Ethics, animal welfare and the 3Rs:

An effective Culture of Care

norecopa.no/ESLAV2018

Adrian Smith

adrian.smith@norecopa.no

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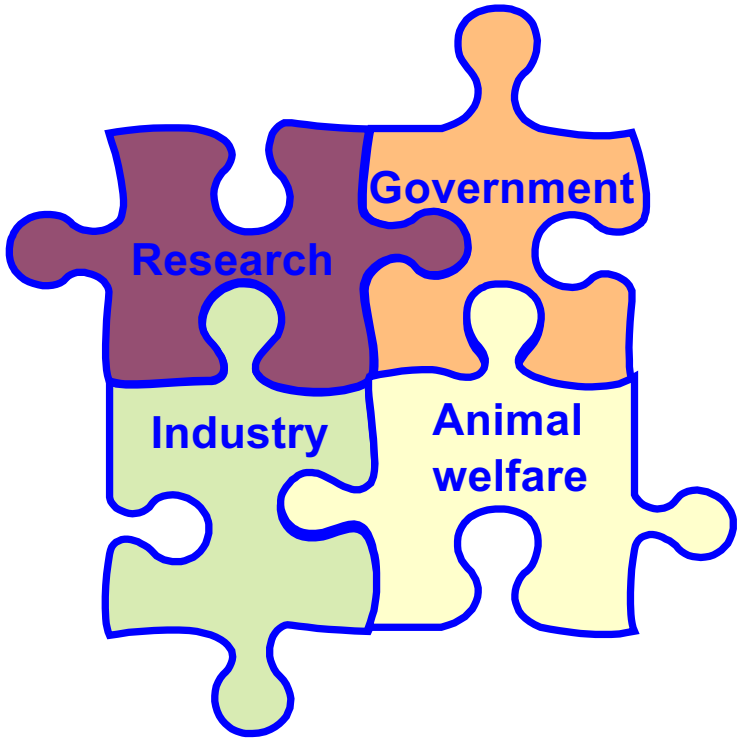
Norecopa

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

European Consensus-Platform for Alternatives

ecopa.eu

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



International consensus meetings

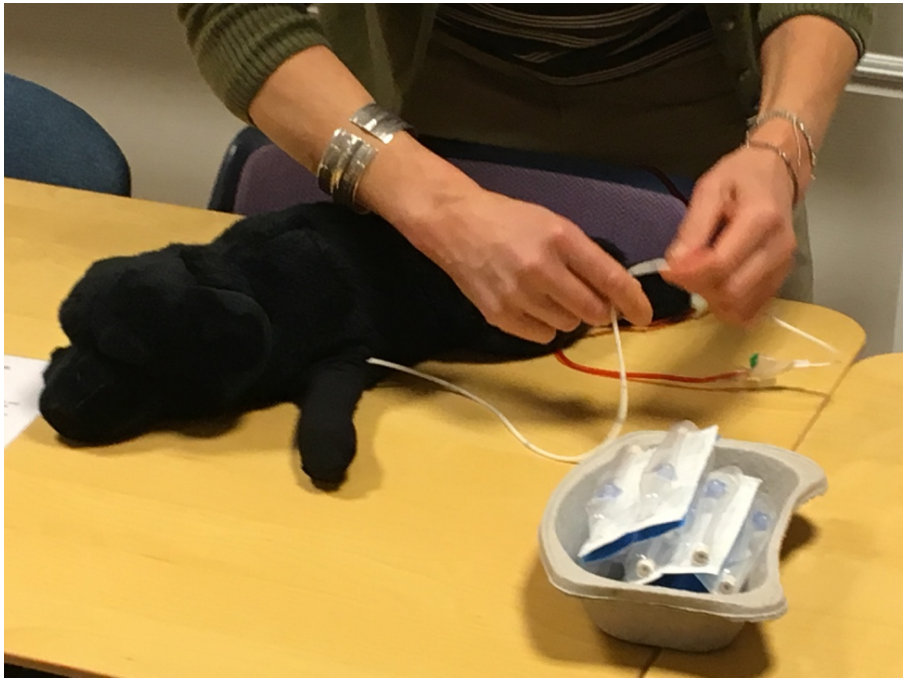
Harmonisation of the Care and Use of:

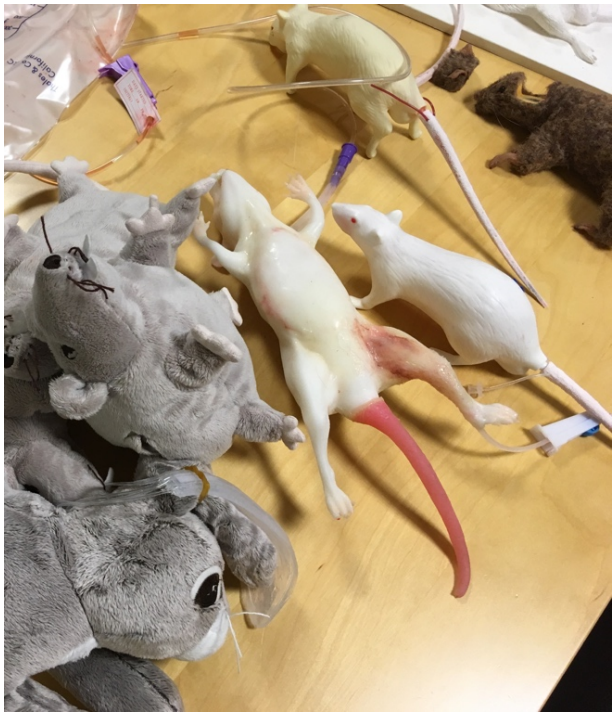
Fish (2005)
Wildlife (2008)
Fish (2009)
Agricultural animals (2012)
Wildlife (2017)

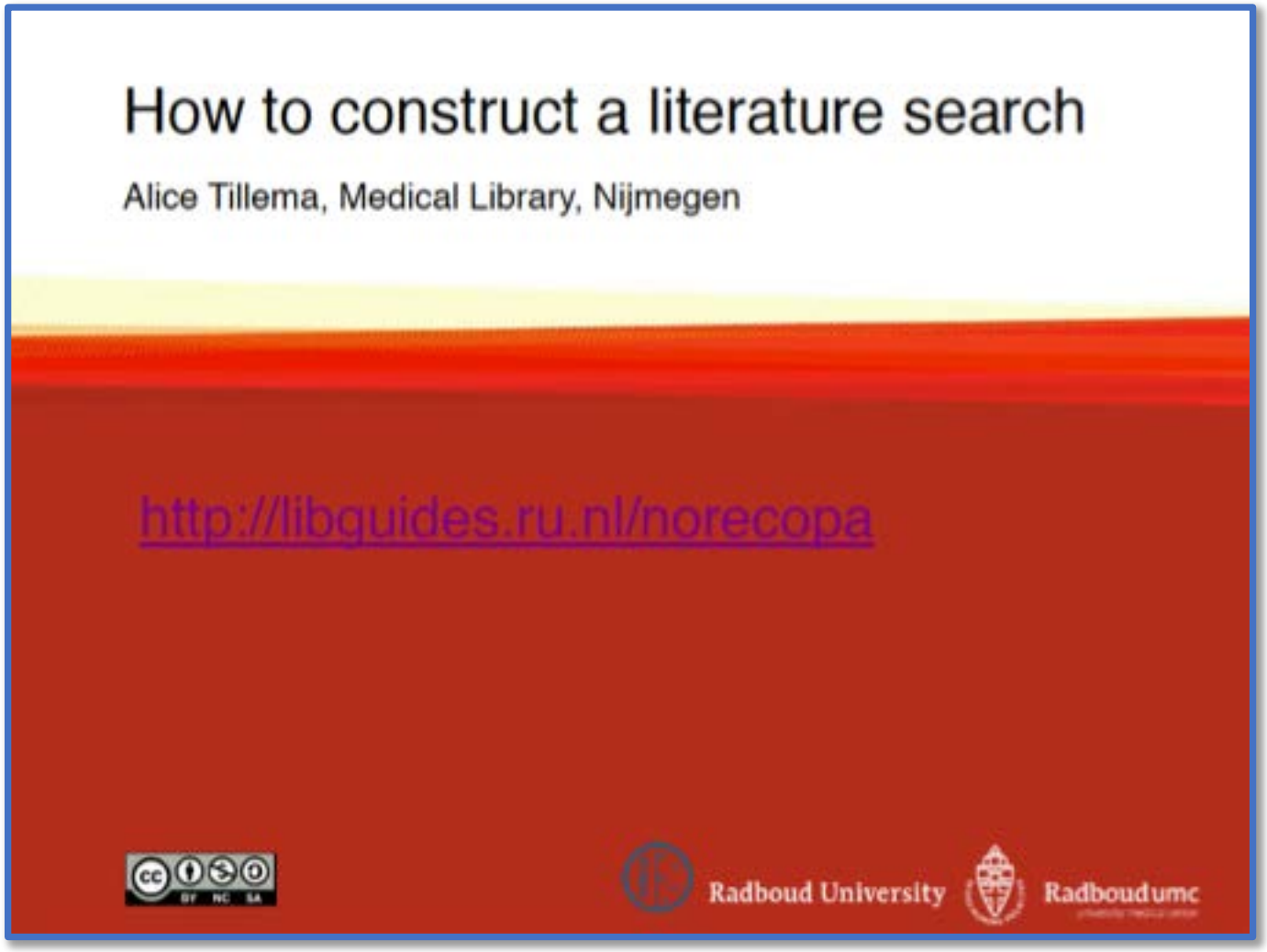
All the presentations + lectures at Norecopa's Annual Meetings on the web:

a lasting resource

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







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

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]

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. This aims 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; 1–8; DOI: 10.1258/la.2011.010101

Background

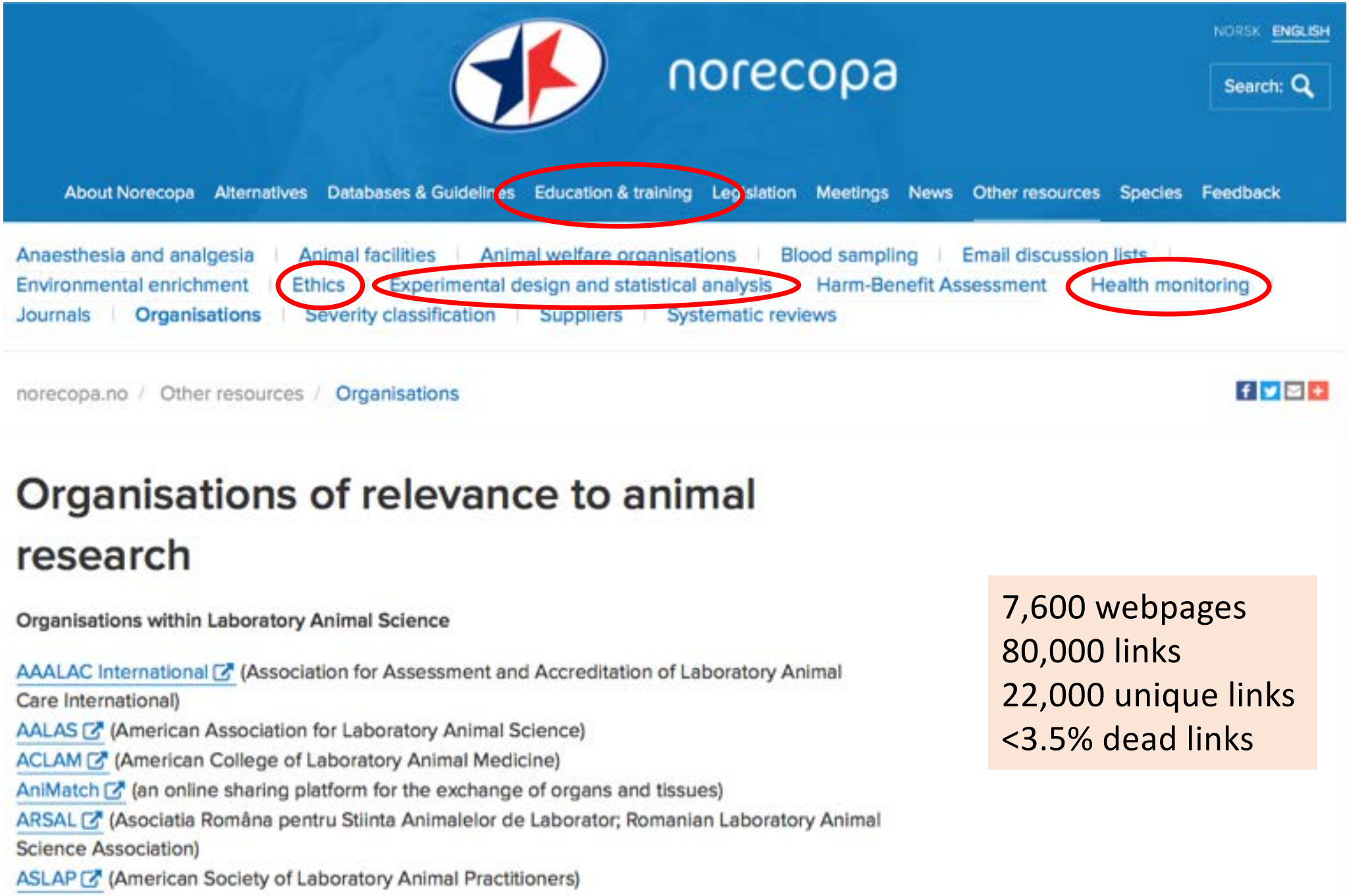
An effective prediction of the effects of a research protocol on the animals concerned helps to ensure that any pain, suffering or distress they may experience will be effectively anticipated, recognized and alleviated. This is essential not only for animal welfare but also for scientific validity, because 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

Guidelines for severity classification of procedures on fish

https://norecopa.no/3r-guide/guidance-on-the-severity-classification-of-scientific-procedures-involving-fish

norecopa.no



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<3.5% dead links

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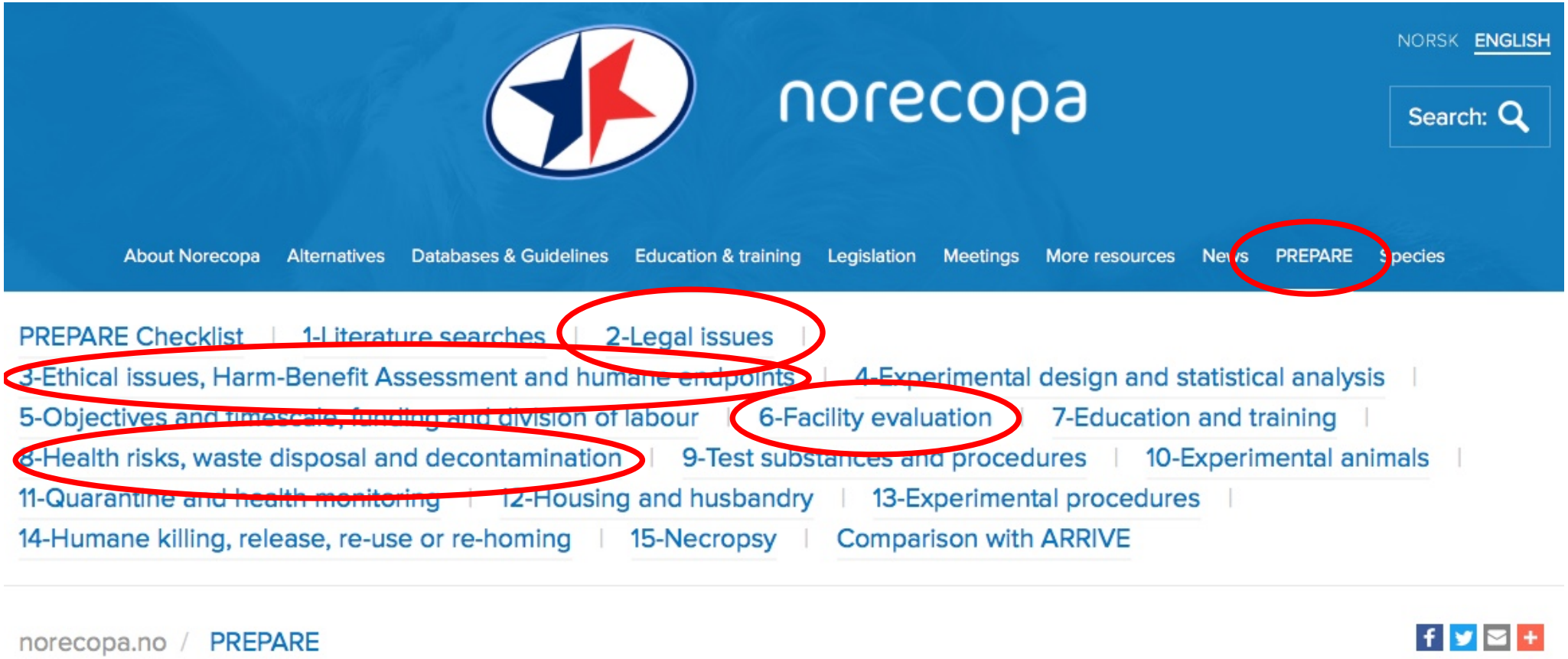
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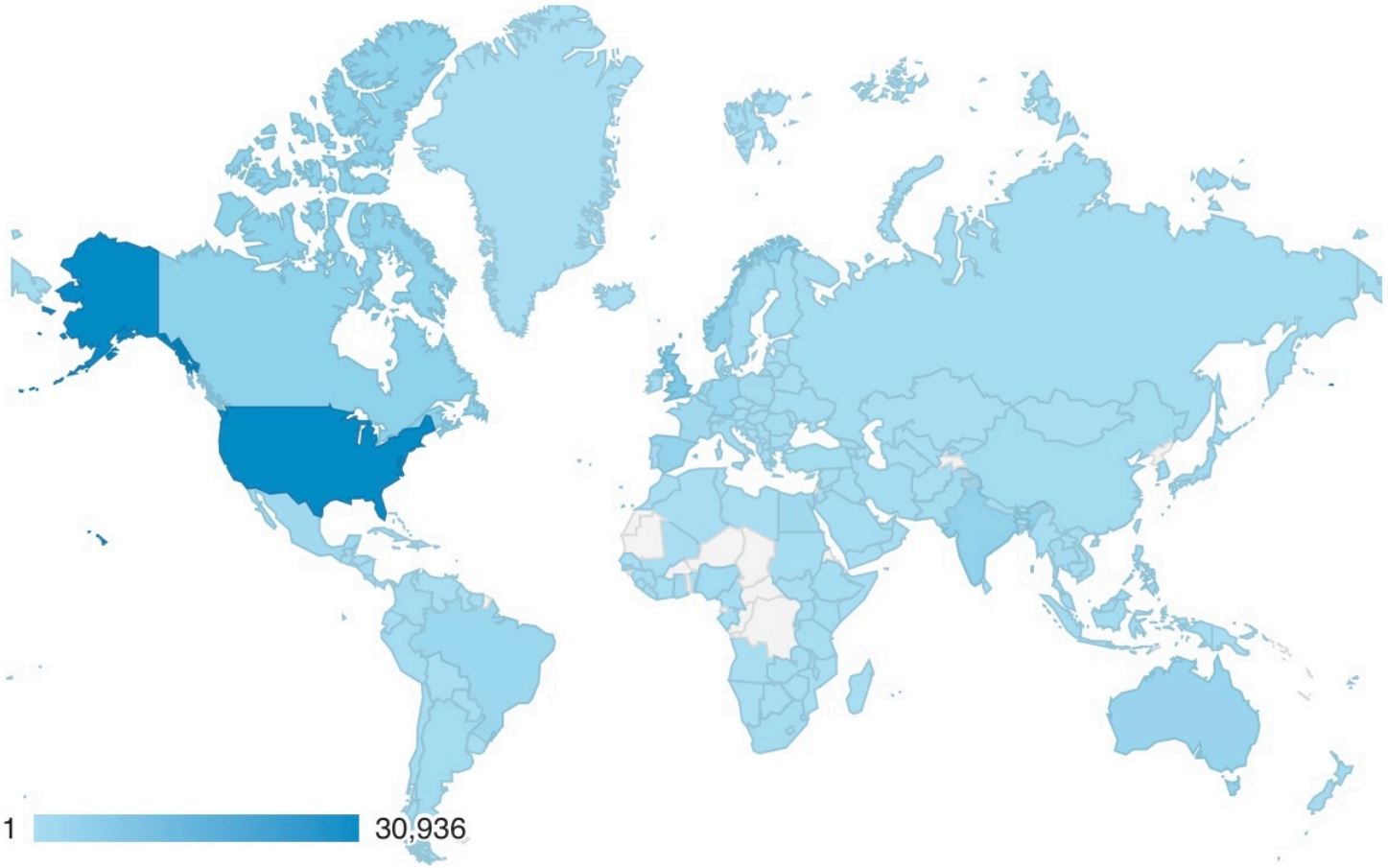
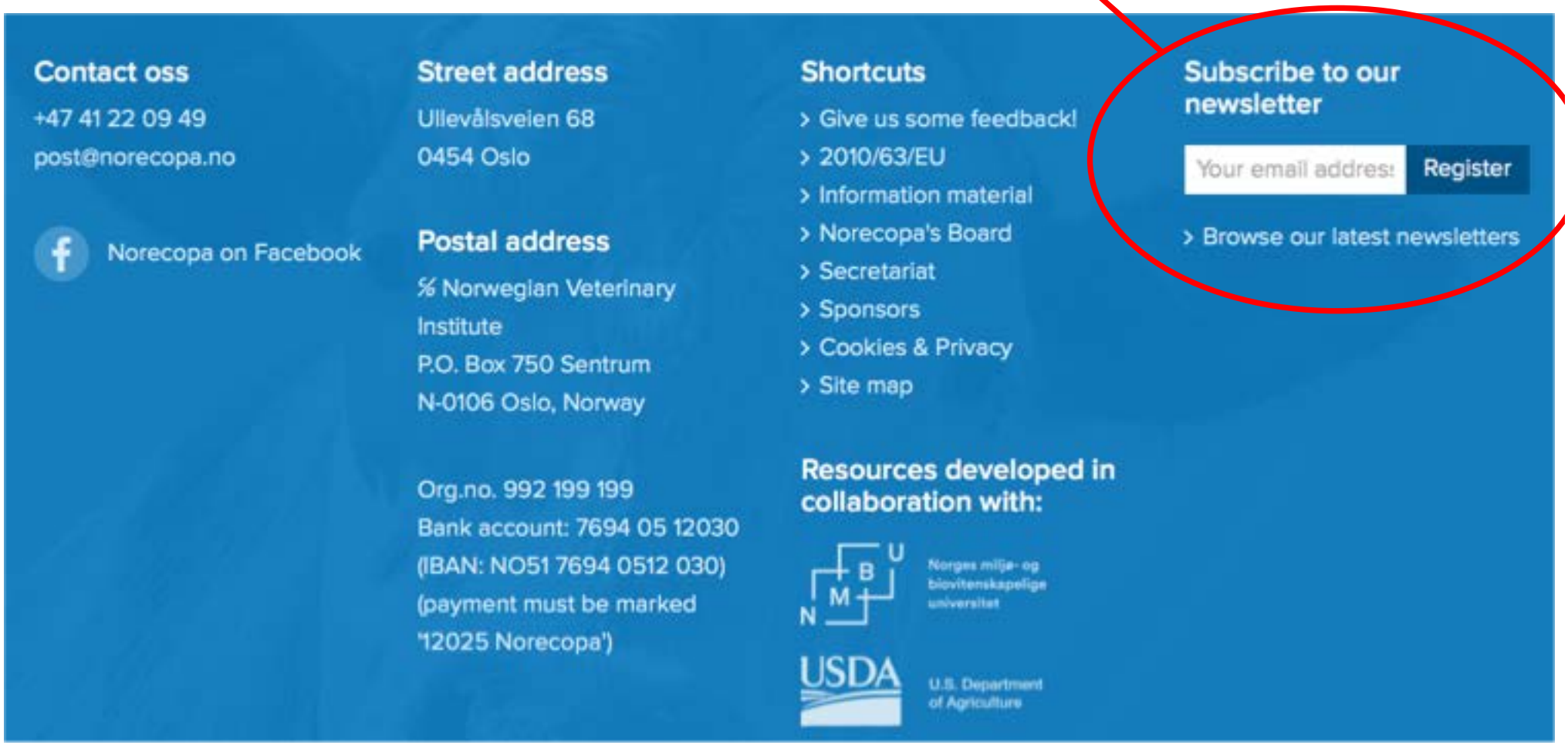
1-Literature searches
2-Legal issues
3-Ethical issues, Harm-Benefit Assessment and humane endpoints
4-Experimental design and statistical analysis
5-Objectives and timescale, funding and division of labour
6-Facility evaluation
7-Education and training
8-Health risks, waste disposal and decontamination
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



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

Averaging 150,000 page views a year at present

English-language newsletters



International Meetings Calendar:

Culture of Care – some reflections

- Why do we have to discuss care at all?
- Doesn't everyone in fact care – or don't they?
- - 'Researchers are more concerned about their number of publications than about the truth, so the results are hyped. As long as they get their work published, they will get the money to continue their research. Why bother to change?'
- 'Animal research and testing is systematic animal abuse'
- But it is in fact an illegal activity, unless you have dispensation
- Trevor Poole: Happy animals make good science
- The 3Rs and a Culture of Care are now embedded in EU Directive 2010/63 and guidance from the EU Commission
- Now we have an international CoC network

Definitions of Culture of Care

Animal caretaker: Pride in being innovative and constantly thinking of improvements to animal welfare and ethical assessment towards animal use

Animal rights: Phrase is intended to reflect a commitment to exceeding the minimal welfare regulations and guidelines governing the treatment of animals in laboratories, in practice.

Senior research scientist: primarily the care of animals where animal health and welfare is critical. In addition the care of personnel involved

Director, 3R Management and Strategy, Industry: Being committed to doing the utmost to handle the animals in the best way. From study design, housing where each individual plays a central role. A spirit embedded in the employees and constantly challenging the way things are done

University scientist working on alternatives: Several factors involved. Utmost is that animals do not suffer pain or distress and that animals have the ability to express their normal behaviour (housing and care)

Animal caretaker: All the values shared by people working with animals, incl. respect, refinement and willingness to replace

Designated vet: Is going beyond the minimum required by legislation and creating an environment where both staff and animals are treated with compassion, care and respect

Lab Manager, industry: All practices, equipment and staff behaviour with the aim of satisfying physiological and psychological needs of animals

Regulatory specialist: The awareness that animals are sentient beings

Animal welfare: right attitudes, values and people with everyone engaged and positively contributing towards making continuous improvement, knowing what is required of them and doing the right thing without prompting

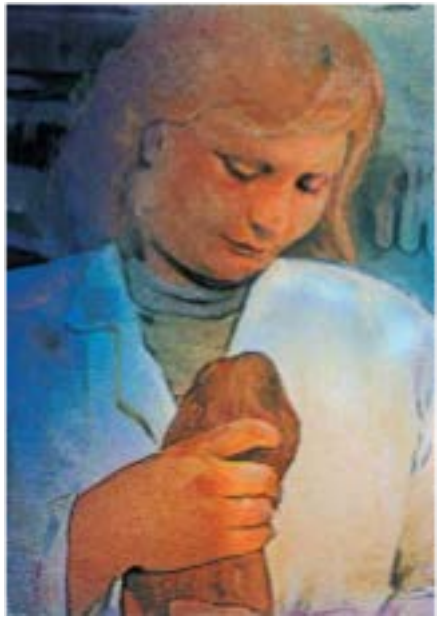
Commission official: no simple answer. It is a result of a combination of essential, complementary building blocks

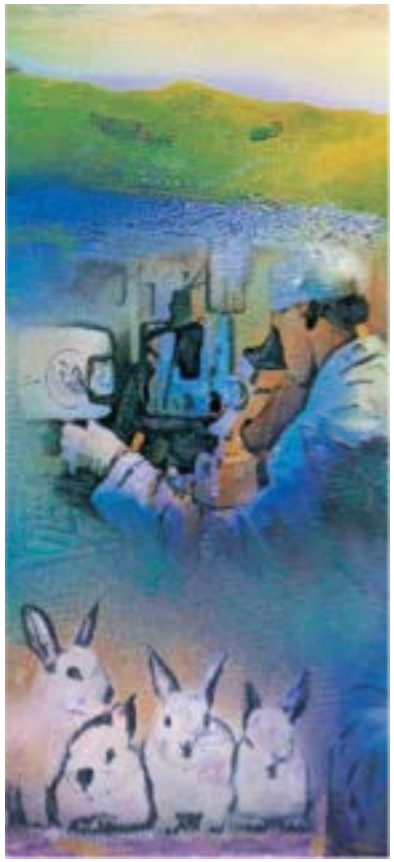
Clinical veterinarian: Knowing how to take care of animals, provide everything they need in a timely manner and not let them suffer

from a questionnaire initiated by Eurogroup for Animals

Culture of Care is used in the laboratory animal community to indicate a commitment to

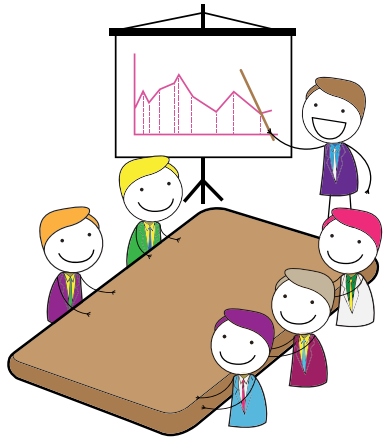
- improving animal welfare,
- improving scientific quality
- taking care of the staff
- and transparency towards the stakeholders.





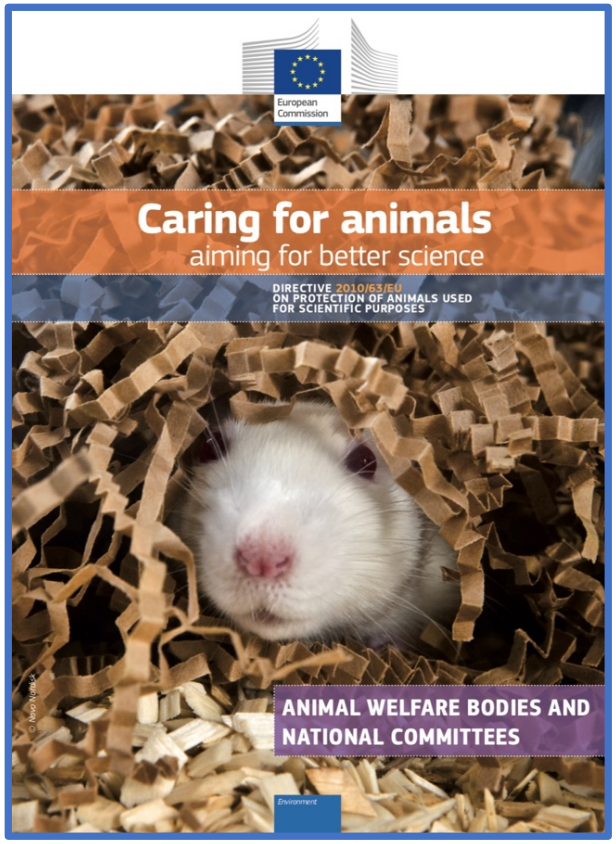
mpi.govt.nz/dmsdocument/1473

A Culture of Care is anchored in the EU Directive 2010/63



Recital 31 states:

Animal-welfare considerations should be given the highest priority in the context of animal keeping, breeding and use. Breeders, suppliers and users should therefore have an ***animal-welfare body*** *in place with the primary task of focusing on giving advice on animal-welfare issues. The body should also follow the development and outcome of projects at establishment level,* ***foster a climate of care*** *and provide tools for the practical application and timely implementation of recent technical and scientific developments in relation to the principles of replacement, reduction and refinement, in order to enhance the life-time experience of the animals. The advice given by the animal-welfare body should be properly documented and open to scrutiny during inspections.*

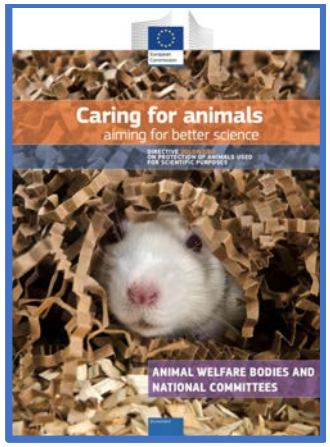


A working document on Animal Welfare Bodies and National Committees to fulfil the requirements under the Directive

A section entitled '**Fostering a Culture of Care**' on:

'establishing and maintaining an appropriate climate of care, often called in practice, and subsequently referred to in this document as, a "culture of care", among the animal user community.'

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/guidance/animal_welfare_bodies/en.pdf



'Fostering a Culture of Care

Ensuring an appropriate culture of care is in everyone's interests, as it will promote improved animal welfare and therefore enhanced scientific outcomes, and give all those involved in the establishment confidence that delivering high quality animal care and use practices is an important priority.

Simply having animal facilities and resources which meet the requirements of the legislation will not ensure that appropriate animal welfare, care and use practices will automatically follow. All those involved in the care and use of animals should be committed to the Three Rs principles and demonstrate a caring and respectful attitude towards the animals bred or used for scientific procedures. ***Without an appropriate culture of care within an establishment, it is unlikely that welfare and scientific outcomes will be optimised.***

The key factors which blend together to foster the appropriate culture of care within an establishment include:

- *Appropriate behaviour and attitude towards animal research from all key personnel is of critical importance. Management should be knowledgeable of animal care and use issues with a commitment to provide high animal welfare standards; staff who work diligently, accept individual responsibility at all levels, and are willing to take the initiative to resolve problems should any arise. In summary, an attitude that is not based on complying with the rules alone but on an individual's positive and proactive mind-set and approach to animal welfare and humane science.*
- *A corporate expectation of high standards with respect to the legal, welfare, Three Rs and ethical aspects of the use of animals, operated and endorsed at all levels throughout the establishment; The establishment will maintain animal facilities to a high standard, and have established policies on animal welfare. Animals will be provided with good veterinary and technical care by well trained staff.*

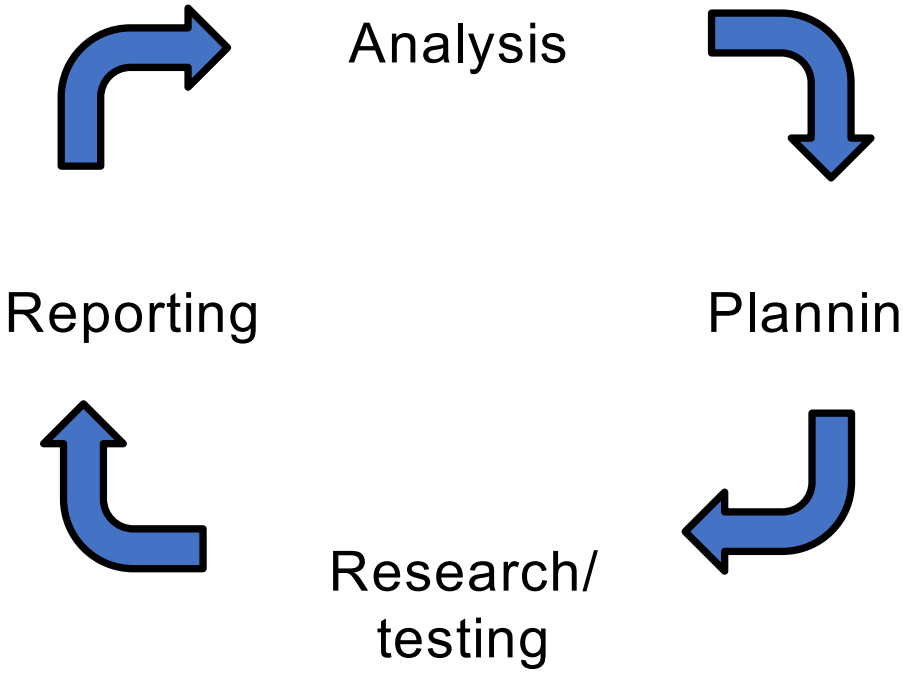
- *Shared responsibility (without loss of individual responsibility) towards animal care, welfare and use.*
- *A pro-active approach towards improving standards, rather than merely reacting to problems when they arise.*
- *Effective communication throughout the establishment on animal welfare, care and use issues and the relation of these to good science;*
- *The importance of compliance is understood and effected.*

Those with specified roles know their responsibility and tasks:

- *Empowered care staff and veterinarians - Animal care and technical staff are respected and listened to and their roles and work are supported throughout the establishment*
- *All voices and concerns are heard and dealt with positively. Personnel at all levels throughout the organisation should be encouraged to raise issues of concern (i.e. there should be a "no blame culture"), and good interaction and communication between researchers and animal care staff should also be encouraged.**

*PREPARE for an experiment!

Reporting is only one part of quality-controlled science…



Space Shuttle, NASA

Identify and ensure the quality of (at least) the **critical points** in the experiment:

critical for animal welfare and scientific value

1) Columbia

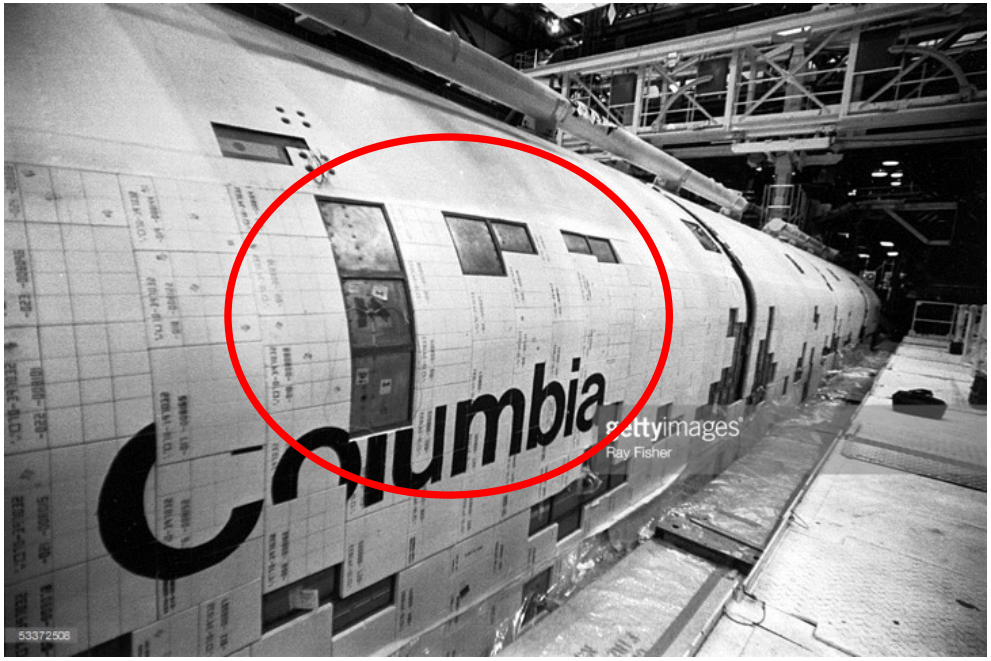
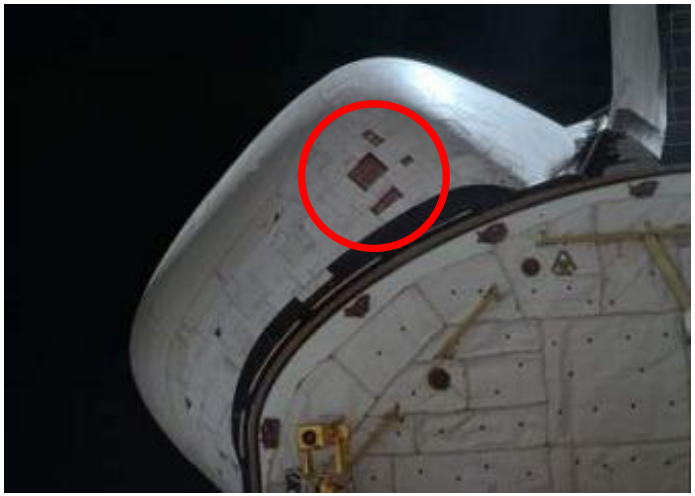


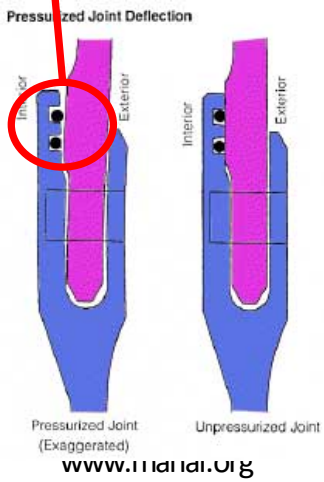
Photo: gettyimages.no



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

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

2) Challenger



Challenger disintegrated in January 1986 killing all 7 crew members

Photo: no.wikipedia.org

Details are important!!

Good planning is critical!

- Complex machines (animals) create *known or unknown unknowns* (interactions between parts that are impossible to foresee until you "fly")
- Possible design weaknesses must be discussed (damage from foam, and susceptibility to low temperature, *which the engineers knew about!)*
- Avoid "pressure to launch" (political, media). = Publish or perish.
- Don't make bad management decisions (pushing the safety envelope):

  "We've got away with it before"
  = "We've managed to publish the experiments before"

- Often a combination of many factors, each of which may be harmless until they occur simultaneously

  Don't ignore "insignificant" issues!
  Pay Attention to Detail

How can a good culture of care be developed?

Although, the culture of care should permeate throughout all levels of the establishment, it is essential that senior staff should take the lead, and visibly demonstrate their commitment to, and support for, a good culture of care within the establishment.

Selection of staff utilising tailored recruitment processes which assist recognition of the desired traits. These processes should preferably apply to selection of all those involved in the care and use of animals.

Management should acknowledge and appreciate efforts of staff to promote an effective culture of care, for example as part of staff appraisal criteria or by developing award programmes for Three R initiatives.

Expectations of the establishment with regard to welfare and care practices should be communicated to all personnel, not just those directly involved with animal care and use. These should be further emphasised and expanded in the induction and ongoing training programmes for all those using and caring for animals.

Encourage development of formal and informal communication channels between researchers and care and technical staff for mutual benefit with respect to science and animal welfare. Encourage links with outside establishments to develop and share good practices, for example inviting in guest lecturers or arranging exchange visits for staff.

Role of the Animal Welfare Body in promoting a good Culture of Care

The AWB is in ideal position to drive the culture of care, and should demonstrate effective leadership in this area. The AWB should ensure, in collaboration with senior management, that there are appropriate structures in place to promote a suitable culture of care, and that these are kept under review to ensure the outcomes are delivered effectively.

All relevant staff should be aware of the role of the AWB and be encouraged to contribute ideas and initiatives to further develop good practices.

The AWB should deliver a collaborative, collegiate and non-confrontational approach whilst maintaining authority and achieving implementation of advice.

Further suggestions to assist the AWB in achieving a good culture of care:

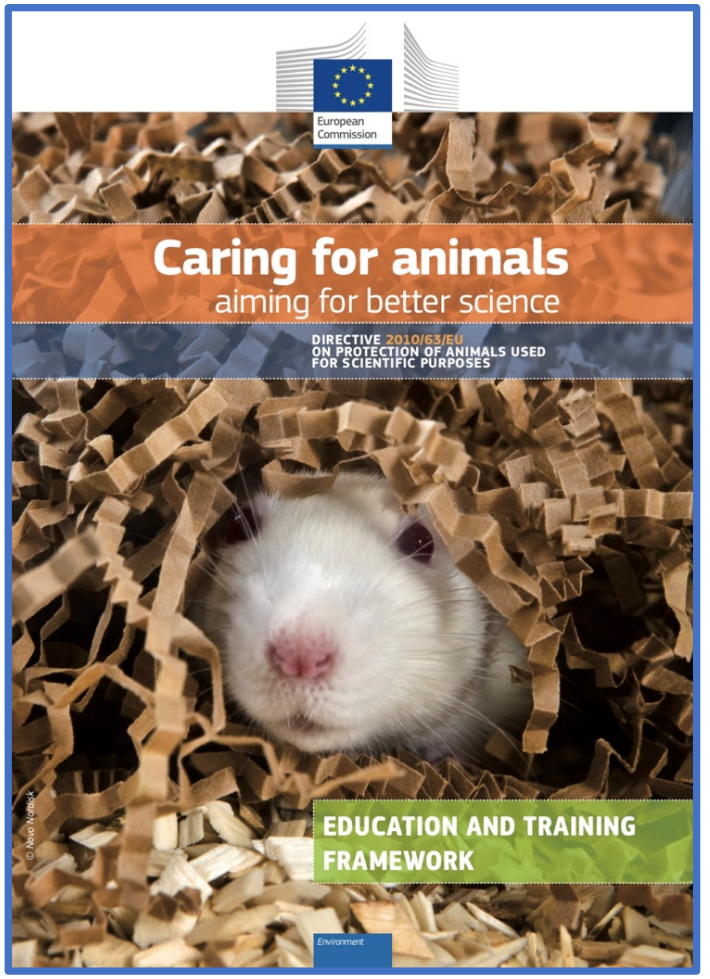
- *Encourage scientists to work with (and value the contribution of) animal care staff*
- *Provide information on the role and functions of the AWB for new staff and encourage their contributions*
- *Provide for on-going involvement of project holders in the AWB*
- *Provide the opportunity and encouragement for any staff member to raise issues with, and to attend AWB meetings*
- *Communicate with all staff (presentations/newsletters/web page) and spread the word about the Three Rs, welfare improvements, policy changes, roles of care staff, training persons and veterinarians, and the AWB itself.*

Later in the document, it states that the National Committee can contribute to the culture of care:

- *Organisation of a national forum to allow sharing of good practice*
- *Ensuring sharing of good practices through the establishment of a national framework to collect, store and disseminate information on good practices*
- *Promoting the importance and relevance of a good culture of care to good scientific and animal welfare outcomes*
- *Making AWBs aware of, and supporting their role as, the promoter of a good culture of care*
- *Utilising the benefits of personal contacts and interactions, in contrast to impersonal 'newsletters' to emphasise the importance of good culture of care.*

Further advice on how to promote a culture of care is given in the Guidance Document entitled **Inspections and Enforcement**, and the Document entitled **Education and Training Framework** indicates how a culture of care can be integrated in these processes.

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/guidance/inspections/en.pdf



http://ec.europa.eu/environment/chemicals/lab_animals/pdf/guidance/education_training/en.pdf

Although an oversight by the competent authorities is an important factor, the development of an effective culture of care and responsibility critically relies on the internal processes, attitudes and practices in place within the establishments. Buy-in from all staff supported by effective leadership is essential. Each individual has to positively contribute. Inspectors can assist in identifying good practice and deficits in internal processes.

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/guidance/inspections/en.pdf

(vii) Understand the role of the Inspector as communicator, promoter of good practices and the Three Rs

Insp.44. Discuss the concept of culture of care

Insp.45. List issues which contribute to a good culture of care (a proactive approach to the Three Rs, clear mechanisms for communication between all staff which are used effectively, effective collaboration among key players)

Insp.46. Describe methods which can be used to promote better quality science and reporting (e.g. the use of ARRIVE guidelines)

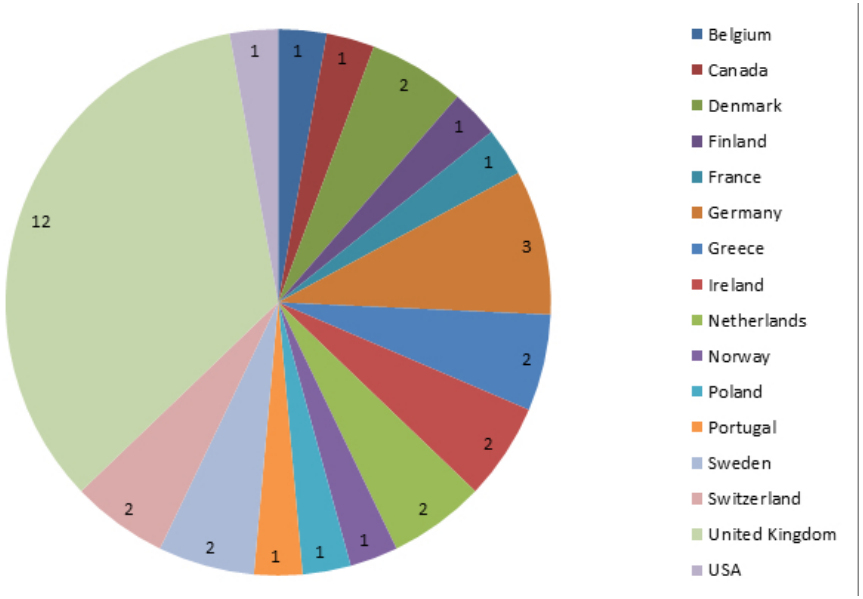
Insp.47. Explain the benefits of a consistent and pro-active inspection system

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/guidance/education_training/en.pdf

The International Culture of Care Network

norecopa.no/culture-of-care

35 members from user establishments, competent authorities, communication and interest organisations, in 16 countries



Proposed by Thomas Bertelsen at the FELASA Congress in Brussels in June 2016, where there were 7 presentations which discussed the culture of care. To share and publish examples of activities fostering a Culture of Care which improve animal welfare.

http://felasa2016.eu/wp-content/uploads/2016/06/DETAILED_PROGRAMME_FELASA_2016_V3.6.pdf

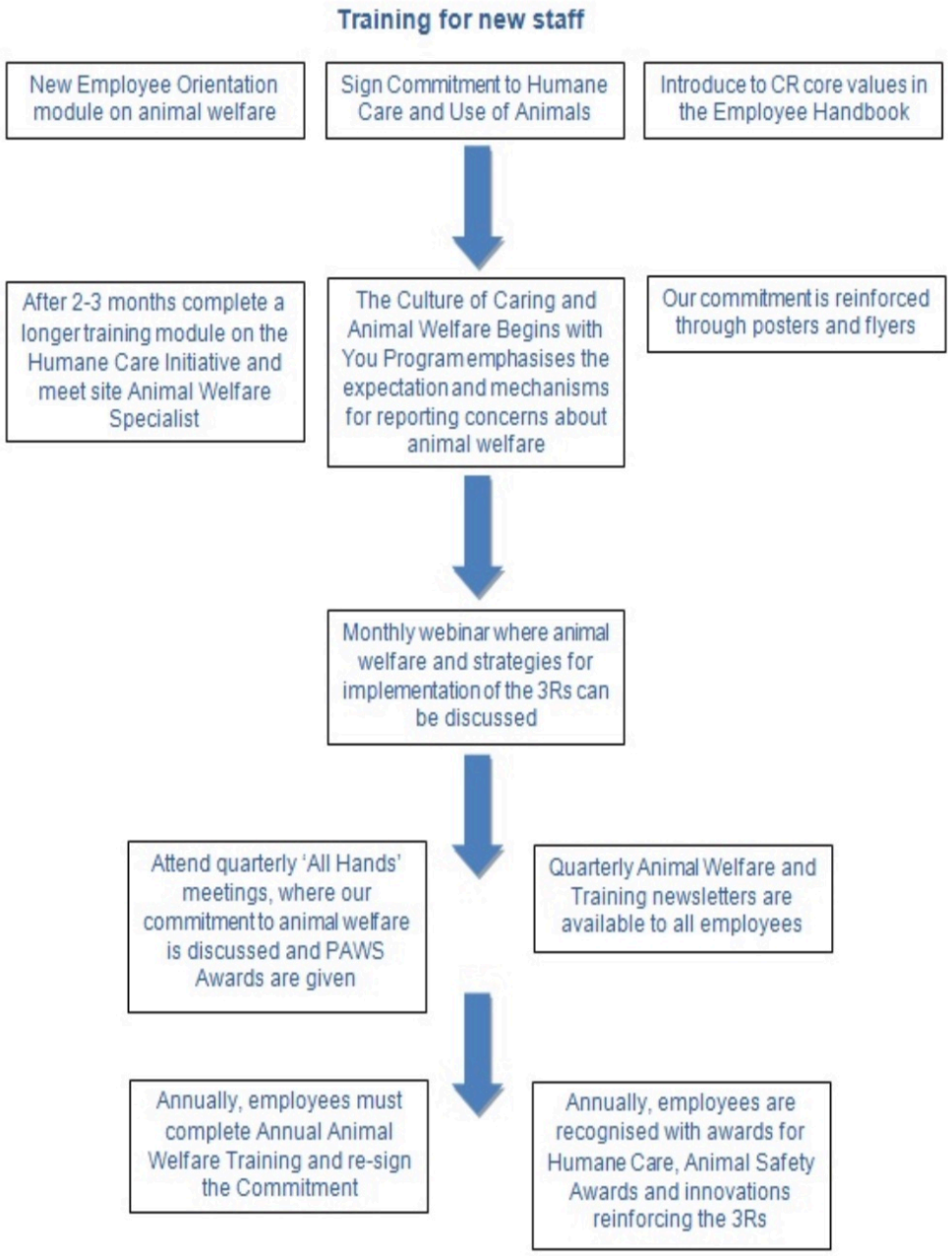
Klein HJ & Bayne KA (2007): Establishing a Culture of Care, Conscience, and Responsibility: Addressing the Improvement of Scientific Discovery and Animal Welfare Through Science-Based Performance Standards. *ILAR Journal*, 43(1), 3-11.
http://ilarjournal.oxfordjournals.org/content/48/1/3.full

A culture of care, conscience, and responsibility relies on the establishment of an effective program of self-monitoring. This process entails building a trust relationship with oversight bodies (e.g., US Department of Agriculture, Office of Laboratory Animal Welfare, and AAALAC International); the application of sound ethical principles, which will ensure an appropriate level of resources for the program; and establishing and sustaining an appropriate institutional organization that includes vigilant monitoring of the program.

As Dr. Alan C. Rosenquist, Chair of the University of Pennsylvania Institutional Animal Care and Use Committee has stated, **“Let's regulate ourselves or someone with a “.gov” address will do it for us.”**

Marilyn Brown, Charles River: Creating a Culture of Care

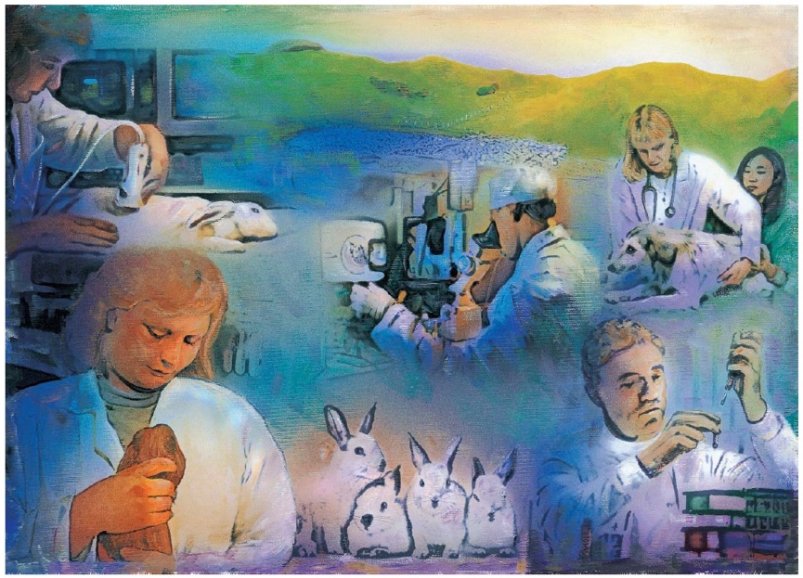
https://www.nc3rs.org.uk/news/creating-culture-care



National Animal Ethics Advisory Committee

A Culture of Care

A guide for people working with animals in research, testing and teaching



mpi.govt.nz/dmsdocument/1473

RSPCA: A one-page summary by Penny Hawkins and Maggy Jennings, endorsed by the Culture of Care Network.

https://norecopa.no/media/7711/culture-of-care-working-concept.pdf

The Culture of Care - a working concept

The text below setting out essential factors for a good Culture of Care is summarised from:

- the *European Commission National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes: A working document on Animal Welfare Bodies and National Committees to fulfil the requirements under the Directive,* pp. 16-18; **ec.europa.eu/environment/chemicals/lab_animals/pdf/endorsed_awb-nc.pdf**
- the *RSPCA/LASA Guiding Principles on Good Practice for Animal Welfare and Ethical Review Bodies: Chapter 11; Promoting a Culture of Care;* **tinyurl.com/RSPCA-LASA-AWERB**

The concept, principles and structural and behavioural elements that contribute to a Culture of Care have been well described in these documents. Establishments need to interpret and implement these within their own organisations, with a clear vision of what a Culture of Care means for them.

The culture of an organisation relates to the beliefs, values and attitudes of its staff and the development of processes that determine how they behave and work together. A Culture of Care is one that demonstrates caring and respectful attitudes and behaviour towards animals and encourages acceptance of responsibility and accountability in all aspects of animal care and use. **This should go beyond simply having animal facilities and resources that meet the minimum requirements of the legislation.**

A healthy Culture of Care requires a shift away from merely responding to externally imposed standards, to one in which leaders and frontline staff are actively committed to improving Three Rs, animal welfare and research and working together to do so.

The key factors which blend together to foster the appropriate Culture of Care within an establishment include:

- Appropriate behaviour and attitude towards animal research from all key personnel.
- A corporate expectation of high standards with respect to the legal, welfare, Three Rs and ethical aspects of the use of animals, operated and endorsed at all levels throughout the establishment.
- Shared responsibility (without loss of individual responsibility) towards animal care, welfare and use.
- A pro-active approach towards improving standards, rather than merely reacting to problems when they arise.
- Effective communication throughout the establishment on animal welfare, care and use issues and the relation of these to good science.
- The importance of compliance is understood and effected.
- Those with specified roles know their responsibility and tasks.
- Care staff and veterinarians are respected and listened to and their roles and work are supported throughout the establishment.
- All voices and concerns at all levels throughout the organisation are heard and dealt with positively.

The Animal Welfare Body (AWB) in every establishment is in ideal position to drive the Culture of Care, and should demonstrate effective leadership in this area. The AWB should ensure, in collaboration with senior management, that there are appropriate structures in place to promote a suitable culture, and that these structures are kept under review to ensure the outcomes are delivered effectively.

The NC3Rs:

An institutional framework for the 3Rs

1. Improving access to information and other resources
2. Championing the 3Rs
3. Involving the wider institutional community
4. Rewarding 3R developments
5. Supporting 3Rs training
6. Disseminating 3Rs advances
7. Taking a strategic approach

https://www.nc3rs.org.uk/institutional-framework-3rs

Recognition of a culture of care: 3R prizes

Norecopa's 3R Prize

In 2010 Norecopa established a prize for outstanding efforts to advance "the 3Rs" (Replacement, Reduction & Refinement) in connection with animal research.
The aim of the prize is to increase awareness and use of the 3R principle in research. Special emphasis is placed on advances in research and development which benefit Norwegian conditions. The prize can be awarded for scientific, technical or administrative work.

The prize consists of NOK **30,000 and a diploma.** It is awarded in connection with Norecopa's Annual General Meetings.

Do you wish to nominate someone, or yourself, for the prize?

The deadline is 15 March each year. Nominations can be sent at any time of year to Norecopa's secretary.

The nomination form can be downloaded here
The statutes for the prize can be read here

More information in Norwegian about the prizewinners and the nominees.

Other 3R Prizes:
3R-prize from the Danish 3R-centre
3R-prize from the British 3R-centre NC3Rs
3R Science Prize and 3R Laboratory Technician Prize from EPAA (European Partnership for Alternatives to Animal Testing)
Nordic Research Prize, awarded by Alternativfondet and Forsøgsdyrenes Værn (won by Adrian og Karina Smith in 2003)
Ursula M. Händel Prize
SGV Award (3R prize from the Swiss Laboratory Animal Science Association)
Global overview of 3R Awards

Closely related to a culture of care is the concept of a **Culture of Challenge** (Louhimies, 2015)**.**

Look for the acceptable, rather than choosing the accepted.

"because we've always done it that way»

«as often as necessary»

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

Carol M. Newton (1925-2014)

National Library of Medicine

The three S's

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

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

https://norecopa.no/3S

nature International weekly journal of science

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News & Comment > News > 2017 > May > Article

NATURE | NEWS

Swiss survey highlights potential flaws in animal studies

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

Ramin Skibba

20 December 2016

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

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

Br J Anaesth (2016) 116 (1): 37-45. **DOI:** https://doi.org/10.1093/bja/aev301
Published: 03 October 2015

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

nature International weekly journal of science

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

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

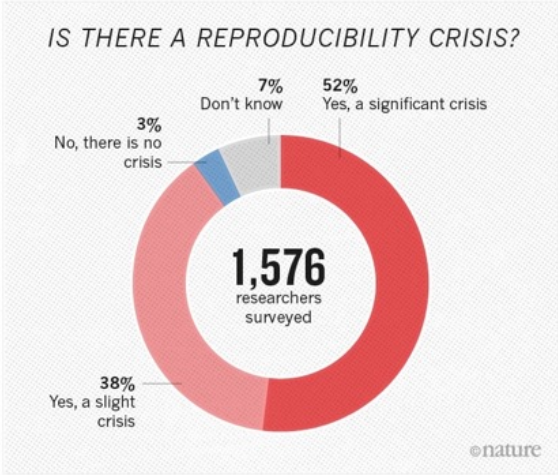
NATURE | NEWS FEATURE

1,500 scientists lift the lid on reproducibility

Survey sheds light on the 'crisis' rocking research.

Monya Baker

25 May 2016 | Corrected: 28 July 2016



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

Berti & Cima 1955, quoted in Öbrink and Rehbinder

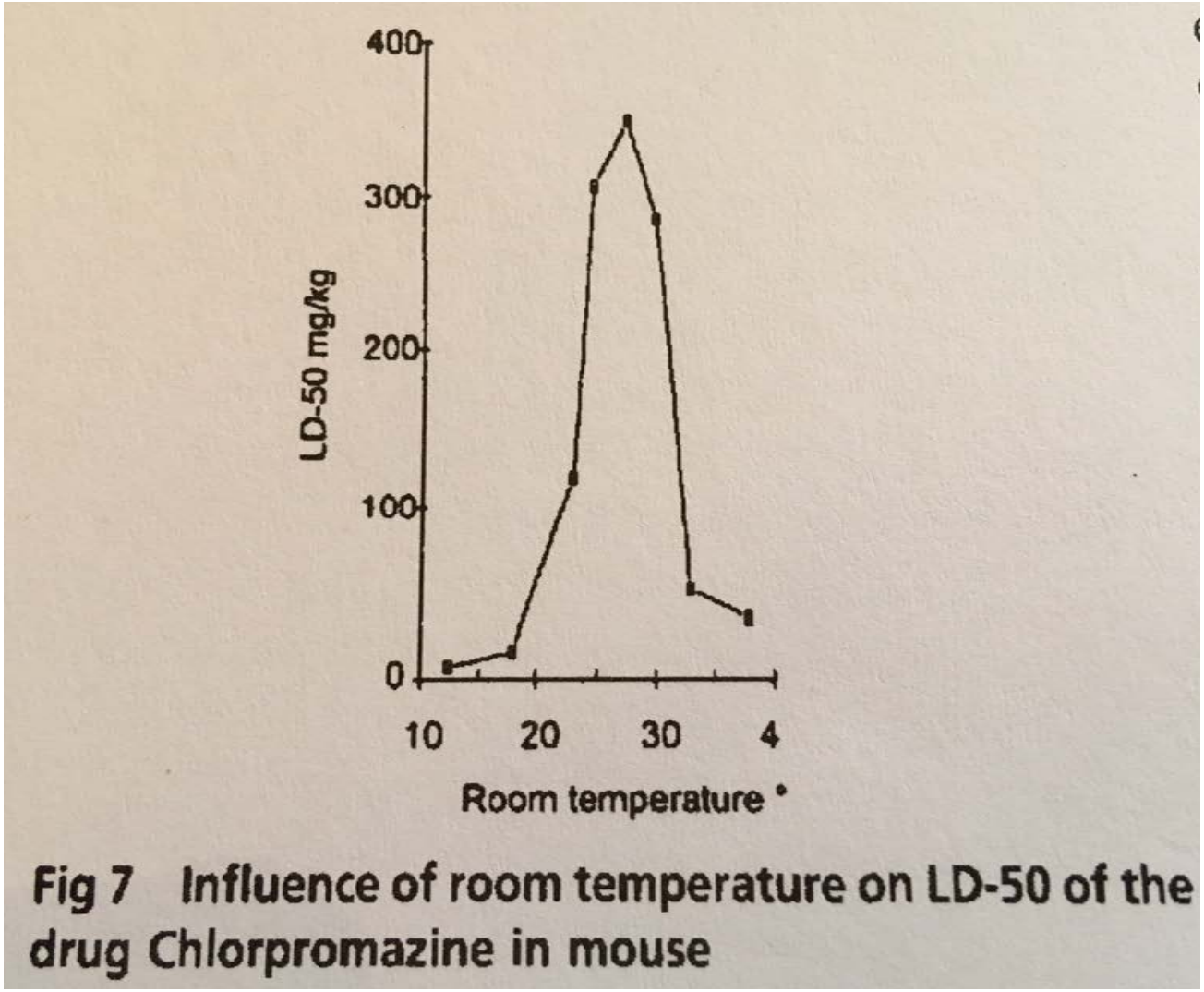


Fig 7 Influence of room temperature on LD-50 of the drug Chlorpromazine in mouse

Hurni 1969, quoted in Öbrink and Rehbinder

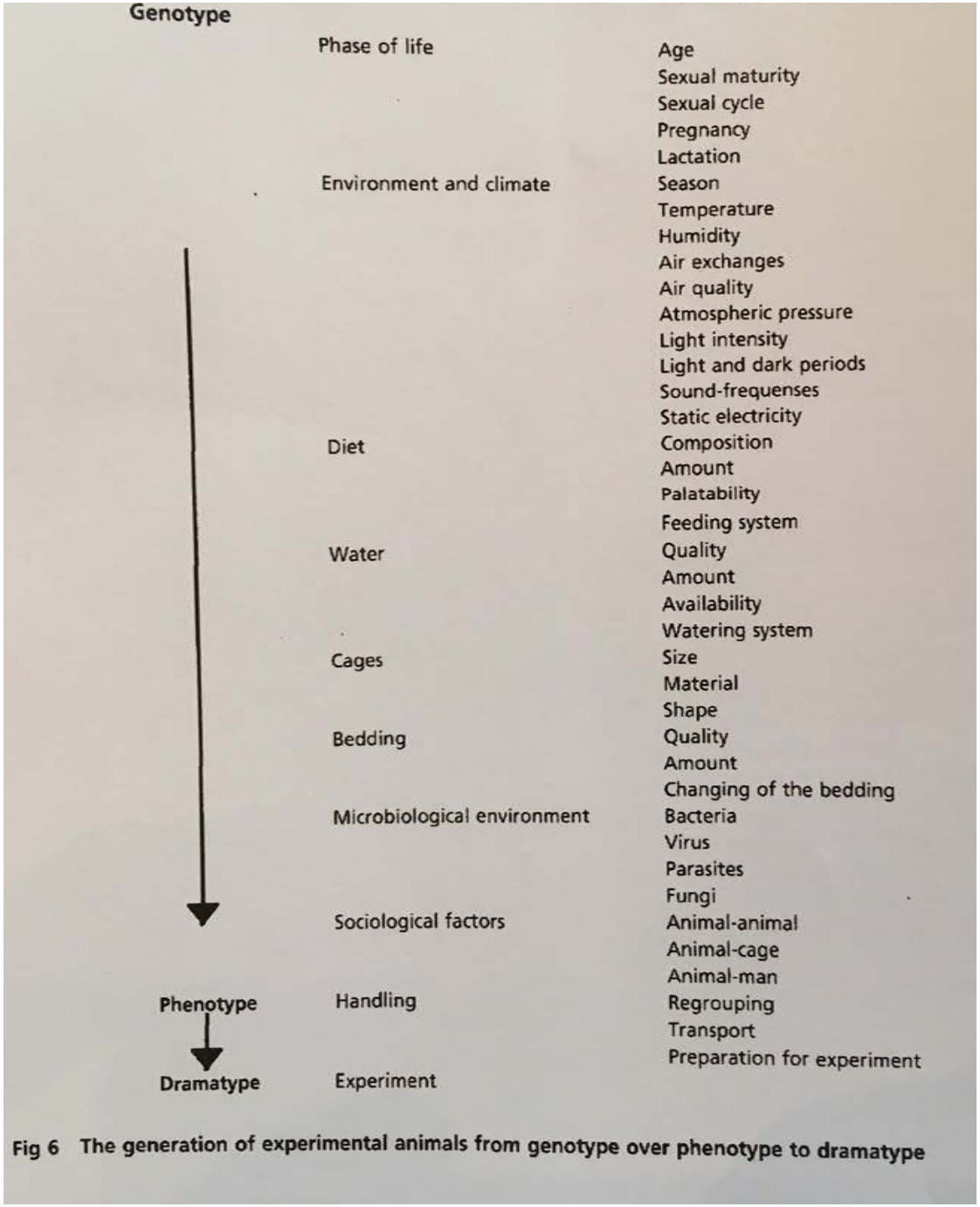


Fig 6 The generation of experimental animals from genotype over phenotype to dramatype

photo: NMBU

Contingent suffering

(not just direct suffering caused by the procedure)

e.g. fear, boredom, discomfort

which may caused by

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

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

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

photo: colourbox.com

INDEPENDENT

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

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

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

”Simple” techniques?

Photo: NMBU

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

‘Simple’ blood sampling techniques?

At the doctor:

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

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

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

medipoint.com/html/for_use_on_mice.html

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

There are many guidelines for *reporting* animal studies

- GV-SOLAS committee, chaired by AW Ellery (1985)
- Öbrink & Waller, 1996
- Jane Smith *et al.*, 1997
- Öbrink & Rehbinder: Animal definition: a necessity for the validity of animal experiments? *Laboratory Animals,* 2000
- ARRIVE Guidelines, 2010 (Kilkenny *et al.*, NC3Rs)
- Gold Standard Publication Checklist, 2010 (SYRCLE)
- Institute for Laboratory Animal Research, NRC, 2011
- Instructions to authors, in many journals

  e.g. Nature's Reporting Checklist

More species- and situation- specific guidance is needed

Guidelines for reporting the results of experiments on fish

Trond Brattelid & Adrian J. Smith

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

Summary

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

Keywords Fish; experiment; study; report; refinement

Laboratory Animals, 2000

Original Article

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

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

PREPARE: guidelines for planning animal research and testing

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

Abstract

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

Keywords

guidelines, planning, design, animal experiments, animal research

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

Introduction

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

[1]Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750, Sentrum, Oslo, Norway
[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

Corresponding author:
Adrian Smith, Norecopa, c/o Norwegian Veterinary Institute, P.O. Box 750 Sentrum, 0106 Oslo, Norway.
Email: adrian.smith@norecopa.no

Why do we need PREPARE when we have ARRIVE?

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

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

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

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

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

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

PREPARE

ARRIVE

https://www.dreamstime.com

PREPARE:

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

PREPARE covers 15 topics:

Formulation of the study

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

Dialogue between scientists and the animal facility

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

Methods

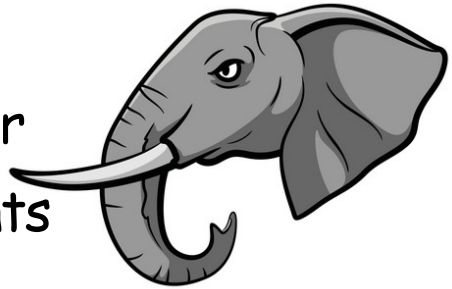
9. Test substances and procedures
10. Experimental animals
11. Quarantine and health monitoring
12. Housing and husbandry
13. Experimental procedures
14. Humane killing, release, reuse or rehoming
15. Necropsy

Items in pink are not highlighted in ARRIVE

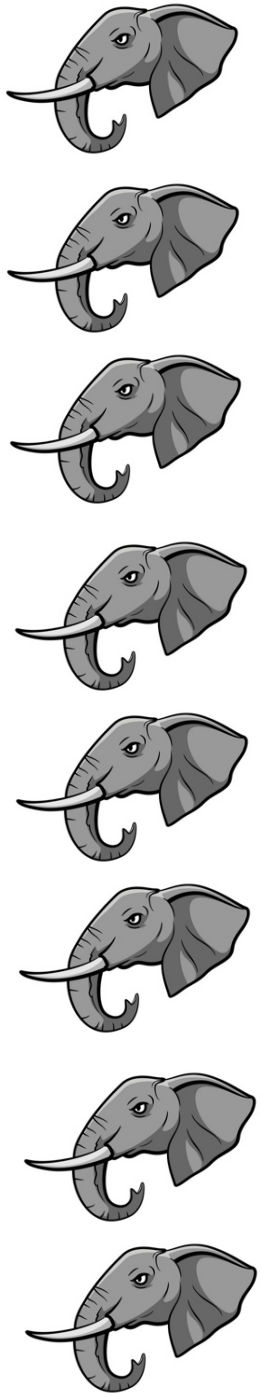
There are several elephants in the room…

reddit.com

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



Some of the elephants in the herd...



- poor literature searches
- lack of humane endpoints
- poor experimental design
- vague distribution of work and costs between the scientists and the animal facility
- insufficient evaluation of the facility's competence and infrastructure
- too little attention to transport and acclimation
- ignoring health risks for all involved
- lack of standard procedures for necropsy
- poor planning of waste disposal
- little discussion about the fate of the animals

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.
(B) Dialogue between scientists and the animal facility	
5. Objectives and timescale, funding and division of labour	☐ Arrange meetings with all relevant staff when early plans for the project exist. ☐ Construct an approximate timescale for the project, indicating the need for assistance with preparation, animal care, procedures and waste disposal/decontamination. ☐ Discuss and disclose all expected and potential costs. ☐ Construct a detailed plan for division of labour and expenses at all stages of the study.
6. Facility evaluation	☐ Conduct a physical inspection of the facilities, to evaluate building and equipment standards and needs. ☐ Discuss staffing levels at times of extra risk.
7. Education and training	☐ Assess the current competence of staff members and the need for further education or training prior to the study.
8. Health risks, waste disposal and decontamination	☐ Perform a risk assessment, in collaboration with the animal facility, for all persons and animals affected directly or indirectly by the study. ☐ Assess, and if necessary produce, specific guidance for all stages of the project. ☐ Discuss means for containment, decontamination, and disposal of all items in the study.
(C) Quality control of the components in the study	
9. Test substances and procedures	☐ Provide as much information as possible about test substances. ☐ Consider the feasibility and validity of test procedures and the skills needed to perform them.
10. Experimental animals	☐ Decide upon the characteristics of the animals that are essential for the study and for reporting. ☐ Avoid generation of surplus animals.
11. Quarantine and health monitoring	☐ Discuss the animals' likely health status, any needs for transport, quarantine and isolation, health monitoring and consequences for the personnel.
12. Housing and husbandry	☐ Attend to the animals' specific instincts and needs, in collaboration with expert staff. ☐ Discuss acclimatization, optimal housing conditions and procedures, environmental factors and any experimental limitations on these (e.g. food deprivation, solitary housing).
13. Experimental procedures	☐ Develop refined procedures for capture, immobilisation, marking, and release or rehoming. ☐ Develop refined procedures for substance administration, sampling, sedation and anaesthesia, surgery and other techniques.
14. Humane killing, release, reuse or rehoming	☐ Consult relevant legislation and guidelines well in advance of the study. ☐ Define primary and emergency methods for humane killing. ☐ Assess the competence of those who may have to perform these tasks.
15. Necropsy	☐ Construct a systematic plan for all stages of necropsy, including location, and identification of all animals and samples.

References

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

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

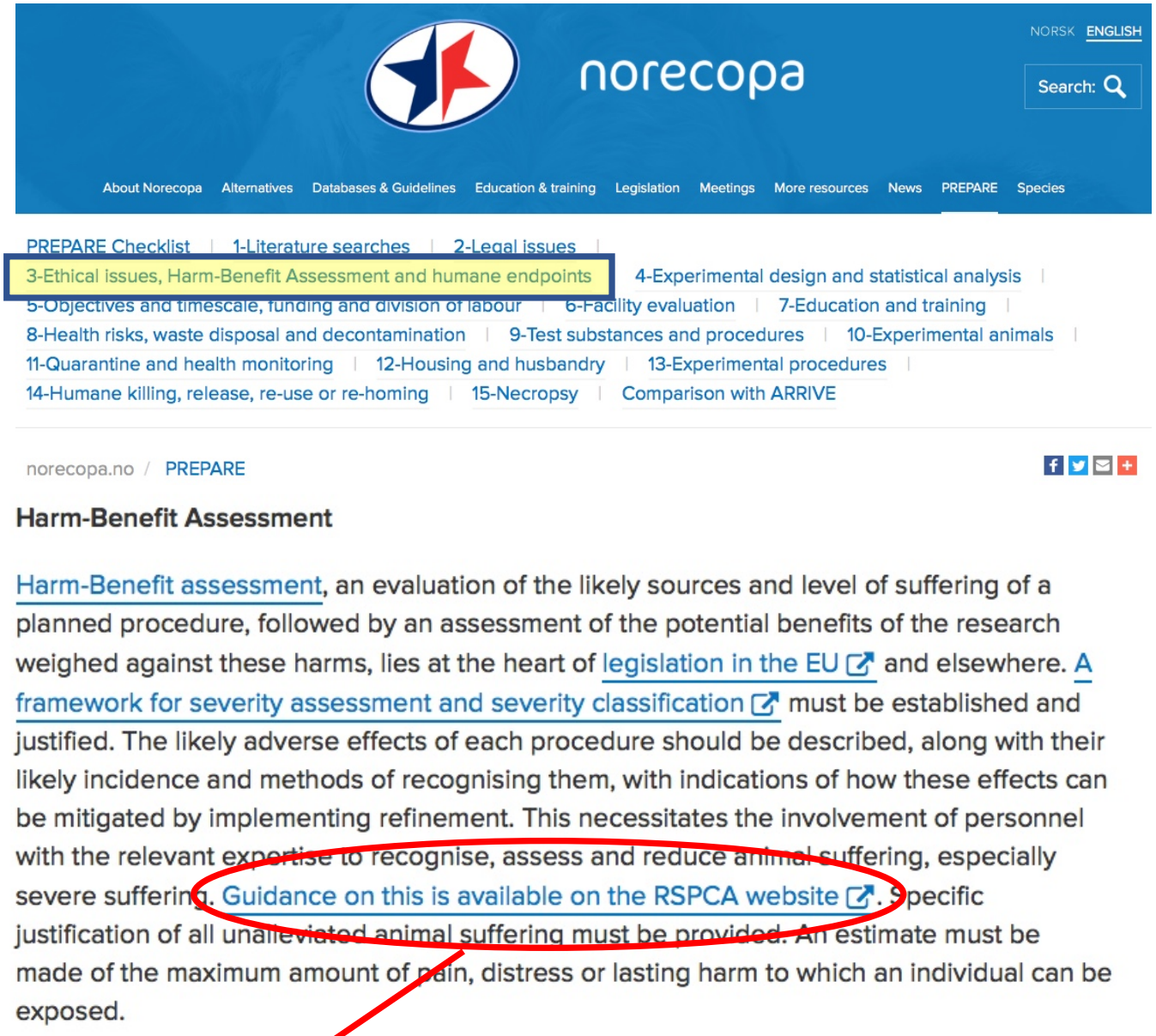
https://norecopa.no/prepare/prepare-checklist

Two pages, translated into 13 languages so far

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

norecopa.no/PREPARE

norecopa.no/PREPARE



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

Health risks: there are many people to think about

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

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

They may:

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

Are we prepared for equipment failure?

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

Photo: NMBU

Are the animals ready for the experiment?

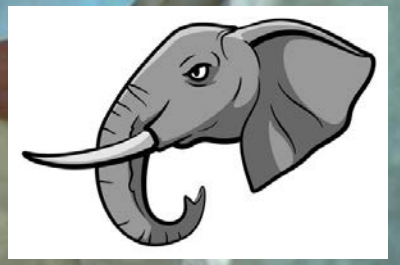


Photo: NMBU

norecopa.no/farm-animals

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

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

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

Contract between the animal facility and the research group

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

	Animal facility	Researcher	Not applicable
Animal:			
Arrival date			
Species			
Strain/stock and substrain			
Supplier (full name and address) or bred on the premises			
Number and sex			
Age, weight, stage of life cycle on arrival			
Pre-treatment (surgical or medical) from supplier			
Quality (e.g. SPF, germ-free, gnotobiotic, conventional)			
Acclimation time before the start of the experiment			
Time and duration of fasting (with/without water and bedding)			
Environment:			
Type of housing: barrier/conventional			
Temperature (mean ± variation)			
Light schedule			
Relative humidity (mean ± variation)			
Number of air changes in the animal room/cabinet per hour			
Environmental enrichment			
Housing:			
Free-range, shelf, cabinet, isolator			
Cage type and size			
Number and method of distribution of animals per cage			

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

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

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

A simple but effective Master Plan

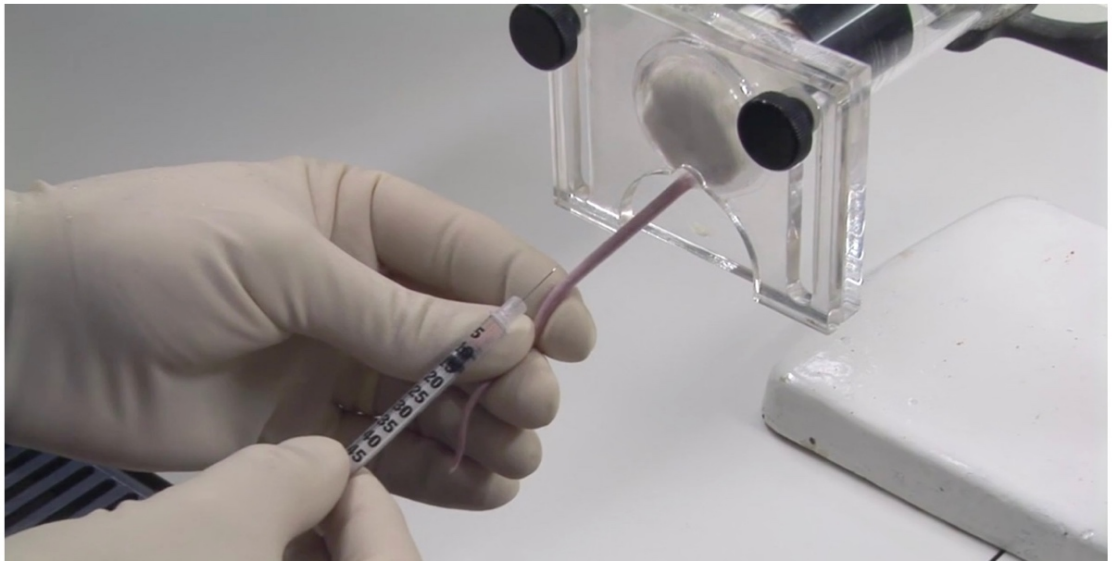
Think ”3R-Alternatives” at all stages

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

Consult the technicians from Day 1:

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

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



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

norecopa.no/PREPARE

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

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

wikipedia.org

Søren Kirkegaard (1813-1855)

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

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

KNOWLEDGE – SKILLS – ATTITUDE

C ommitment to continually improve standards of animal welfare, ethics, health and safety
U ndertake training regularly and keep informed of the latest 3R developments
L ip service banned: a positive and optimistic mind-set is needed
T ransparency, including the general public and all other stakeholders
U nderstand the need for individual responsibility to nurture the culture
R ight to challenge and question the use of animals, the choice of husbandry methods and the procedures
E ducate about alternatives at an early stage of employment

O n the ball: a pro-active approach, rather than just reacting to problems when they arise
F ind the time needed

C oncerns can be aired without consequences for the whistleblower
A ward good initiatives and promote individual thinking
R esearchers and staff interact well, ensuring research integrity and quality
E veryone, from leadership downwards, is willing to implement a CoC

EU PRIZE for
WOMEN INNOVATORS
2018

Winner (Rising Innovator): Karen Dolva, Norway

No Isolation

Passion
Stamina
Optimism

youtube.com/watch?v=MGLOnzQH2x0

Thanks to our main sponsors:

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

Graphics: colourbox.com