\\*](#)

[Video presentation of the Norecopa website](#)

[Short cut: Guidelines for animal research](#)

[Short cut: European 3R Centres](#)

[Search engine help file](#)

More about the databases: [3R Guide](#) - [NORINA](#) - [TextBase](#) - [Classic AVs](#) - [NAL](#) - [European Commission Inventory of 3Rs Knowledge Sources](#)

[Norecopa: the first 10 years \(2007-2017\)](#)

[Reviews of the website](#)

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## Meetings calendar

- > [Anaesthesia Workshop](#), Newcastle, 8-10 October 2019
- > [Recent advances in assessing the emotional component of pain in animals](#), Stockholm, 10 October 2019
- > [3rd RSPCA International Meeting: Focus on Severe Suffering - Avoiding Mortality](#), Athens, 10-11 October 2019
- > [EUSAAT congress](#), Linz, 10-13 October 2019
- > [Animal Handler Risk Assessment](#), webinar, 11 October 2019
- > [70th AALAS National Meeting](#), Denver, 13-17 October 2019
- > [Scientific Procedures, Supply, Husbandry and Culture of Zebrafish](#), Basel, 14 October 2019
- > [Annual meeting for animal welfare bodies](#), Gothenburg, 17 October 2019



## ***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***



[norecopa.no/education-training/homemade-educational-materials](http://norecopa.no/education-training/homemade-educational-materials)



+ the NORINA database of 3,100 audiovisual aids for use in education and training  
Established in 1991, updated weekly. [norecopa.no/NORINA](http://norecopa.no/NORINA)





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EURL ECVAM

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### **Inventory of the 3Rs knowledge sources**

In the context of the European Commission's Communication published in response to the European Citizens' Initiative "Stop Vivisection", Action 1 aimed to conduct an assessment...

<https://norecopa.no/european-commission-inventory-of-3rs-knowledge-sources>



### **Three Rs Education and Training Courses and Resources**

The purpose of the collection of these data undertaken between June and September in 2018 was to provide a snapshot overview of education and training courses and resources on...

<https://norecopa.no/education-training>



**EURL ECVAM**

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**Refinement Wiki**

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**EUSAAT**

*European Society for  
Alternatives to Animal Testing*

*The European 3Rs Society*

Edward Everett Hale



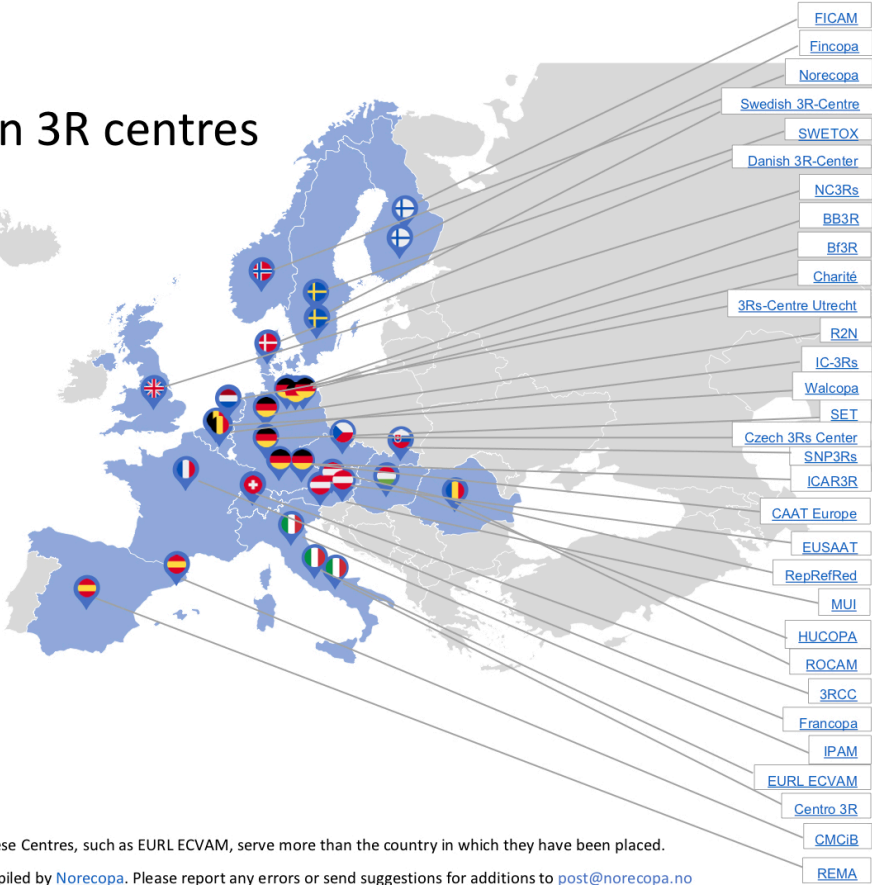
### Interactive map of European 3R Centres

- *European network of 3R Centres established*
- *Plans for a global 3R network?*

### European 3R centres

Map:  
[norecopa.no/3REuropeOverview](http://norecopa.no/3REuropeOverview)

List of 3R centres:  
[norecopa.no/3REurope](http://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](http://Norecopa). Please report any errors or send suggestions for additions to [post@norecopa.no](mailto:post@norecopa.no)  
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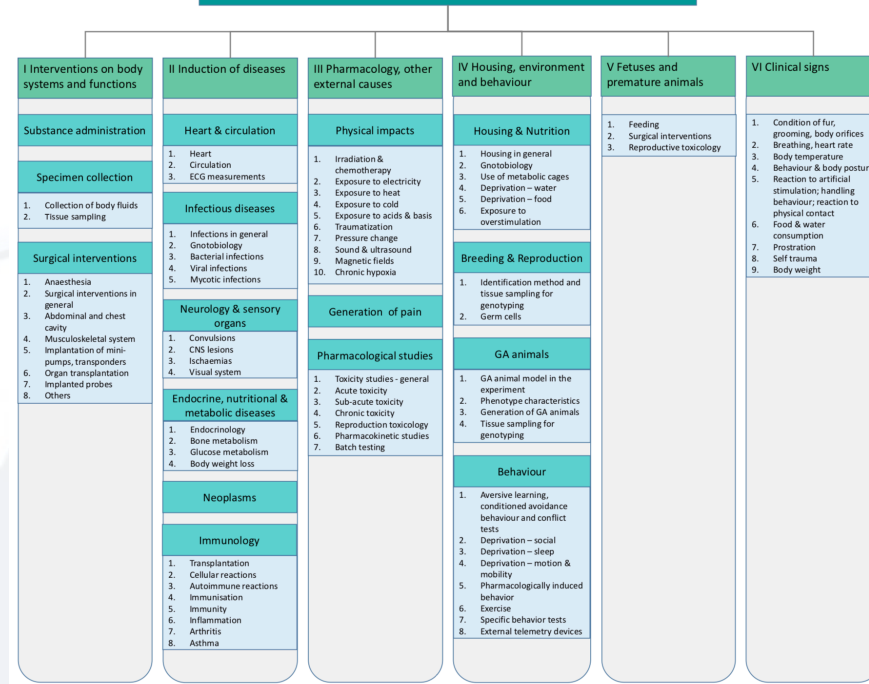
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# Mild, Moderate or Severe? A compilation of severity classification



[norecopa.no/severity](https://norecopa.no/severity)

## COMPILATION OF SEVERITY CLASSIFICATIONS ACROSS EUROPE



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Anne Zintzsch, Nikolaos Kostomitsopoulos & Jan-Bas Prins

**'One Europe': The challenge of consistency in severity classification**

Anne Zintzsch<sup>1</sup>, Adrian Smith<sup>2</sup>, Nikolaos Kostomitsopoulos<sup>3</sup> & Jan-Bas Prins<sup>4</sup>  
<sup>1</sup> UK Centre for Animal Welfare, University of Glasgow & Professorship for Laboratory Animal Science and Animal Welfare, Germany; <sup>2</sup> Norwegian Biomedical Research Association of the Academy of Health Sciences; <sup>3</sup> The French CNRS Institute, UK & London University Medical Centre, The Netherlands

<https://norecopa.no/severity>

**Background**  
 Severity classification is an important factor in the proper authorization of animal experiments and, accordingly, according to Directive 2003/60/EC. The requirement for a specific severity category needs careful evaluation of the impact on the animal and being 'to facilitate a common understanding and avoid decisions on a subjective basis, several guidelines are available on how experimental interventions could be classified. The guidelines are used by Animal Welfare Bodies (AWB) in a systematic way to assess the severity of procedures, such as cumulative severity, setting early end points or other alternatives, must be taken into account on a case-by-case basis, and they modify the recommended severity classification.

**Compilation as the first step**  
 As a first step in the efforts being made to harmonize severity classification, we have collected existing guidelines and developed their contents into tables, making it easier to compare them. Severity classifications have been included from:  
 • The UK Home Office  
 • The European Commission  
 • The Working Group of Berlin Animal Welfare Centres  
 • Others

**A compilation of severity classifications is available online**

The compilation gives an overview of systems currently in use in Europe. The severity classification of techniques and procedures, and the generally agreed laboratory animals.

**The way forward**  
 The next step is to review the severity classifications, add more guidance notes and include more examples of severity classifications those compiled by ELIAS working group. A systematic review of available literature is planned to supplement the compilation. Our aim is to offer a comprehensive tool to aid harmonization of severity classification. It may assist future decisions on severity classification, be utilised as the compilation, please see [www.norecopa.no/severity](http://www.norecopa.no/severity)

<sup>1</sup>Classification and reporting of severity experienced by animals used in scientific procedures. F12, ANA-51, ANE/ELAW Working Group report  
 David Smith, David Anderson, Anne Thompson, Daphne Cude, Bill, Ann C. O'Leary, Alison Evans, Marie-Thérèse Fournier, Brian Courtney, Sam M. O'Connell, Greta O'Connell, Cindy's Tapp, Hanna Maria Vignar, Laboratory Animals, vol. 52, 1, pp. 33-41, 2010. Published January 15, 2010.

<https://norecopa.no/severity>

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# Mild, Moderate or Severe? A compilation of severity classification



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

## COMPILATION OF SEVERITY CLASSIFICATIONS ACROSS EUROPE

I Interventions on body systems and functions	II Induction of diseases	III Pharmacology other external causes	IV Housing, environment and behaviour	V Foetuses and premature animals	VI Clinical signs
<b>Substance administration</b> 1. Subcutaneous 2. These varying	<b>Heart &amp; circulation</b> 1. Heart 2. Circulation 3. Circulation 4. Circulation	<b>Physical impacts</b> 1. Irradiation 2. Irradiation 3. Irradiation 4. Irradiation 5. Irradiation 6. Irradiation 7. Irradiation 8. Irradiation 9. Irradiation 10. Irradiation 11. Irradiation 12. Irradiation 13. Irradiation 14. Irradiation 15. Irradiation 16. Irradiation 17. Irradiation 18. Irradiation	<b>Housing &amp; Nutrition</b> 1. Housing 2. Nutrition 3. Nutrition 4. Nutrition 5. Nutrition 6. Nutrition 7. Nutrition 8. Nutrition 9. Nutrition 10. Nutrition 11. Nutrition 12. Nutrition 13. Nutrition 14. Nutrition 15. Nutrition 16. Nutrition 17. Nutrition 18. Nutrition	1. Foetus 2. Premature animals 3. Premature animals 4. Premature animals	1. Clinical signs 2. Clinical signs 3. Clinical signs 4. Clinical signs 5. Clinical signs 6. Clinical signs 7. Clinical signs 8. Clinical signs 9. Clinical signs 10. Clinical signs 11. Clinical signs 12. Clinical signs 13. Clinical signs 14. Clinical signs 15. Clinical signs 16. Clinical signs 17. Clinical signs 18. Clinical signs

The compilation covers

- > [Interventions on body systems and functions](#)
  - ▶ [Substance administration](#)
  - ▶ [Specimen collection](#)
  - ▶ [Surgical interventions](#)
- > [Induction of diseases](#)
  - ▶ [Heart and circulation](#)
  - ▶ [Infectious diseases](#)
  - ▶ [Neurology and sensory organs](#)
  - ▶ [Endocrine, nutritional and metabolic diseases](#)
  - ▶ [Neoplasms](#)
  - ▶ [Immunology](#)
- > [Pharmacology and other external causes](#)
  - ▶ [Physical impacts](#)
  - ▶ [Generation of pain](#)
  - ▶ [Pharmacological studies](#)
- > [Housing, environment and behaviour](#)
  - ▶ [Housing and nutrition](#)
  - ▶ [Breeding and Reproduction](#)
  - ▶ [GA animals](#)
  - ▶ [Behaviour](#)
- > [Foetuses and premature animals](#)
- > [Clinical signs](#)

Source	Non-harmful / below threshold / severity degree 0	Mild / severity degree 1	Moderate / severity degree 2	Severe / severity degree 3
<a href="#">Directive 2010/63/EU, Annex VIII</a>		Administration of substances via subcutaneous, intramuscular, intraperitoneal routes, gavage and intravenously via superficial blood vessels, where the substance has no more than mild impact on the animal, and the volumes are within appropriate size and species animal.	Frequent application of test substances which produce moderate clinical effects, and withdrawal of blood samples (> 10 % of circulating volume) in a conscious animal within a few days without volume replacement.	
<a href="#">Home Office (2014 a)</a>		Injection routes, i.e. intravenous or intramuscular, or intraperitoneal, and that the procedure is performed in accordance with the guidelines and that the needle size is followed) by these in the cul are no cu		
<a href="#">Federal Food Safety and Veterinary Office FSVO (2018)</a>	Single injection of small volumes s.c. and i.v. (species-specific), including repeated injections at long intervals (at least 24 hours).	I.v. or i.p. injections in sedated animals by catheter or tube and substances introduced into the body such as enemas. Implants and permanent accesses that can be created and used by means of a minimally invasive (superficial) procedure. Examples: Repeated iv or sc injection of small volumes (species-specific). Insertion of cannulae into peripheral blood vessels. Subcutaneous injection of tumour tissue. Single subcutaneous implantations of osmotic minipumps and transponders. Subcutaneously channelled venous catheters.	Repeated injections at short intervals (several times within 24 hours). Implants and permanent accesses that have to be created by means of a deep surgical procedure or causing mild long-term constraint on an animal. Examples: Chronic iv catheters. Duodenal infusion cannula. Hepatic portal vein catheter. Gastric tube or chronic intragastric infusion cannula. Intraperitoneal or intravenous osmotic minipumps. Gavage. Telemetry transmitters. Implanted iv catheters with pumps in a jacket worn by dogs. Implantation of indwelling catheters in	Implants and permanent accesses that have to be created by means of a deep surgical procedure and causing severe long-term strain on an animal. Examples: Attachment of implants on the locomotor apparatus or other large implants that restrict movement (e.g. dorsal skinfold chamber in mice), implantation of catheters in the abdominal aorta or bile duct. Implantation of an arterial blood-pressure catheter in the aortic arch via the left carotid artery or in the abdominal aorta via the femoral artery. Implantation of a combination of a venous and arterial catheter.





**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)<sup>1</sup>, N Dennison<sup>2</sup>, G Goodman<sup>3</sup>, S Hetherington<sup>4</sup>, S Llywelyn-Jones<sup>5</sup>, K Ryder<sup>6</sup> and A J Smith<sup>6</sup>**

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Corresponding author: P Hawkins. Email: phawkins@rpa.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 severity classes of 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](http://www.norecopa.no/categories)) where more information on severity classification for procedures using fish, including field research, will be made available.

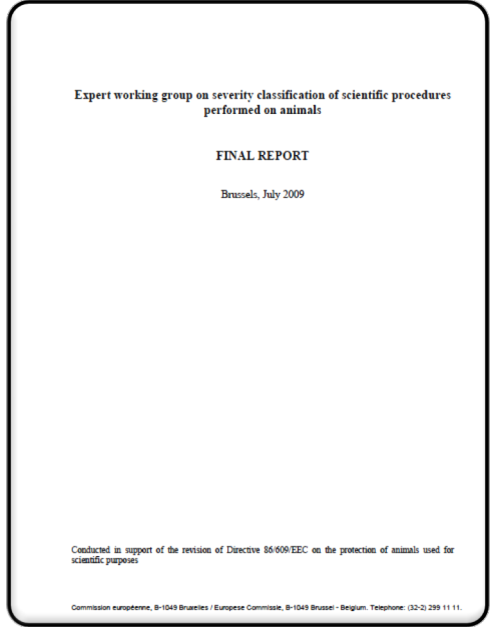
**Keywords:** Fish, harm-benefit assessment, humane endpoints, refinement, severity  
**Laboratory Animals** 2011; 1-6. DOI: 10.1258/la.2011.010181

**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<sup>1</sup> which is now an integral part of the legislation on animal research and testing in many countries. Predictions of animal welfare 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.<sup>2</sup> 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



[http://ec.europa.eu/environment/chemicals/lab\\_animals/pdf/report\\_ewg.pdf](http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf)

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

Laboratory Animals, 45: 219-224, 2011  
[norecopa.no/categories](http://www.norecopa.no/categories)

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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.



NATURE | NEWS

## Animal studies produce many false positives

Examination of neurological disease research shows pervasive 'significance bias'.

Heidi Ledford

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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

## 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

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## There are many guidelines for *reporting* animal studies

- 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** (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



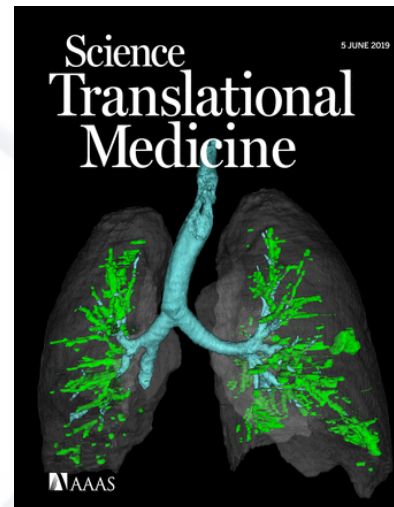
norecopa



## PREPARE *from day 1*

## ARRIVE

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



<https://www.dreamstime.com>

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Original Article

**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

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



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

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## **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**

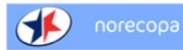
9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Items in pink are  
not highlighted in  
ARRIVE

# A downloadable checklist



## 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 9HS, 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<sup>1</sup> 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 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
<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"/> Decide upon databases and information specialists to be consulted, and construct search terms. <input type="checkbox"/> 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. <input type="checkbox"/> Assess the reproducibility and transatability 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"/> Address the 3Rs (replacement, reduction, refinement) and the 3Ss (good science, good sense, good sensibilities). <input type="checkbox"/> Consider pre-registration and the publication of negative results. <input type="checkbox"/> Perform a harm-benefit assessment and justify any likely animal harm. <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> Allocate a severity classification to the project. <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"/> Consider pilot studies, statistical power and significance levels. <input type="checkbox"/> Define the experimental unit and decide upon animal numbers. <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 evaluation	<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. Education and training	<input type="checkbox"/> 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	<input type="checkbox"/> Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. <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"/> Decide upon the characteristics of the animals that are essential for the study and for reporting. <input type="checkbox"/> Avoid generation of surplus animals.
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"/> Attend to the animals' specific instincts and needs, in collaboration with expert staff. <input type="checkbox"/> Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).
13. Experimental procedures	<input type="checkbox"/> Develop refined procedures for capture, immobilisation, marking, and release or rehoming. <input type="checkbox"/> Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	<input type="checkbox"/> Consult relevant legislation and guidelines well in advance of the study. <input type="checkbox"/> Define primary and emergency methods for humane killing. <input type="checkbox"/> Assess the competence of those who may have to perform these tasks.
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: 10.1177/002367217724823.
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](mailto:post@norecopa.no) | [@norecopa](#)

Norecopa: PREPARE for better Science

EUSAAT Congress, Linz, 10-13 October 2019



- 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



# Aviation and Animal Research: Human Factors

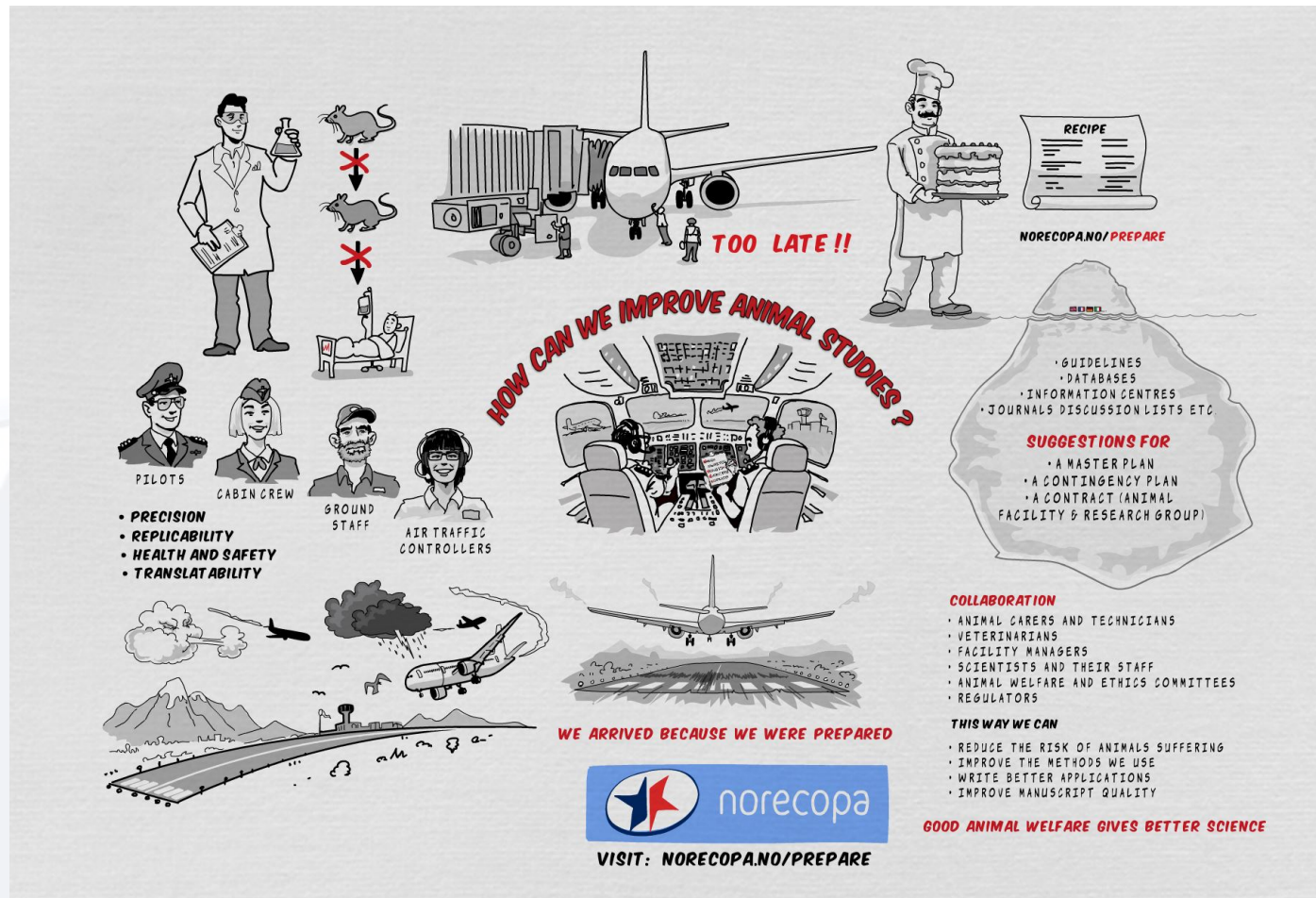


## **A Pilot's Perspective** **By Jake Hannabuss**

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

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


3-minute cartoon film



Norecopa: PREPARE for better Science

EUSAAT Congress, Linz, 10-13 October 2019



**PREPARE** 

**The PREPARE Guidelines Checklist**  
*'Planning Research and Experimental Procedures on Animals: Recommendations for Excellence'*  
 Adrian J. Smith, R. Eddie Clifton, Eilert Lilien, Kristine G. Au, Hansson & Trond Bratberg\*

\*Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0748 Oslo, Norway; \*Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, UK; \*Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwell, Nottingham, NG12 3JG, UK; \*Sector of Experimental Biomedicine, Department of Professor Anne-Claire Schoenenberger, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, P.O. Box 8148 Dep., 0203 Oslo, Norway; \*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†. 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
<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"/> Decide upon databases and information specialists to be consulted, and construct search strategies. <input type="checkbox"/> Assess the relevance of the species to be used, its biology and welfare, and the ethical and practical questions with the least suffering, and the most scientific value. <input type="checkbox"/> Assess the reproducibility of the study.
2. Level of care	<input type="checkbox"/> Consider the level of care and the 3Rs (Replacement, Reduction, Refinement) and the 3Ss (Good science, good sense, good standards). <input type="checkbox"/> Consider pre-approval and the publication of negative results. <input type="checkbox"/> Perform a harm-benefit assessment and justify any likely animal harm. <input type="checkbox"/> Discuss the learning objectives, if the animal use is for educational or training purposes. <input type="checkbox"/> Allocate a severity classification to the project. <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"/> Consider pilot studies, statistical power and significance levels. <input type="checkbox"/> Define the experimental unit and decide upon animal numbers. <input type="checkbox"/> Choose methods of randomisation, prevent observer bias, and decide upon inclusion and exclusion criteria.

[norecopa.no/prepare/prepare-checklist](https://norecopa.no/prepare/prepare-checklist)

Will you be an ambassador for PREPARE in your country or institution?

- ✓ **Coming together is a beginning**
- ✓ **Keeping together is progress**
- ✓ **Working together is success**



Danish 3R-Center  
**RRR**

Edward Everett Hale

## Are you PREPARED? How to Design Animal Experiments 17 September 2019 at NTNU

### DESCRIPTION

The PREPARE guidelines ([www.norecopa.no/PREPARE](http://www.norecopa.no/PREPARE)) offer a checklist for planning and conducting animal studies. Based on PREPARE, this course gives an overview of all topics you need to consider when planning your study. We will introduce you to resources which will ease your way to the optimal study design. The course contains lectures, tips and resources on the following topics:

**Literature searches:** Form a clear hypothesis, consider the use of systematic reviews, decide upon databases and assess the reproducibility and translatability of the project.

**Harm benefit analysis & severity classification:** Justify any likely animal harm and define objective, easily measurable and unequivocal humane endpoints. Allocate a severity classification to the project.

**Communication between scientists and the animal facility:** Good and clear communication is likely to be essential for the outcome of your study - but who should you talk to and what needs to be agreed upon?

**Experimental design:** How to decide on methods for evaluating data - before you conduct the study.

**Health monitoring and the impact of the microbiota and nutrition on animal studies:** Consider whether these factors are likely to influence your study.

**How to write a non-technical summary:** Short and understandable for laymen.

**Refinement of procedures:** Resources on refinement of the care and use of laboratory animals.

### EDUCATORS

**Adrian Smith** is the secretary of Norecopa and for many years worked as a professor at the Norwegian School of Veterinary Science. Adrian is one of the authors of the PREPARE guidelines.

**Axel Kornerup Hansen** is Professor & Head of the Section of Experimental Animal Models, University of Copenhagen. Axel's research focus is on reduction and refinement, in particular the impact of nutrition and microbiota on health and disease.

**Aurora Brønstad** is PhD, Chief Veterinarian & researcher at University of Bergen. Aurora is a SYRACLE Ambassador – from the Systematic review centre for Laboratory animal experimentation, Nijmegen, the Netherlands.

Adrian, Axel & Aurora have arranged and lectured at numerous courses in Laboratory Animal Science.

**Kirsten Bayer Andersen**, DVM, PhD. Scientific Affairs Manager at SCANBUR. Kirsten has been working for the Danish Animal Experiments Inspectorate and helped numerous researchers define humane endpoints, allocate severity classification and describe their research with lay man terms.

## One-day courses on the design of animal experiments



# An International Culture of Care Network

[norecopa.no/CoC](http://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**



### The International Culture of Care Network

Thomas Bertelsen, Novo Nordisk A/S, Denmark; Nikolaos Kostomitsopoulos, Biomedical Research Foundation Academy of Athens, Greece; Anja Petrie, University of Aberdeen, UK; Adrian Smith, Norecopa, Norway

**Background**

Recital 31 of the Directive 2010/63/EU states that breeders, suppliers and users of research animals should have an animal-welfare body which fosters a **climate of care** and provides tools for implementation of the 3Rs. Many user establishments use the phrase 'Culture of Care' on their websites, but no clear definition of this exists.

**Network**

Efficiently create a culture of care that continuously improves the quality of life of laboratory animals. This requires a strong commitment and a willingness to go beyond the status quo. The network will be useful for all those who are interested in this.

**Our members**

The network consists of people with a large range of backgrounds:

- Laboratory animal scientists & technicians
- Laboratory animal veterinarians
- Members of Animal Welfare Bodies & National Committees
- Representatives of National competent authorities
- Communications experts
- Members of animal welfare organisations

This diversity of competency and perspectives ensures that the network encourages a culture of care both for the animals used in research and those working with them.

We are currently 28 members in 14 countries.

**Interested in joining?**

Members are expected to work actively with Culture of Care. Please contact Thomas Bertelsen ([tb@novonordisk.com](mailto:tb@novonordisk.com))

**References:**

- M H Lloyd, B W Foden, S E Wolfensohn. Refinement: promoting the three Rs in practice. *Laboratory Animals* 2008; 42:284-293
- J Klein, K A Bayne: Establishing a Culture of Care. *ILAR Journal* 2007; 48(1):3-11
- H Herzog: Ethical Aspects of Relationships Between Humans and Research Animals. *ILAR Journal* 2002; 43(1):27-32
- <https://norecopa.no/alternatives/culture-of-care>
- [http://ec.europa.eu/environment/chemicals/lab\\_animals/pubs\\_guidance\\_en.htm](http://ec.europa.eu/environment/chemicals/lab_animals/pubs_guidance_en.htm)

## The challenge of academic research





## The challenge of academic research



**We need to disseminate an updated version of the  
Three Rs**

- not just a reduction in inhumanity**
- not just refinement of existing animal models**





Food for Thought ...

## Beyond the 3Rs: Expanding the Use of Human-Relevant Replacement Methods in Biomedical Research

Kathrin Herrmann<sup>1</sup>, Francesca Pistollato<sup>2</sup> and Martin L. Stephens<sup>1</sup>

<sup>1</sup>Johns Hopkins University, Bloomberg School of Public Health, Center for Alternatives to Animal Testing (CAAT), Baltimore, MD, USA; <sup>2</sup>European Commission, Joint Research Centre (JRC), Ispra, Italy

### Abstract

This year marks the 60<sup>th</sup> anniversary of Russell and Burch's pioneering book, *The Principles of Humane Experimental Technique*. Their 3Rs framework has helped to inspire humane and scientific progress in experimental technique. However, it is time to update its strategic application. The 21<sup>st</sup> century has already seen the development of promising, high-tech non-animal models, such as organs-on-a-chip and computational approaches that, in our view, will replace animals as the default option in biomedical experimentation. How fast this transition will take place will depend on the pace at which these new models are optimized to reflect the biology of humans, rather than that of non-human animals. While the new methods are likely to reshape all areas in which animals are currently used in science, we particularly encourage their application in biomedical research, which accounts for the bulk of animals used. We call for the pursuit of a three-prong strategy that focuses on (1) advancing non-animal methods as replacements of animal experiments, (2) applying them to biomedical research, and (3) improving their relevance to human biology. As academics and scientists, we feel that educational efforts targeted at young scientists in training will be an effective and sustainable way to advance this vision. Our strategy may not promise an imminent end to the use of animals in science, but it will bring us closer to an era in which the 3Rs are increasingly perceived as a solution to a receding problem. Russell and Burch themselves surely would have welcomed these positive changes.

### 1 Introduction

*The Principles of Humane Experimental Technique*, the landmark book that gave us the 3Rs framework of replacement, reduction, and refinement, turns 60 this year. First published in 1959, *Principles* was the outcome of a project spearheaded by the Universities Federation for Animal Welfare (UFAW), overseen by a committee that included future Nobel Prize-winning scientist Peter Medawar, and carried out by the British scientists William Russell and Rex Burch (Russell and Burch, 1959). The 3Rs framework helped to inspire and guide humane progress in experimental technique during the second half of the 20<sup>th</sup> century and beyond (Stephens and Mak, 2013; Balls et al., 2019).

The 60<sup>th</sup> anniversary of *Principles* falls in the midst of substantial developments in non-animal methods, i.e., potential replacement technology. Indeed, scientific experimentation is at the cusp of a new era of techniques hardly imagined in the mid-

20<sup>th</sup> century. Relevant techniques include (among others) organs-on-a-chip (microdevices containing cells and fluids intended to simulate physiological processes in organs); organoids (three-dimensional spheroids containing multiple cell types and intended to simulate physiological processes); high-throughput systems (rapid screening of large numbers of chemicals for biological activity against panels of different cells or biomolecules); induced pluripotent stem cells (adult cells that have been genetically reprogrammed to an embryonic stem cell-like state); and computational modeling (using computation to study the behavior of complex systems).

In our view, these methods (and no doubt others in various stages of development) have the potential to replace the use of animals as the default option in both safety testing and biomedical research. That is, these methods will come to comprise the rule, with animal experiments being the exception. This is consistent with Dutch efforts to expeditiously end animal experi-

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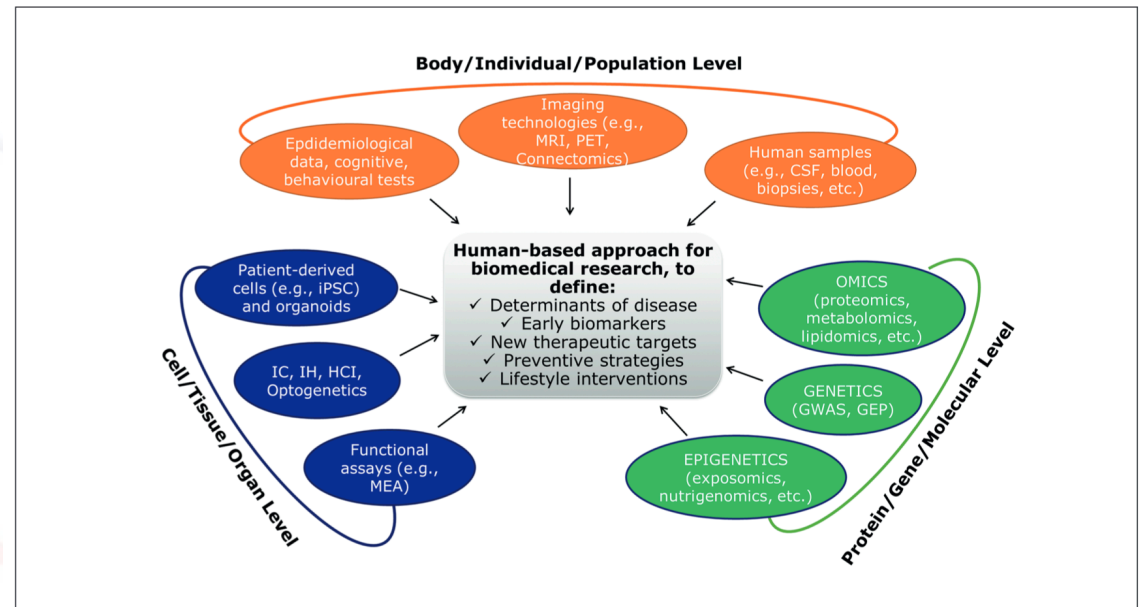
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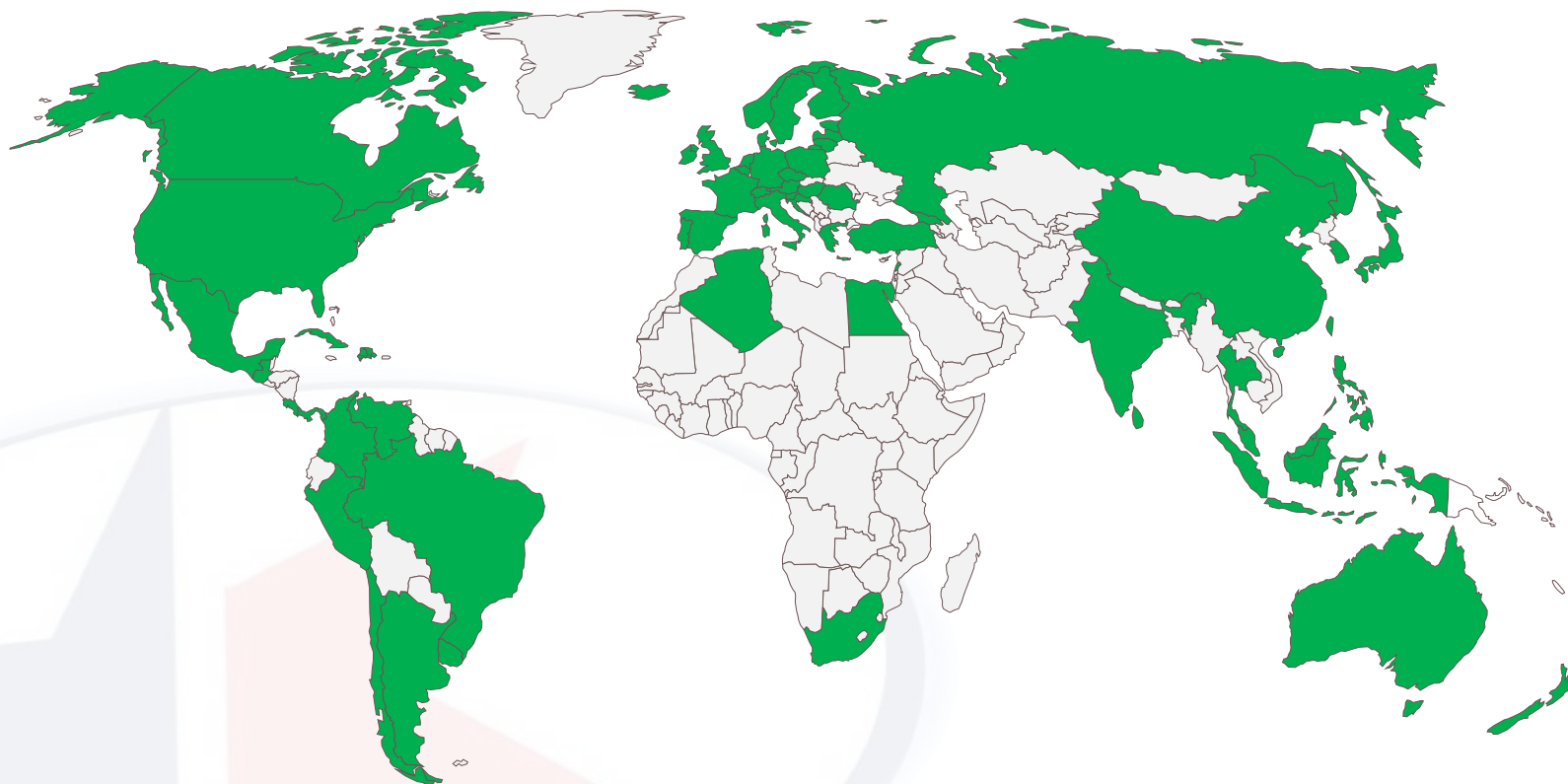
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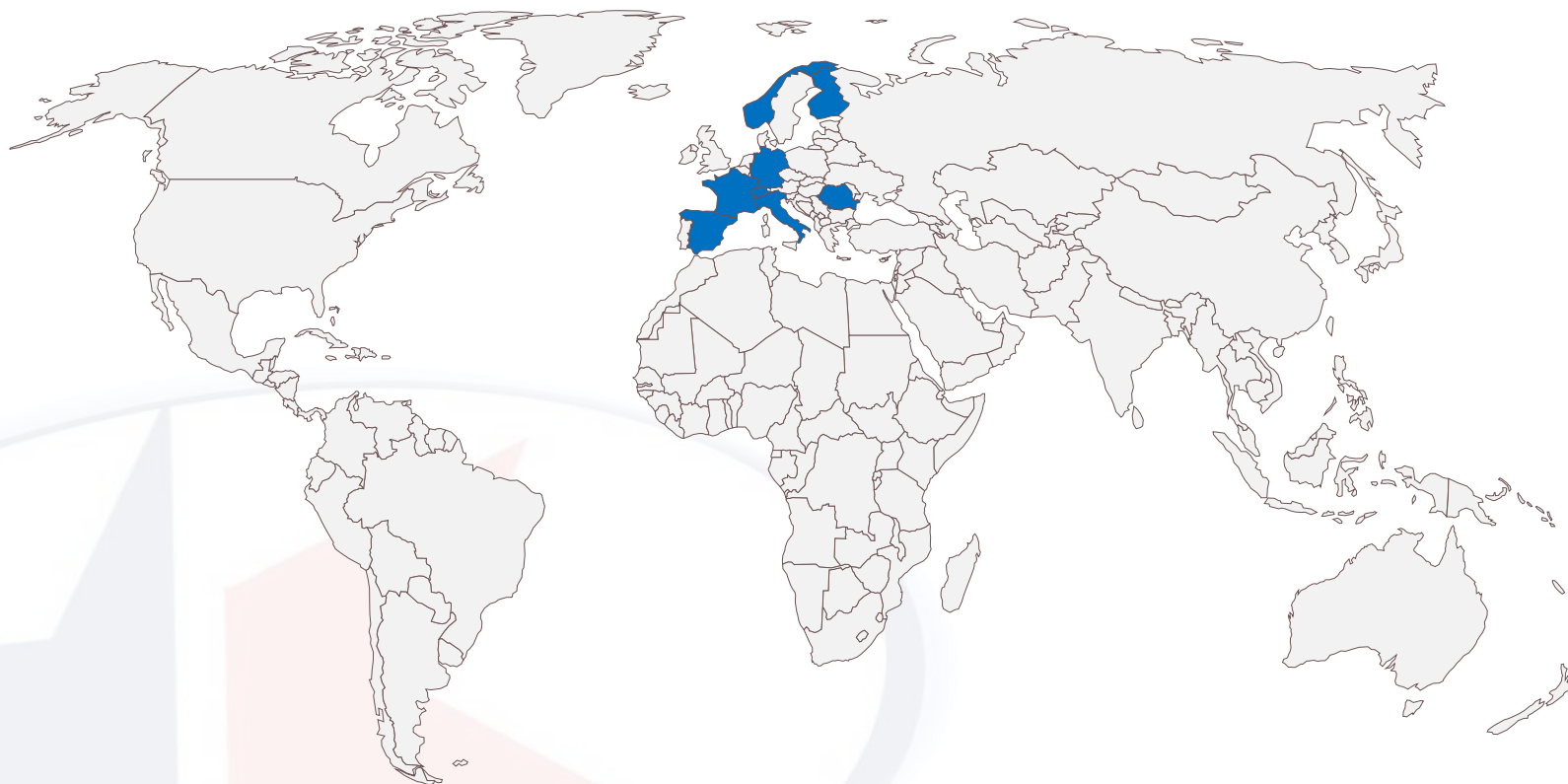
1. Advancing non-animal methods
2. Applying them to basic research
3. Improving their relevance to human biology

A more human-based approach to science, rather than refinement of animal models





**Countries with a LAS organisation or affiliated to a regional organisation**



**8 National Consensus Platforms affiliated to *ecopa***

**I am only one, but I am one.**

**I can't do everything, but I can do something.**

**The something I ought to do, I can do.**

**And by the grace of God, I will.**

Edward Everett Hale

## Thanks to Norecopa's main sponsors:



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