

Charles River Excellence in Refinement Award

in collaboration with

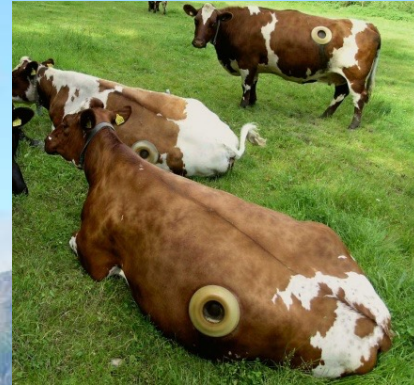
the Johns Hopkins University Center for Alternatives to Animal Testing (CAAT)

Thank you!

norecopa.no/CR

Adrian Smith

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





scientists



animal care staff



local competent person



animal welfarists

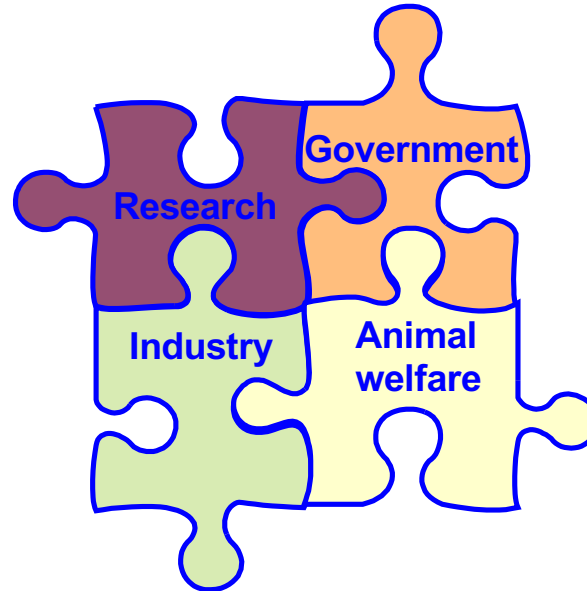


central authority

European Consensus-Platform for Alternatives
ecopa.eu



Recognises **National Consensus Platforms** (NCPs) with **4 stakeholders** equally represented:



Norecopa: PREPARE for better Science

ACKNOWLEDGEMENTS

At the risk of ignoring the Norwegian expression “no one mentioned, no one forgotten” we wish to thank in particular the following for their support during the development of a National Consensus Platform and the activities of Norecopa (in approximately historical order with their affiliation at that time):

Richard Fosse, University of Bergen
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Gunvor Knudsen and colleagues at the Research Animals Unit, Norwegian Food Safety Authority

The competent persons at Norway's animal research facilities

Former Director Harald Gjein, Norwegian Veterinary Institute

Past and present Board Members of *ecopa*
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Past and present members of Norecopa's 3R Prize Committee
Institutional and individual members of Norecopa

Penny Hawkins and colleagues, RSPCA, UK
The Norwegian Animal Protection Alliance
Knut Carlberg, Nordic Society against Painful Animal Experiments
The Norwegian Society for Protection of Animals

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David Anderson
Jan L. Ottesen and colleagues, Novo Nordisk
Tom Bengtson and colleagues, secretariat of Denmark's 3R-Center and National Committee
The Board Members of Denmark's 3R-Center
Tim Allen, Kristina Adams and colleagues, Animal Welfare

Information Center, Maryland, USA

Siri Anzjøn, Kjell Emil Naas, Kristin Danielsen and colleagues,
Research Council of Norway

Ingvill Løken, Norwegian Medicines Agency

Laboratory Animals Ltd.
Jon Richmond and colleagues, Scottish Accreditation Board
The Stiansen Foundation
The Universities Federation for Animal Welfare (UFAW), UK

Past and present members of the Standing Parliamentary Committee on Business and Industry

Øyvind Wærenskjold, Bitfarm
Kjell Ingvar Torvik and colleagues, NetLab AS

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and a multitude of friends and colleagues worldwide in the field of Laboratory Animal Science, animal welfare and 3R alternatives.

Responsible Editor: Adrian Smith, Norecopa
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Front cover photos (clockwise from top left):
Novo Nordisk; Jon Terje Hellgren Hansen; Terje Aamodt, Nofima;
Vibeke D. Valderhaug, Sandvig Laboratory, NTNU
Pigs (p. 32): Novo Nordisk
Goats (p. 33): Birte Graeber Bredahl, Norwegian Veterinary Institute
Rabbits (p. 35): Novo Nordisk
Salmon (p. 35): Terje Aamodt, Nofima
Zebrafish (p. 35): Tom Ask, Aleström Lab, NMBU

Norecopa's 3R Prize – approx. \$ 3,300



norecopa.no/about-norecopa/3r-prize

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- Standing Committee on Business Affairs, Norwegian Parliament
- Norwegian Ministries of Agriculture and Fisheries
- Research Council of Norway
- Laboratory Animals Ltd.
- Architect Finn Rahn's Legacy
- Nordic Society Against Painful Experiments (NSMSD)
- Norwegian Society for Animal Protection (Dyrebeskyttelsen Norge)
- Norwegian Animal Protection Alliance (Dyrevernalliansen)
- Novo Nordisk
- Sanofi
- Scottish Accreditation Board (SAB)
- Stiansen Foundation
- Universities Federation for Animal Welfare (UFAW)
- US Department of Agriculture (USDA)

Graphics: colourbox.com



SCOTTISH ACCREDITATION BOARD



Dyrebeskyttelsen Norge



Dyrevernalliansen



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Friends and colleagues...



Rafael Frías

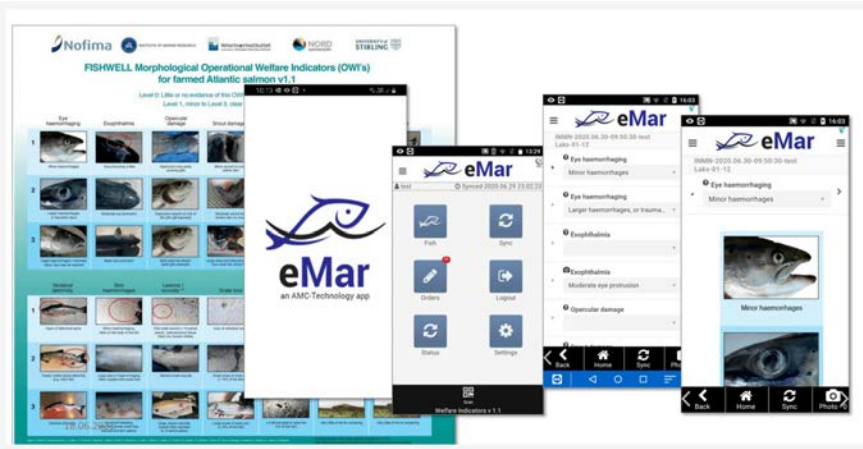
ki.se/en/km/education-in-laboratory-animal-science



Anne Zintzsch

norecopa.no/severity

Charles River Award for Animal Welfare 2016
Aurora Brønstad



<https://www.innovationnewsnetwork.com/ensuring-fish-welfare-in-aquaculture-with-new-digital-app/12855>



ECVAM workshop, Neubiberg, Munich, September 1996:

*Current status and future developments of databases
on alternative methods*

<https://journals.sagepub.com/doi/abs/10.1177/026119299702500404>



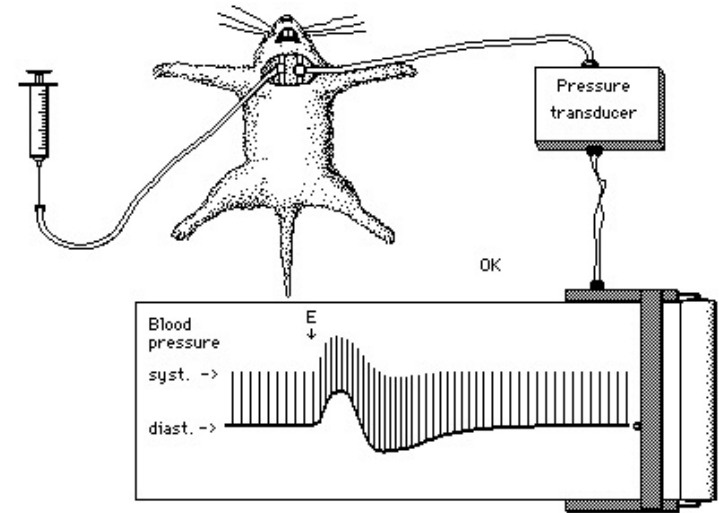
*'Internet access has not yet become
a universal phenomenon'*



wikipedia.org



Richard Fosse



Pharmatutor

laboratory
animals



*Rees Griffiths, Macquarie University
Sydney, Australia*

Norecopa: PREPARE for better Science

norecopa.no : an updated overview of global 3R resources



norsk ENGLISH

norecopa

Databases & Guidelines | Education & training | Legislation | Meetings | More resources | News | PREPARE

al facilities | Animal welfare organisations | Blood sampling | Culture of
tal enrichment | Ethics | Experimental design and reporting | Harm-Ber
ng | Humane endpoints | Humane killing | Journals |
views | fication

approx. 8,500 webpages
300,000 hits annually
7-8 detailed newsletters per year

Search filters

Order by:
Relevance
Typo tolerance:
Default

Database

- 3R Guide database (403)
- Classic AVs database (118)
- European Commission Inventory of 3Rs Education & Training Resources (567)
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- Publisher
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- Record Number

Design and reporting of animal experiments

This page supplements advice given in [Section 4 of the PREPARE guidelines](#). PREPARE covers all aspects of design (including animal and facility related issues).

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Baard Johannessen, Nettforsk



Øyvind Wærenskjold, Bitfarm

Nettforsk
Bitfarm
NetLab
Sourceit
Getonnet
Webhuset
Apsis

The NORINA database: norecopa.no/NORINA



Frog Dissection

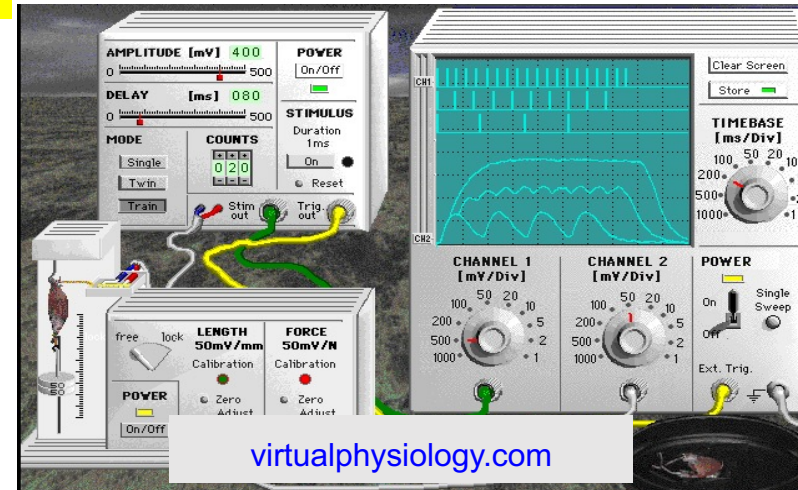
In-store Educational Discount Available

Virtual Frog Dissection Educational App

The Frog Dissection App is an ethical and educative alternative to live animal dissections. Help your students learn all about frogs and their biological functions, without the messy lab work or controversial questions

app screens
Click to view

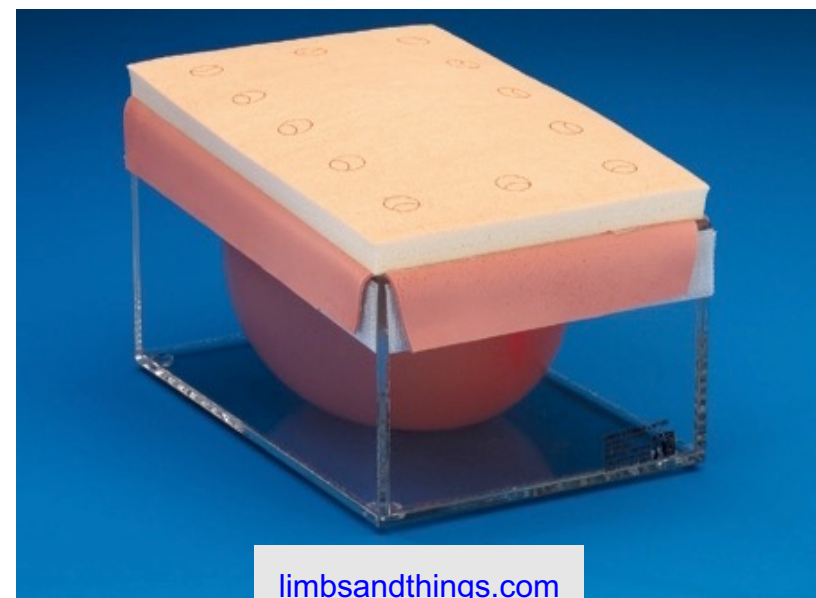
Key Dissection
Anatomy
Internal Organs
External Features
Head
Respiratory System
Circulatory System



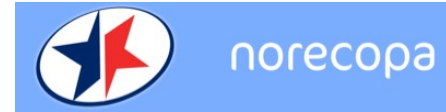
AMPLITUDE [mV] 400
DELAY [ms] 080
MODE Single
COUNTS 020
STIMULUS Duration 1ms
POWER On/Off
Trig. out

CHANNEL 1 [mV/Div] 100
CHANNEL 2 [mV/Div] 100
TIMEBASE [ms/Div] 100
POWER Single Sweep

virtualphysiology.com



The NORINA database



Karina Smith:
1991-2017

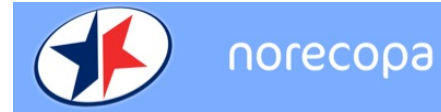
Elisabeth Pagels:
2018-



Nordic Society Against Painful Animal Experiments

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norecopa.no/NORINA



'We may need the animals, as it were, on the night;
but the machines will do very well at rehearsals'

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Laura-Kim Schüller, Veterinary School, Berlin



Rikke Langebæk, University of Copenhagen



Workshop in Oslo, April 2018

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



Laura-Kim Schüller, Veterinary School, Berlin



vetiqo.com





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3R Guide - Tim Allen (AWIC, NAL)

approx. 400 guidelines on the care and use of animals in research and testing

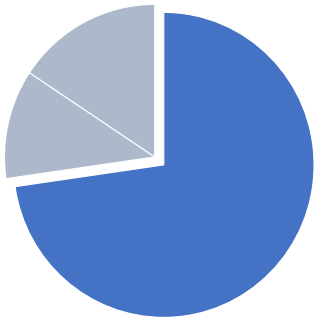
Guidance on the severity classification of procedures involving fish

Report from a Working Group convened by Norecopa



Penny Hawkins and colleagues, RSPCA

What has the award been used for?



EU3Rnet – European 3R centres
International Culture of Care Network

norecopa.no/global3r

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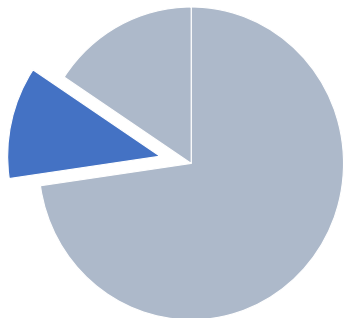
Centres

- [Replacement](#) i
- [Reduction](#) i
- [Refinement](#) i
- [ecopa](#) i

Associations

- [AFLAS \(includes South Korea\)](#) i
- [Culture of Care Network](#) i
- [EU-NETVAL](#) i
- [EU3Rnet](#) i
- [FELASA](#) i
- [FESSACAL](#) i
- [Norecopa](#) i
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- [ecopa](#) i

What has the award been used for?



Prepare



Care



Share




Flag

norecopa.no/PREPARE-CARE-SHARE-FLAG


PREPARING, CARING, SHARING and FLAGGING

The scientific and welfare benefits of increased collaboration and transparency
 Adrian Smith, Norecopa, Norway (adrian.smith@norecopa.no)

This poster presents a set of four icons which were made by Norecopa (the Norwegian platform for Replacement, Reduction & Refinement of animal experiments) to illustrate the 4 essential steps of good preclinical science.

 Prepare <i>Ensure that scientists and animal care staff collaborate closely from day one, to ensure all aspects of a study that potentially uses animals have been addressed</i> norecopa.no/PREPARE	 Share <i>Promote examples of improvements in the care and use of animals, for example by using the Refinement Wiki</i> norecopa.no/wiki
 Care <i>Encourage a strong Culture of Care around animal research, promoting mutual respect, animal and human wellbeing, and safety</i> norecopa.no/CC	 Flag <i>Highlight advances made within the 3Rs in scientific papers, if necessary in a separate methodology paper</i> norecopa.no/3R

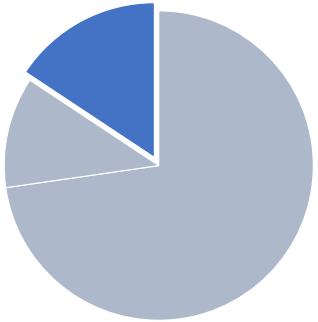
These icons can be downloaded as jpg and mp4 files from norecopa.no/PREPARE-CARE-SHARE-FLAG and used freely.
 Thanks to Per Trystad for the artwork.

 **norecopa** PREPARE for better Science



norecopa

What will the award be used for?



Further development of

- *the PREPARE website*
- *the Refinement Wiki*



Original Article

Laboratory Animals
0011-7
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journals.sagepub.com/home/lan
SAGE

PREPARE: guidelines for planning animal research and testing

Adrian J Smith¹, R Eddie Clutton², Elliot Litley³,
Kristine E Aa Hansen⁴ and Trond Brattelid⁵

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

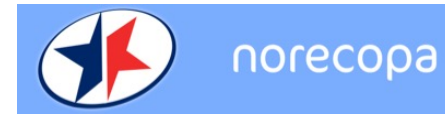
Date received: 5 April 2017; accepted: 27 June 2017

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

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Email: adrian.smith@norecopa.no



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

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



Reached 20,000 downloads/reads during WC11

norecopa.no/PREPARE

Norecopa: PREPARE for better Science

PREPARE:

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

PREPARE covers 15 topics:

Formulation of the study

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

Dialogue between scientists and the animal facility

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

Methods

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

Items in pink are not typically highlighted in reporting guidelines

The burnt cake fallacy:

We can improve research by

- "better reporting"
- "courses in "Experimental Design" that leave out the animal & facility-related issues"

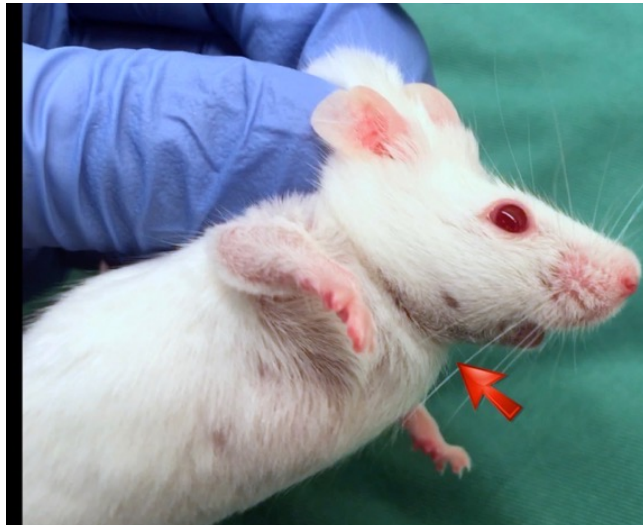


reddit.com



reddit.com

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Fire, flooding
Water, power and ventilation failures

Health and safety issues:
Bites, kicks, scratches
Allergy
Zoonoses
Corrosives, isotopes, radiation
etc. etc.



reddit.com

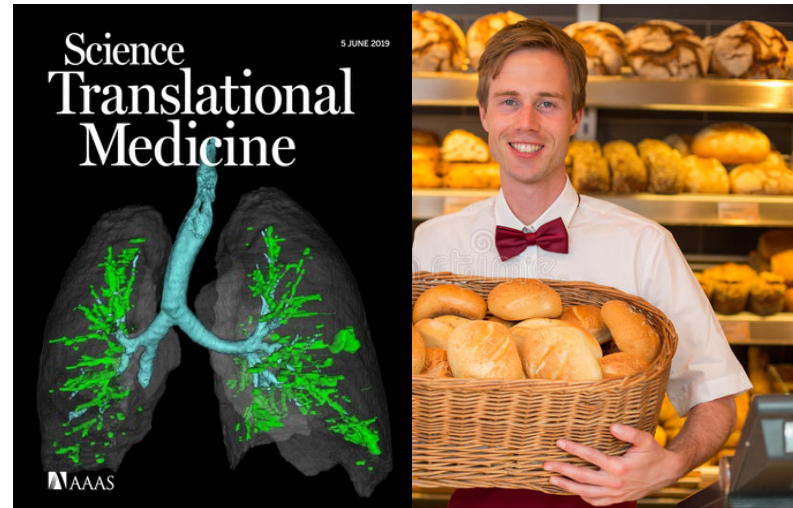


<https://www.bls.gov/ooh/images/3077.jpg>



PREPARE *from day 1*

ARRIVE



<https://www.dreamstime.com>

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norecopa.no/PREPARE/film
3-minute film

TOO LATE!!

HOW CAN WE IMPROVE ANIMAL STUDIES?

RECIPES
NORECOPA.NO/PREPARE

GUIDELINES
• DATABASES
• INFORMATION CENTRES
• JOURNALS, DISCUSSION LISTS, ETC.

SUGGESTIONS FOR
• A MASTER PLAN
• A CONTINGENCY PLAN
• A CONTRACT (ANIMAL FACILITY & RESEARCH GROUP)

COLLABORATION
• ANIMAL CARERS AND TECHNICIANS
• VETERINARIANS
• FACILITY MANAGERS
• SCIENTISTS AND THEIR STAFF
• ANIMAL WELFARE AND ETHICS COMMITTEES
• REGULATORS

THIS WAY WE CAN
• REDUCE THE RISK OF ANIMALS SUFFERING
• IMPROVE OUR METHODS - DO BETTER SCIENCE!
• WRITE BETTER APPLICATIONS
• IMPROVE MANUSCRIPT QUALITY

PRECISION
• **REPLICABILITY**
• **HEALTH AND SAFETY**
• **TRANSLATABILITY**

PILOTS
CABIN CREW
GROUND STAFF
AIR TRAFFIC CONTROLLERS

WE ARRIVED BECAUSE WE WERE PREPARED
VISIT: NORECOPA.NO/PREPARE

norecopa
PREPARE FOR BETTER SCIENCE

Norecopa: PREPARE for better Science

norecopa.no/prepare/endorsements



Report of the Advisory Committee to the Director of the NIH

PREPARE is mentioned as one of the standards which can strengthen critical elements 'across the life of a study, from planning to execution and publication, which will result in a **higher quality knowledge base** and will **better inform future research.**'

<https://acd.od.nih.gov/working-groups/eprar.html>

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ACD WORKING GROUP ON
ENHANCING RIGOR,
TRANSPARENCY, AND
TRANSLATABILITY IN ANIMAL
RESEARCH

FINAL REPORT
June 11, 2021



NASA



cbsnews.com

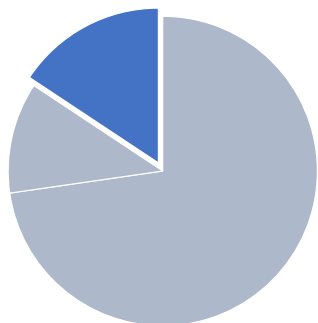


no.wikipedia.org

- Complex machines / animals create ***known or unknown unknown interactions***
- **Design weaknesses** (*which the engineers knew about!*)
- **External pressure to launch** - Publish or perish.
- **Management decisions:**
 - "We've got away with it before"*
 - "We've managed to publish before"*
- **A combination of many factors, each of which may be harmless until they occur simultaneously**

What will the award be used for?

Refinement Wiki



wiki.norecopa.no

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Clicker training

Clicker training is an operant conditioning based on positive reinforcement. When the animal offers the desired behavior, a click or another distinctive sound (secondary reinforcer) is delivered and within the following few seconds the reward is presented (primary reinforcer)^[1]. The click bridges the time between the desired behavior and the presentation of the reward^[1]. A target stick providing a visual guide for the animal can be used for the training.

Animals are usually trained individually, though it is also possible to perform clicker training in a groups, e.g. in mice, rats, and rabbits. For rats, it was demonstrated that they learned tasks by observing the clicker training of their cage mates^[2].

Clicker training can be used to train animals in a stress-free way. The following behaviours are examples for what this technique can be used for:

Mice: entering a tunnel, following a target stick, climbing on the palm of the hand^[3]

Rats: following a target stick, voluntarily change to a cage, observational learning^[2]

Rabbits: following a target stick, rearing/standing up to inspect the abdomen, approaching a human, being touched and lifted by a human, trimming nails, coming on command

Pigs: Pigs can be easily trained to cooperate if they are treated empathetically and desired behavior is reinforced by providing food stuff in form of treats and apple juice^[4].



Clicker training with mice using a target stick. *Left:* The mouse is following the target stick and is climbing on the experimenter's hand. If the hand is lifted, the mouse will remain on the palm of the hand. *Right:* The mice are trained in a group. Two mice are following the target stick on the palm of the experimenter's hand.

- ¹ ^{1.0} ^{1.1} Feng, Lynna C.; Howell, Tiffani J.; Bennett, Pauleen C. (1 August 2016). "How clicker training works: Comparing Reinforcing, Marking, and Bridging Hypotheses" *Applied Animal Behaviour Science*. **181**: 34–40. doi:10.1016/j.applanim.2016.05.012. ISSN 0168-1591.
- ² ^{2.0} ^{2.1} Leidinger, Charlotte Sophie; Kaiser, Nadine; Baumgart, Nadine; Baumgart, Jan (25 October 2018). "Using Clicker Training and Social Observation to Teach Rats to Voluntarily Change Cages" *JoVE (Journal of Visualized Experiments)* (140): e58511. doi:10.3791/58511. ISSN 1940-087X. PMC 6235608. PMID 30417890.
- ³ Leidinger, Charlotte; Herrmann, Felix; Thöne-Reineke, Christa; Baumgart, Nadine; Baumgart, Jan (6 March 2017). "Introducing Clicker Training as a Cognitive Enrichment for Laboratory Mice" *JoVE (Journal of Visualized Experiments)* (121): e55415. doi:10.3791/55415. ISSN 1940-087X. PMC 5408971. PMID 28287586.
- ⁴ "Positive Reinforcement Training in Large Experimental Animals" (PDF).

Experts for clicker training in mice and rats: [TARC](#), Mainz, Germany

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This page was last edited on 27 May 2020, at 11:23.

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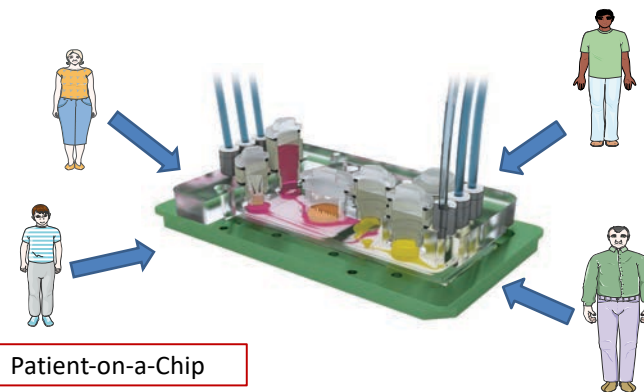
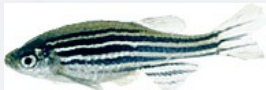


Collaboration, collaboration and collaboration...

Also highly relevant to One Health...



Society is unity in diversity
George Herbert Mead



Patient-on-a-Chip

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Leopold Koenig – NORECOPA – 10.10.2017

TSSUSE
Emulating Human Biology



24th August

Shaun Khoo, @EpistemeHealth

'Siloing is a huge barrier. Papers on refinement are published in specialist vet sci lab animal journals. The scientists who do animal research do not read these journals and the journals they do read don't tend to publish updates on best practice.'

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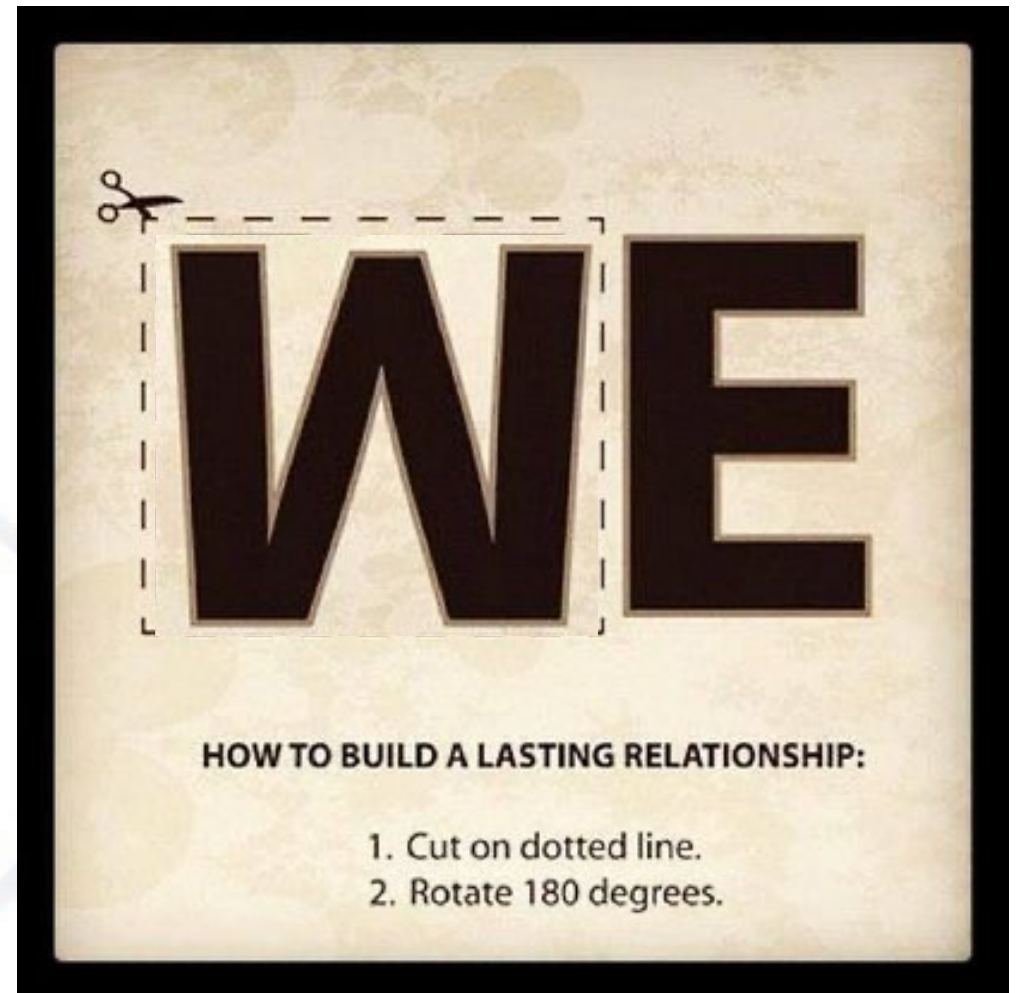


International Society for Transgenic Technologies

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Aggregation of marginal gains

Instead of hoping for a paradigm shift (= immediate animal replacement):

Small improvements of many small components

Lilley E, Jennings M (2013): Refinement: Lessons from the 2012 Olympics

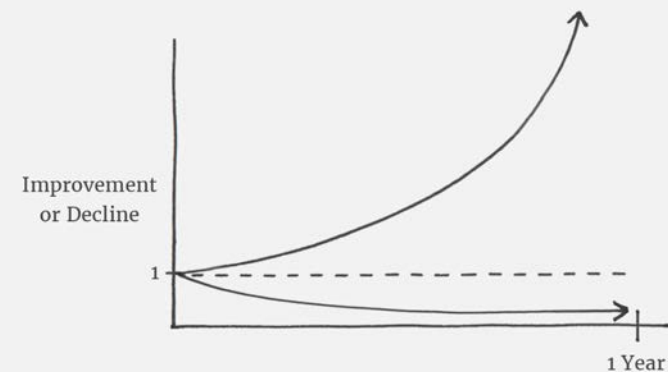
Alternatives to Laboratory Animals (ATLA) 41(3):P28-P29.
doi:10.1177/026119291304100309

rspca.org.uk/webContent/staticImages/Downloads/2012Olympics.pdf

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The Power of Tiny Gains

1% better every day $1.01^{365} = 37.78$
1% worse every day $0.99^{365} = 0.03$



JamesClear.com

jamesclear.com/marginal-gains



Norecopa: A hub of international resources norecopa.no/WC11

The PREPARE guidelines norecopa.no/WC11-PREPARE

Wildlife research norecopa.no/WC11-wildlife

The Refinement Wiki norecopa.no/WC11-wiki

Feedback

English-language newsletters

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