Norecopa:

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

norecopa.no/Linz2019

Adrian Smith
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https://norecopa.no

Coming together is a beginning

Keeping together is progress

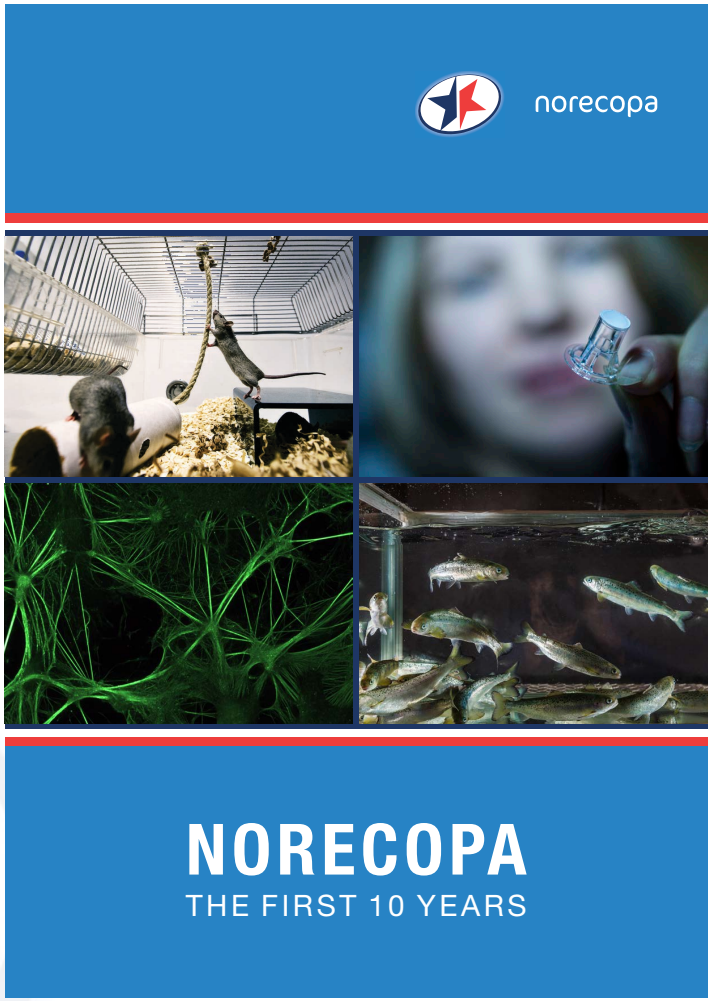
Working together is success

Edward Everett Hale

Norecopa:

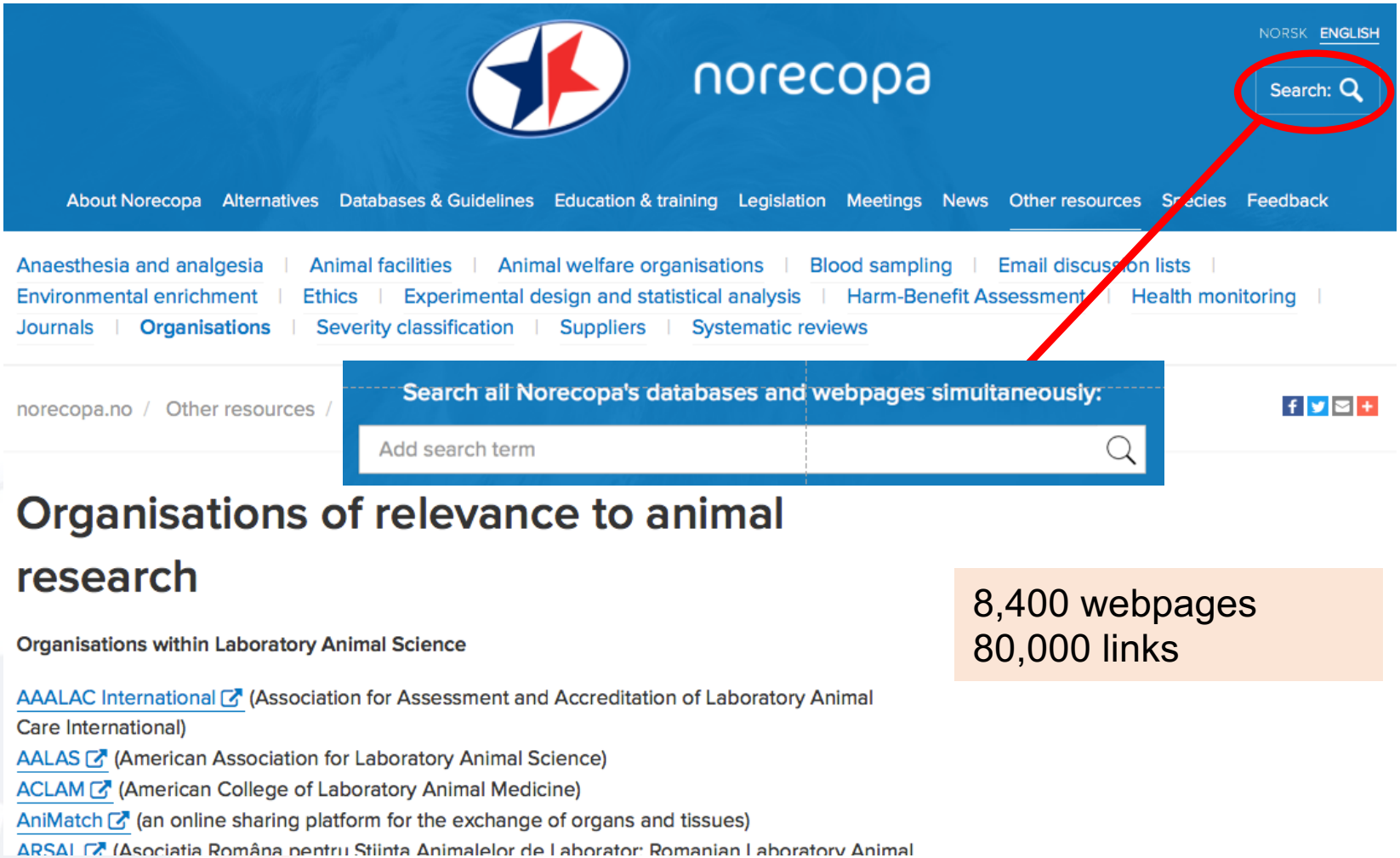
Norway's consensus platform for the 3Rs

founded 10.10.2007



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

norecopa.no

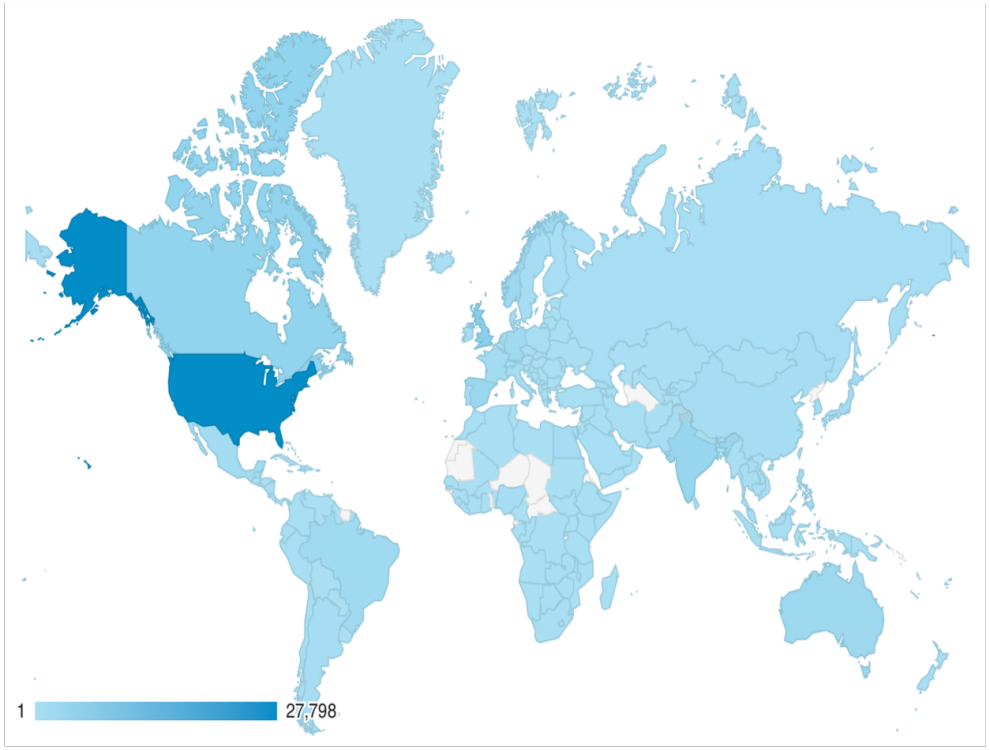


8,400 webpages
80,000 links

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

nbcnews.com

Red Adair



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

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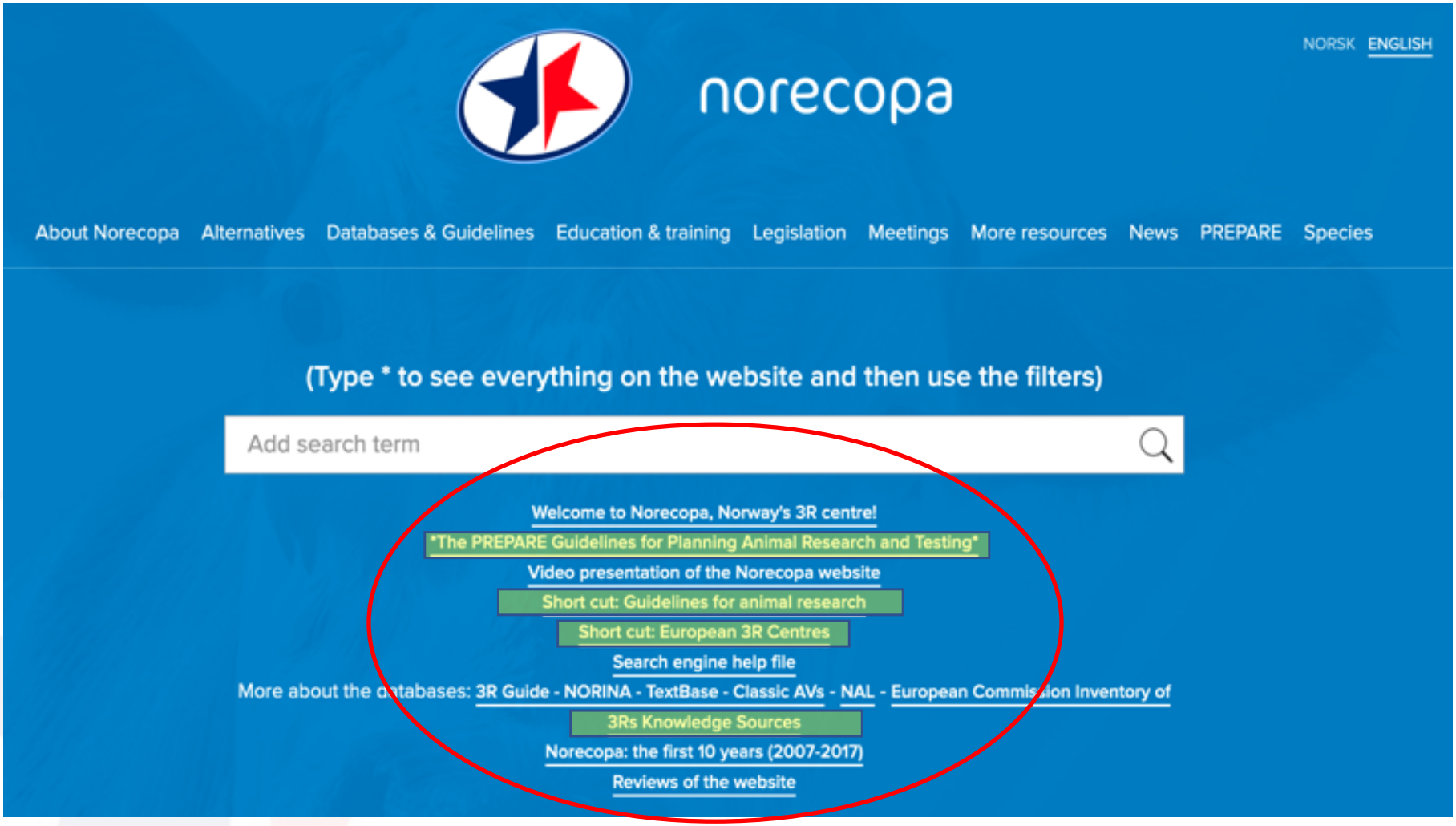
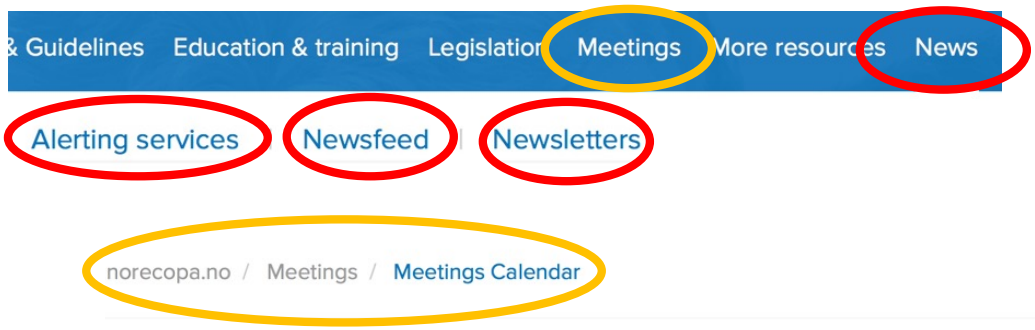
norecopa.no


NORSK ENGLISH
norecopa
About Norecopa Alternatives Databases & Guidelines Education & training Legislation Meetings More resources News PREPARE Species
(Type * to see everything on the website and then use the filters)
Add search term
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



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

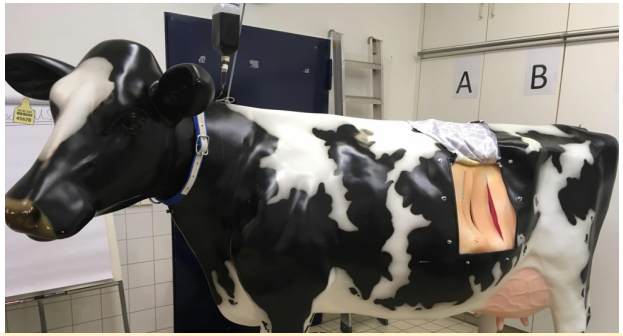
Harmonisation of the Care and Use of:

- *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



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

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

EURL ECVAM

Edward Everett Hale

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

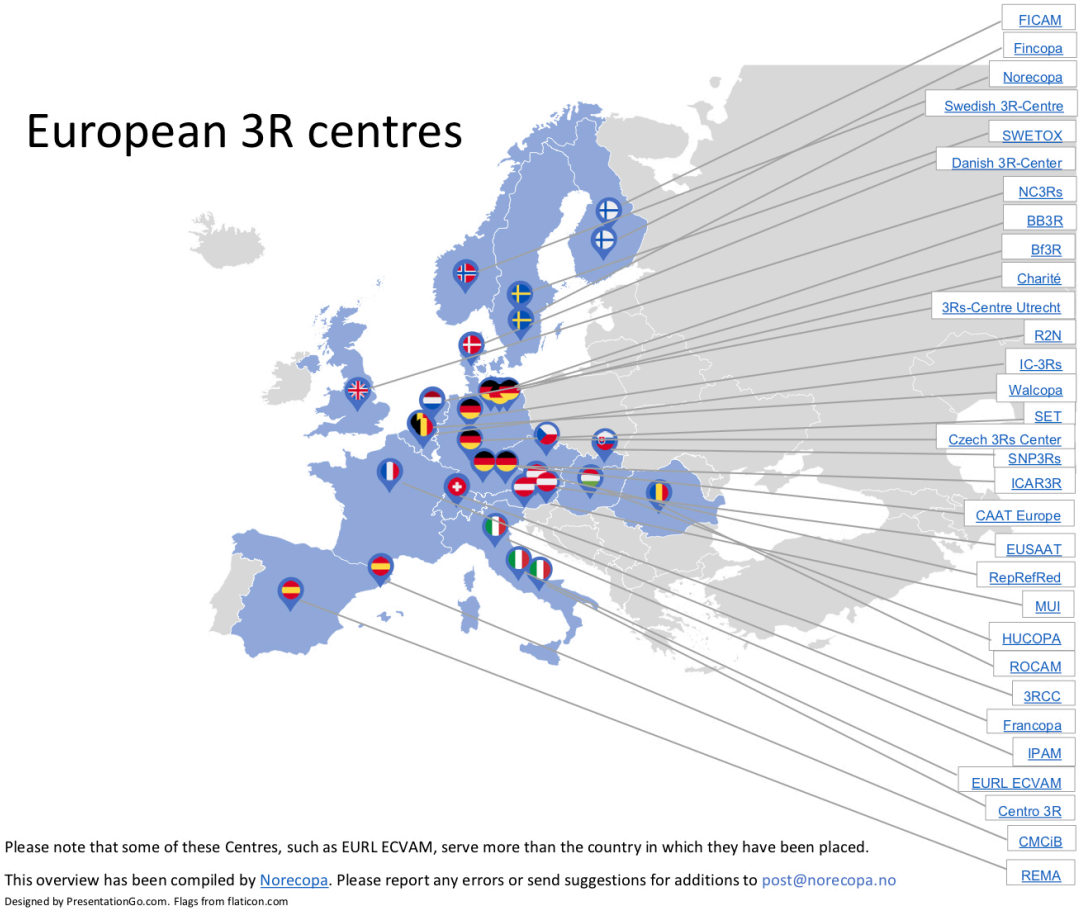
Edward Everett Hale

Interactive map of European 3R Centres

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

Map:
norecopa.no/3REuropeOverview

List of 3R centres:
norecopa.no/3REurope



- **Coming together is a beginning**
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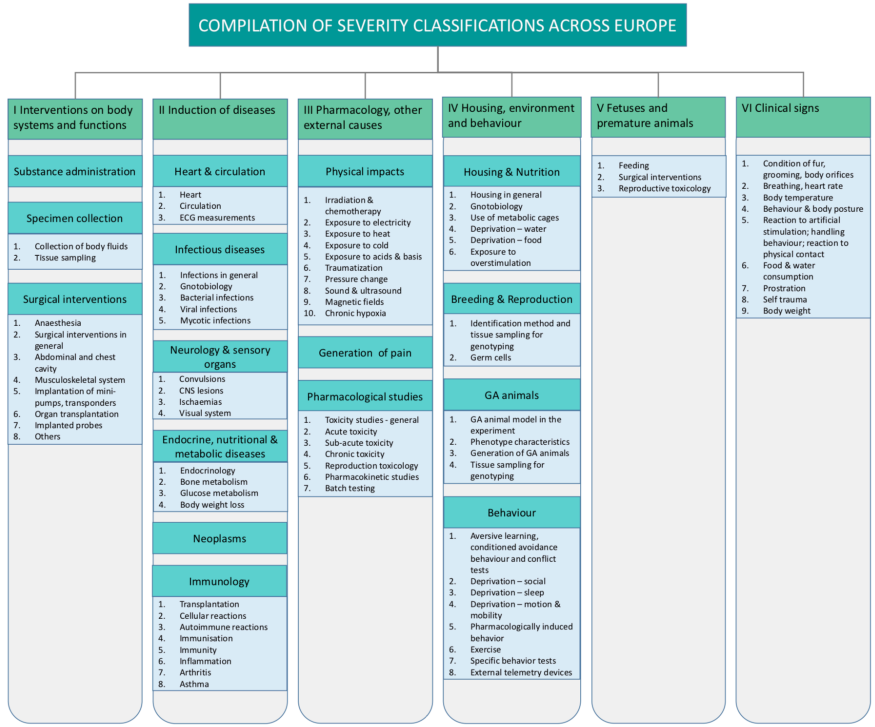
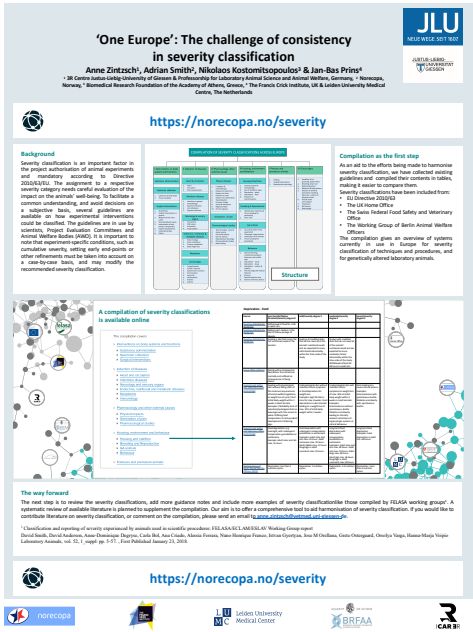
Edward Everett Hale

Mild, Moderate or Severe? A compilation of severity classification

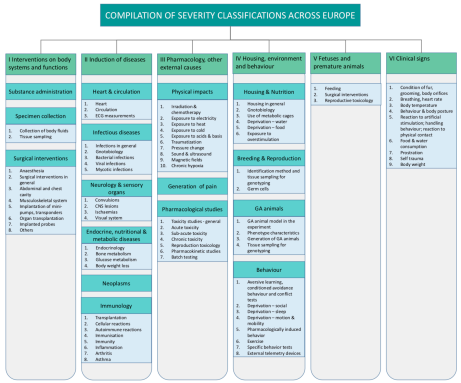
norecopa.no/severity

Anne Zintzsch, Nikolaos Kostomitsopoulos
& Jan-Bas Prins





Mild, Moderate or Severe? A compilation of severity classification

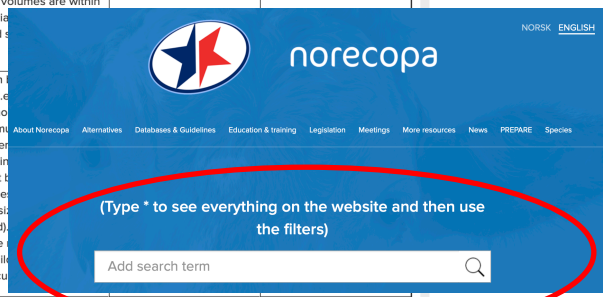


norecopa.no/severity

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
Directive 2010/63/EU, Annex VIII		Administration of substances by 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 appropria… size and s… 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.	
Home Office (2014 a)		Injection … routes, i.e … intraveno… or intramu… competen… performin… and that b… guideline… needle siz… followed)… by these … in the mil… are no cu…		
Federal Food Safety and Veterinary Office FSVO (2018)	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)[1], N Dennison[2], G Goodman[3], S Hetherington[4], S Llywelyn-Jones[5], K Ryder[2] and A J Smith[6]

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

Abstract

The severity classification of procedures using animals is an important tool to help focus the implementation of refinement and to assist in reporting the application of the 3Rs (replacement, reduction and refinement). The recently revised Directive that regulates animal research and testing within the European Union requires Member States to ensure that all procedures are classified as 'non-recovery', 'mild', 'moderate' or 'severe', using assignment criteria set out by the European Commission (EC). However, these are focused upon terrestrial species, so are of limited relevance to fish users. A Working Group set up by the Norwegian Consensus-Platform for the 3Rs (Norecopa) has produced guidance on the classification of severity in scientific procedures involving fish, including examples of 'subthreshold', 'mild', 'moderate', 'severe' and 'upper threshold' procedures. The aims are to complement the EC guidelines and help to ensure that suffering in fish is effectively predicted and minimized. Norecopa has established a website (www.norecopa.no/categories) where more information on severity classification for procedures using fish, including field research, will be made available.

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

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

Background

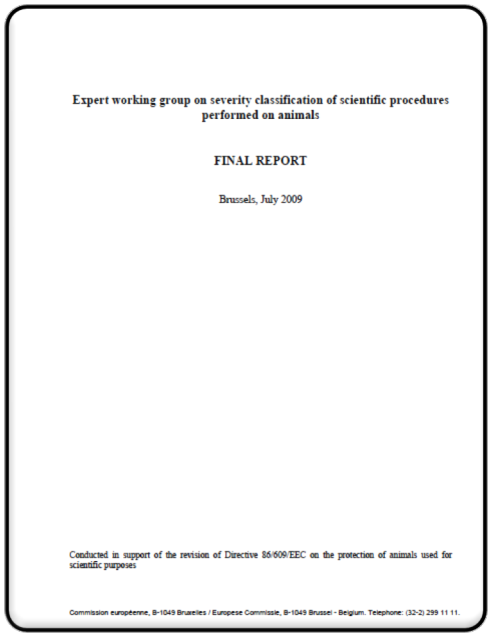
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because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

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

Laboratory Animals 2011; 1–6

Guidance on the severity classification of procedures involving fish

Report from a Working Group
convened by Norecopa



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

FINAL REPORT

Brussels, July 2009

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

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

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

NATURE | NEWS

Swiss survey highlights potential flaws in animal studies

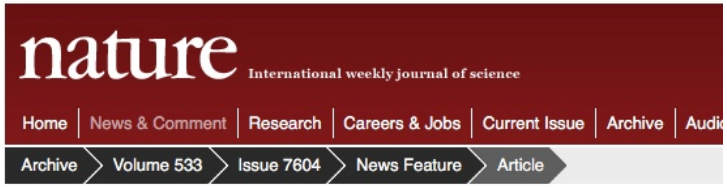
Poor experimental design and statistical analysis could contribute to widespread problems in reproducing preclinical animal experiments.

NATURE | NEWS

Animal studies produce many false positives

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

Heidi Ledford



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

There are many guidelines for *reporting* animal studies

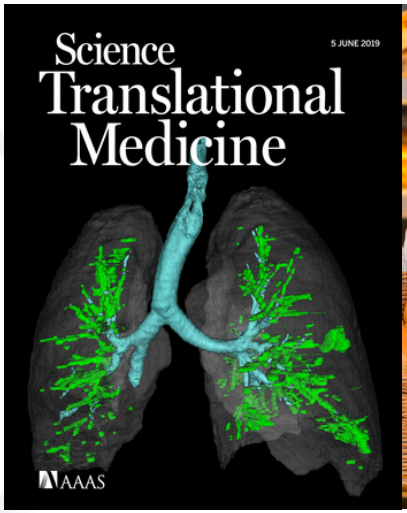
- Guidelines for specification of animals and husbandry methods when reporting the results of animal experiments (GV-SOLAS, 1985)
- Reporting animal use in scientific papers (Jane Smith *et al.)*, 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals,* 2000
- Guidelines for reporting the results of experiments on fish (2000)
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*, NC3Rs)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals

  e.g. Nature's Reporting Checklist

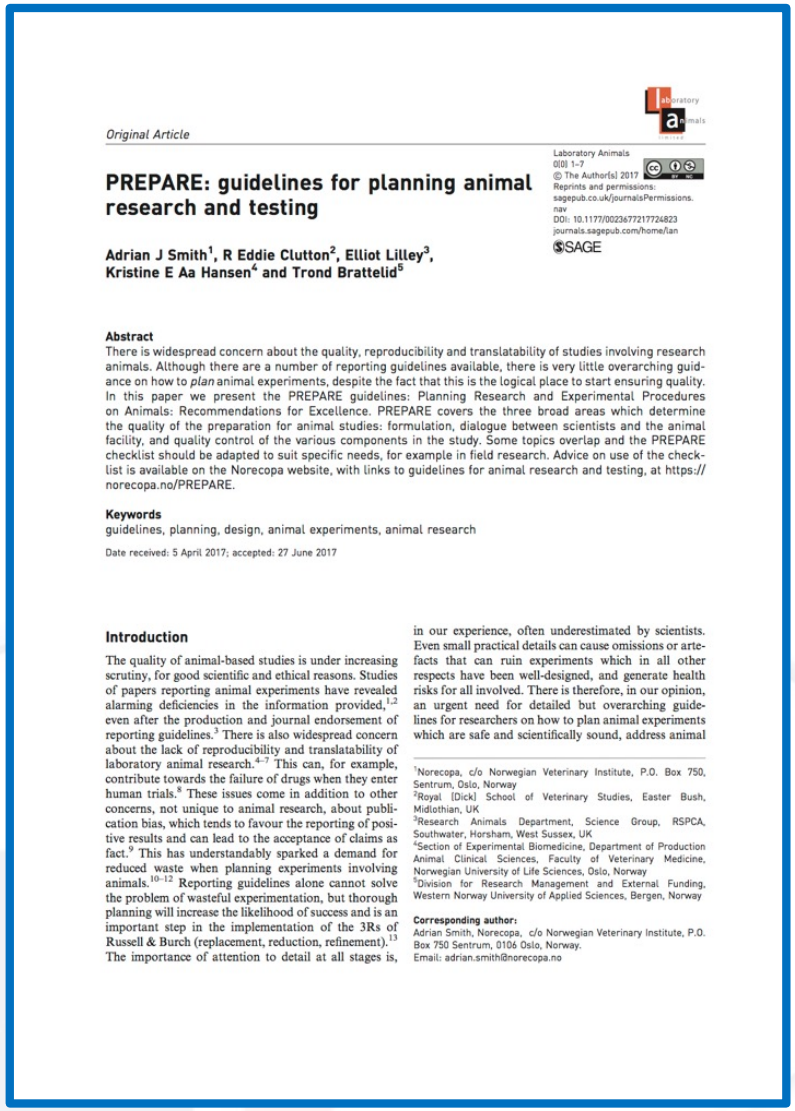
https://www.bls.gov/ooh/images/3077.jpg

PREPARE *from day 1*

ARRIVE



https://www.dreamstime.com



Original Article

PREPARE: guidelines for planning animal research and testing

Adrian J Smith[1], R Eddie Clutton[2], Elliot Lilley[3], Kristine E Aa Hansen[4] and Trond Brattelid[5]

Laboratory Animals
0(0) 1–7

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

Abstract

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

Keywords

guidelines, planning, design, animal experiments, animal research

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

Introduction

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

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[2]Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, UK
[3]Research Animals Department, Science Group, RSPCA, Southwater, Horsham, West Sussex, UK
[4]Section of Experimental Biomedicine, Department of Production Animal Clinical Sciences, Faculty of Veterinary Medicine, Norwegian University of Life Sciences, Oslo, Norway
[5]Division for Research Management and External Funding, Western Norway University of Applied Sciences, Bergen, Norway

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

https://doi.org/10.1177/0023677217724823

UFAW
Established 1926

Over 10,000 downloads from the journal website so far

Also downloadable from
norecopa.no/PREPARE

PREPARE:

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

PREPARE covers 15 topics:

Formulation of the study

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

Dialogue between scientists and the animal facility

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

Methods

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

Items in pink are not highlighted in ARRIVE

A downloadable checklist

PREPARE

norecopa

The PREPARE Guidelines Checklist

Planning Research and Experimental Procedures on Animals: Recommendations for Excellence

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

[a]Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway; [b]Royal (Dick) School of Veterinary Studies, Easter Bush, Midlothian, EH25 9RG, U.K.; [c]Research Animals Department, Science Group, RSPCA, Wilberforce Way, Southwater, Horsham, West Sussex, RH13 9RS, U.K.; [d]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; [e]Division for Research Management and External Funding, Western Norway University of Applied Sciences, 5020 Bergen, Norway.

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

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

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

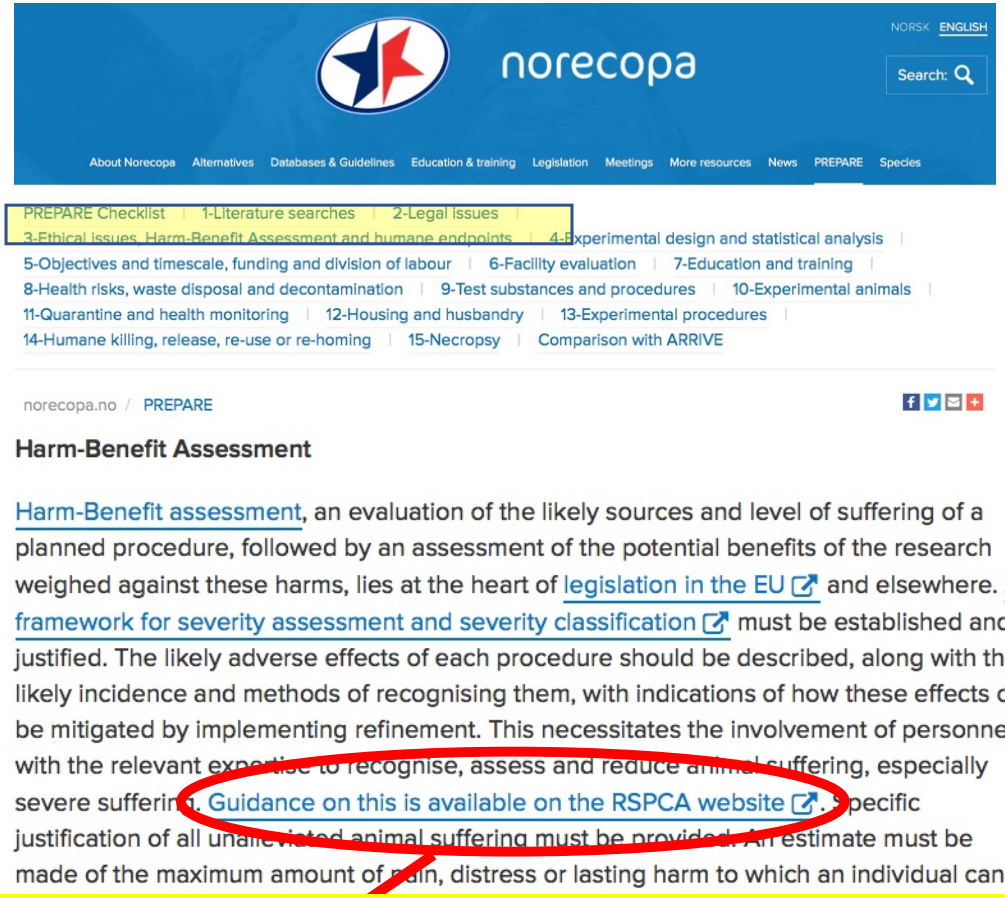
Topic	Recommendation
(A) Formulation of the study	
1. Literature searches	☐ Form a clear hypothesis, with primary and secondary outcomes. ☐ Consider the use of systematic reviews. ☐ Decide upon databases and information specialists to be consulted, and construct search terms. ☐ Assess the relevance of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

References

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

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

norecopa.no/PREPARE



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

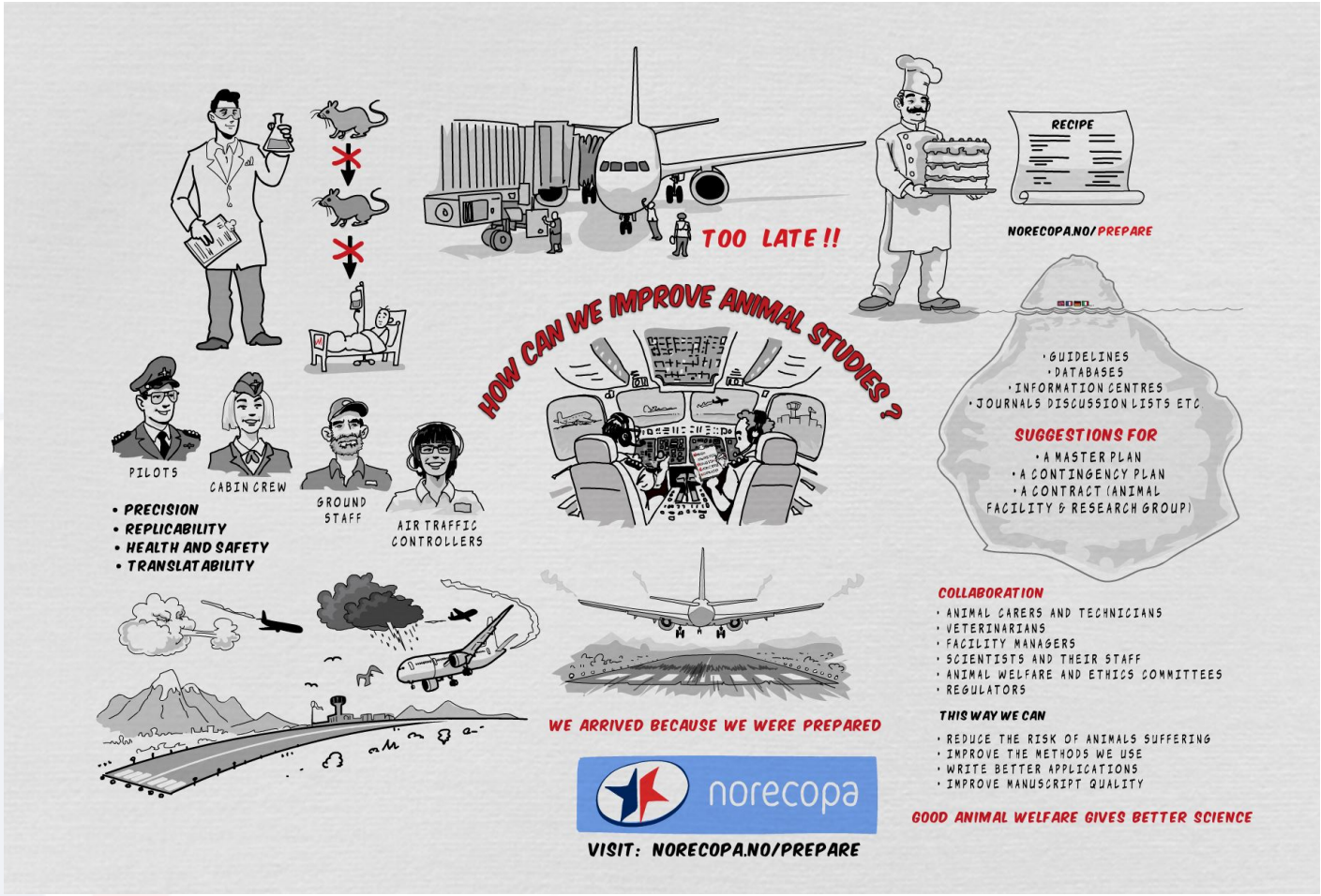
A Pilot's Perspective

By Jake Hannabuss

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

vimeo.com/358069203 or norecopa.no/PREPARE

3-minute cartoon film



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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**

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

DESCRIPTION
The PREPARE guidelines (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 SYRCLE Ambassador – from the Systematic review centre for Laboratory animal experimentation, Nijmegen, the Netherlands.

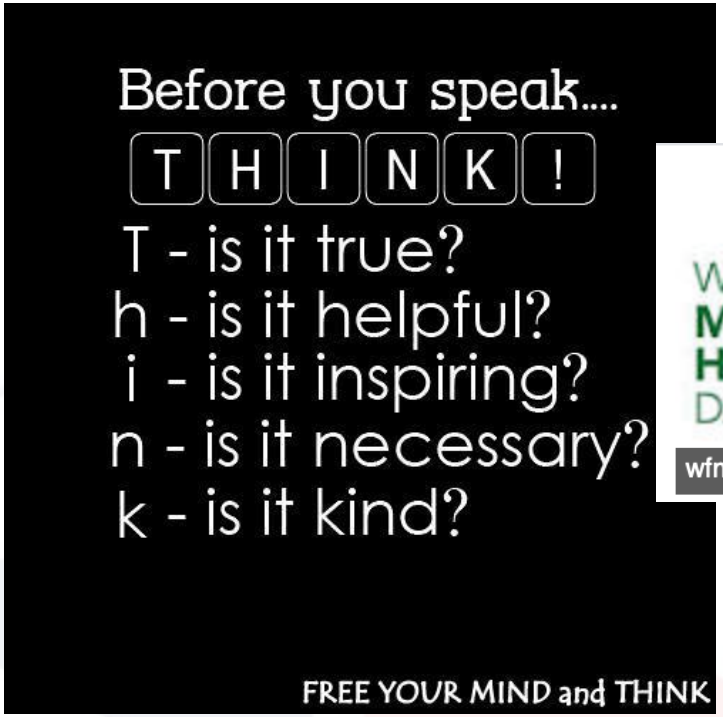
Adrian, Axel & Aurora have arranged and lectured at numerous courses in Laboratory Animal Science.

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



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[1], Francesca Pistollato[2] and Martin L. Stephens[1]

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

Abstract

This year marks the 60th 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 21st 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 20th century and beyond (Stephens and Mak, 2013; Balls et al., 2019).

The 60th 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-20th 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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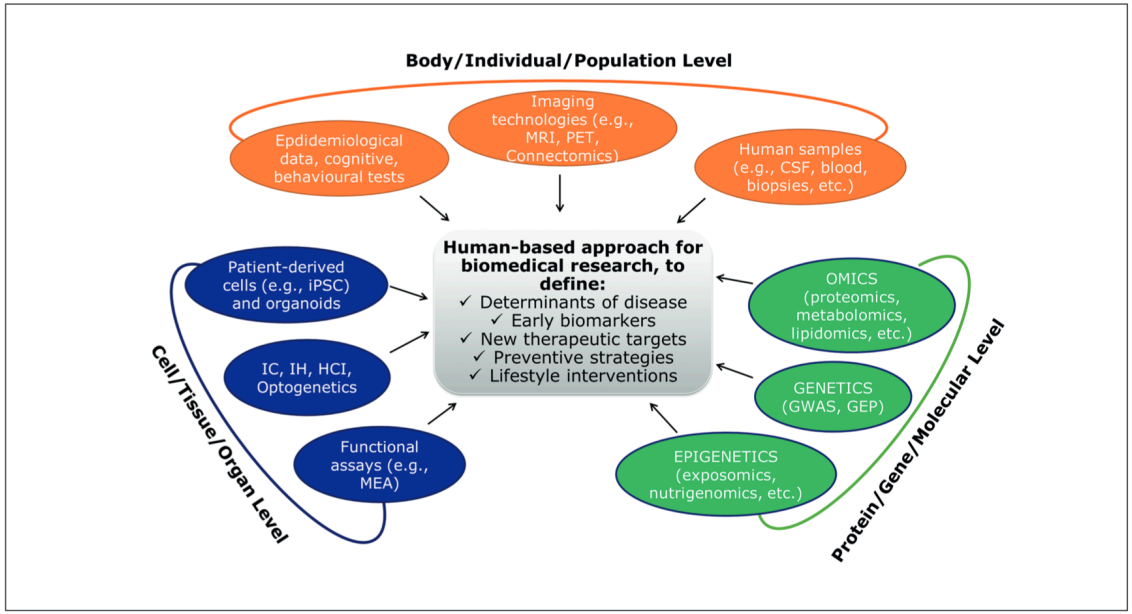
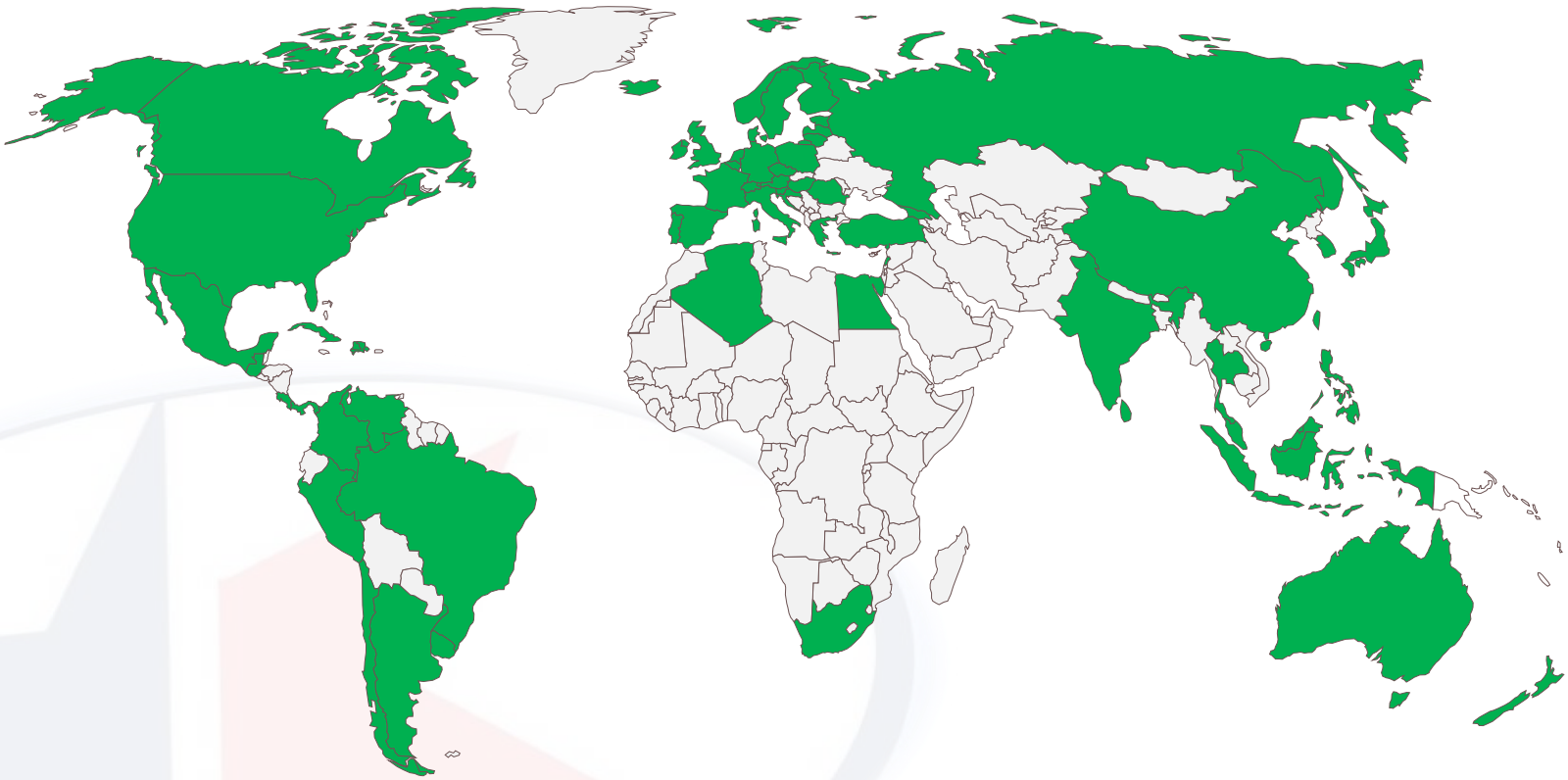
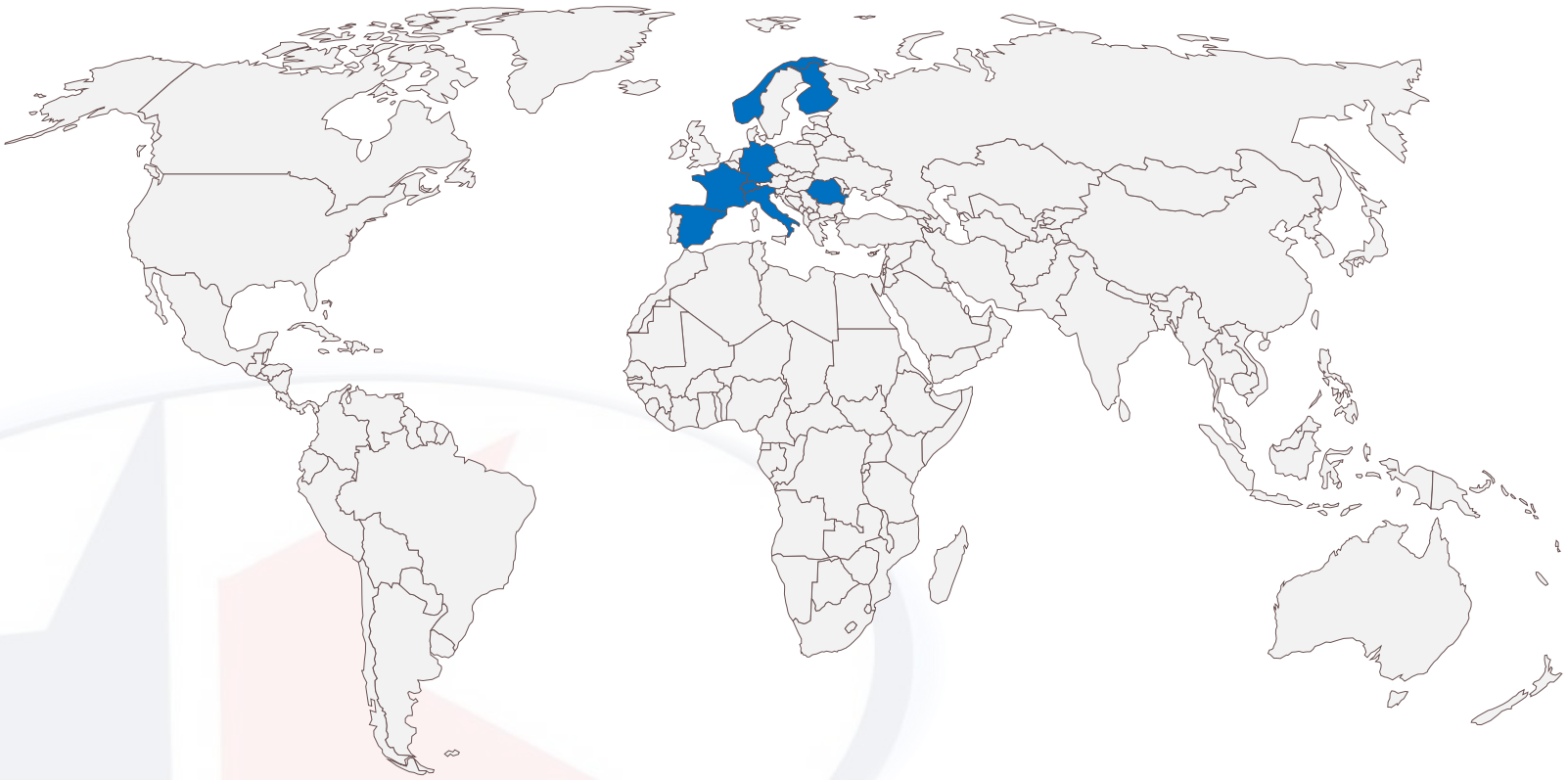
1. Advancing non-animal methods
2. Applying them to basic research
3. Improving their relevance to human biology

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

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