

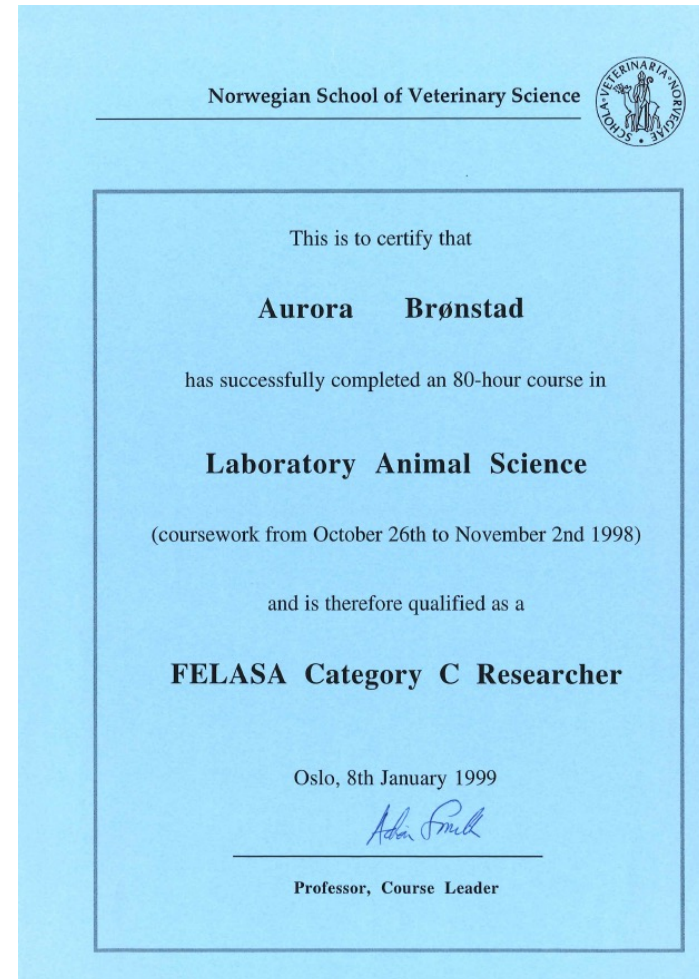


My 3R journey

Aurora Brønstad



Journey starts



The 3R's

The Principles of Humane Experimental Technique – 1959 Russell & Burch

- Replacement
- Reduction
- Refinement



3R are internationally recognized

The three R's

Russell & Burch - The Principles of Humane Experimental Technique 1959

Replacement

Substitution for conscious living higher animals of insentient animals, or methods not involving animals (in vitro methods)

Reduction

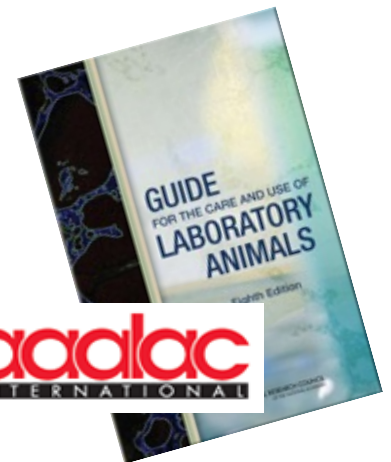
Reduction in the number of animals used to obtain information of a given amount and precision

Refinement

Decrease in the incidence or severity of inhumane procedures

3Rs in regulations and guidelines

- Norwegian animal research regulation
 - §9 – Erstatning, Reduksjon og Forbedring
- EU directive 2010/63
 - Article 4 - Principle of replacement, reduction and refinement
- The guide to the care and use of laboratory animals
- AAALAC Position statement on 3R (2024)



Pregnancy test (1959)

Sprøyter man derimot inn urin fra en gravid kvinne i de første 2-3 måneder av graviditeten, vil det etter 100 timer komme tydelige forandringer i ovariene deres. Denne reaksjonen kalles Aschheim-Zondeks reaksjon etter dem som først beskrev den. (Det skal be-

sen av Aschheim-Zondeks reaksjon består i at man gjentatte ganger sprøyter inn litt urin under huden på musunger som veier ca. 8 g. Etter 100 timer drepes musungen med f. eks. kloroform og obduseres. De forandringer man finner i ovariene, er dels en forstørrelse av hele ovariet, dels blodpunkter på overflaten av ovariet samt større eller mindre corpora lutea.

JØRGEN LØVSET OG EBBE BRANDSTRUP

Lærebok i obstetrikk for jordmødre

ASCHEHOUG

Løvset, J., & Brandstrup, E. (1959). *Lærebok i obstetrikk for jordmødre* (p. 54-56). Aschehoug.

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Pregnancy test (1959)

Etter at man hadde holdt på med denne graviditetsreaksjon endel år, viste det seg at den praktiske nytte av den ikke var så stor fordi den tok for lang tid. Man begynte da å se seg om etter andre biologiske graviditetsreaksjoner, og den første som kom etter Aschheim-Zondeks, var Friedmans reaksjon. Friedman sprøytet inn urin fra gravide på kaniner. Kaniner har som katter ikke noen egglosning

Det har vist seg at man også kan få graviditetsreaksjon på hunpadder, særlig på *Xenopus laevis* (Hogben test). Der sprøyter man urin i lymfesekken på ryggen av padden, og senest etter et døgn vil det komme egglegging hos hunnen dersom reaksjonen er positiv. En enda hurtigere test har man funnet i den såkalte Galli-Mainini-testen. Det er en test som utføres på hanfrosk, og teknikken ved innsprøytingen er den samme som på padde, men allerede etter få timer kan man ta en prøve fra kloakken (det felles uttømmingssted for urin og avføring) på frosken, og hvis reaksjonen er positiv, finner man spermier.

Løvset, J., & Brandstrup, E. (1959). *Lærebok i obstetrikk for jordmødre* (p. 54-56). Aschehoug.

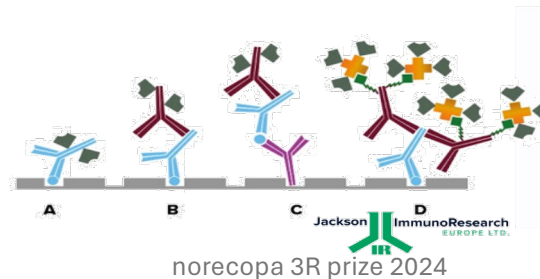
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Pregnancy tests (2024)

- An enzyme-linked immunosorbent assay (ELISA)
 - robust and sensitive technique
 - quantify specific proteins
- Facilitates high volume , fast throughput
- Cheap!



05.06.2024

APOTEK 1 Meny Søk blant 10 000 produkter og råd Mine resepter Min Side Kasse

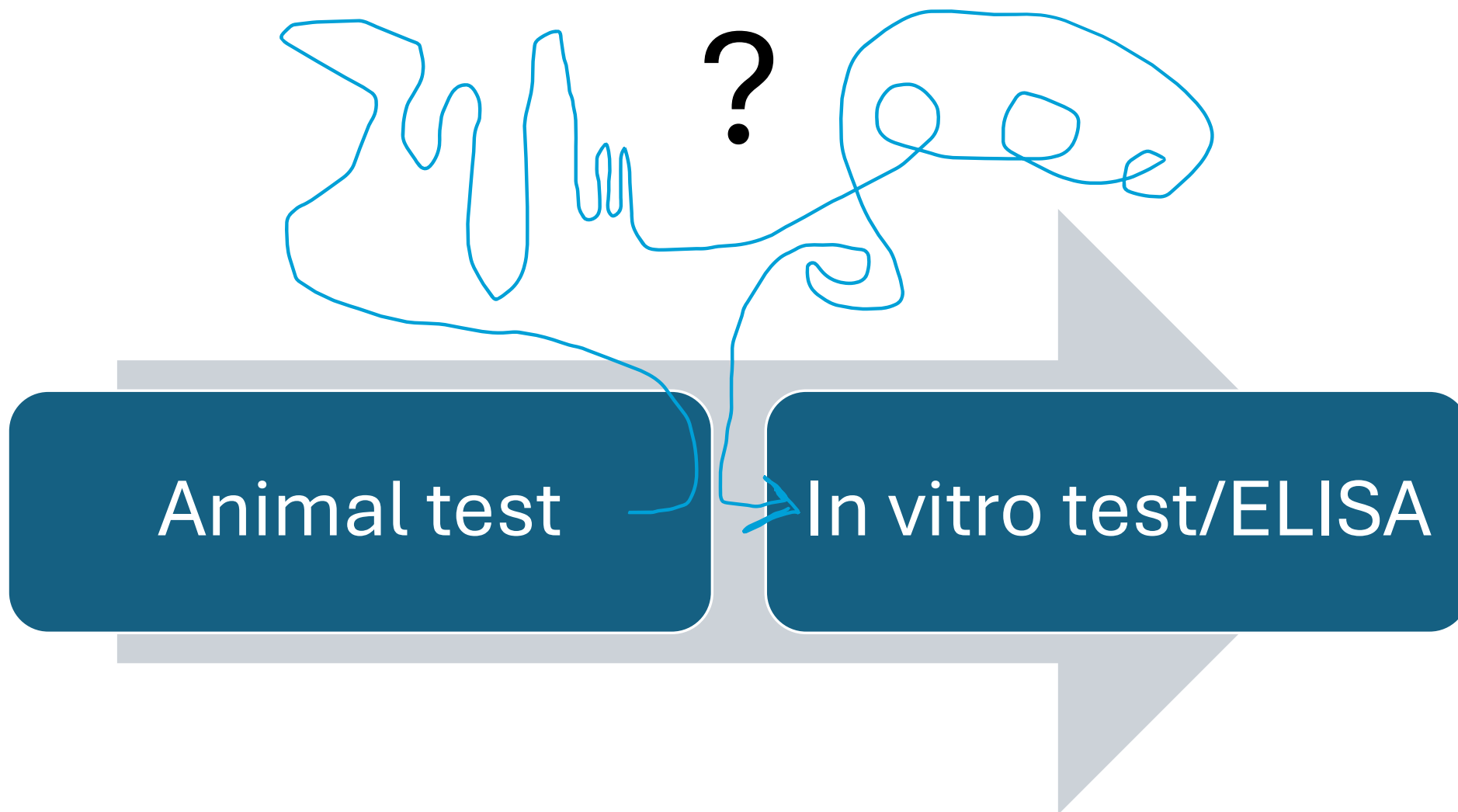
Graviditetstester

Med en graviditetstest kan du raskt og enkelt finne ut om du er gravid. Hvor tidlig du kan teste deg avhenger av graviditetstesten, men det sikreste resultatet får du ved testing fra den dagen du skulle hatt menstruasjon. Les pakningsvedlegg nøye før bruk.

Sorter etter: Relevanse Produktnavn A-Å Pris lav-høy Pris høy-lav På kampanje Kundenmeldelser

17 produkter i kategorien

Product Name	Rating	Price (kr)	Price per unit (kr/stk)	Action
RFSU Test Tidlig graviditetstest 1 stk	★★★★★	99,90	(99,90 kr/stk)	Kjøp
Clearblue Digital ul-tratidlig graviditets...	★★★★★	259,90	(129,95 kr/stk)	Kjøp
RFSU Test Ofte graviditetstest 8 stk	★★★★★	167,90	(20,99 kr/stk)	Kjøp
Metode graviditets-test tidlig strimler...	★★★★★	199,90	(19,99 kr/stk)	Kjøp
Clearblue digital graviditetstest med...	★★★★★	309,90	(154,95 kr/stk)	Kjøp
Clearblue digital graviditetstest ukeindi...	★★★★★	204,90	(204,90 kr/stk)	Kjøp
RFSU Test ofte graviditetstest 25 stk	★★★★★	334,90	(13,40 kr/stk)	Kjøp
Clearblue Rask de-teksjon graviditets...	★★★★★	249,90	(124,95 kr/stk)	Kjøp



3Rs at



UNIVERSITETET I BERGEN



[Alternatives lab at Dyreavdelingen | The Laboratory Animal Facility | UiB](#)

[Cell culture labs | Center for Translational Oral Research \(TOR\) | UiB](#)

[O'Farrell | Fruit Fly Lab \(uib.no\)](#)

Alternatives lab at Dyreavdelingen

Spend some time in our AltLab to get more training in handling and procedures! The use is free of charge

3R

AltLab
Training room for
alternative methods

R
r
R

At our AltLab (Alternatives lab for work with lab animal models) you can find models that can replace use of live animals for training and education.

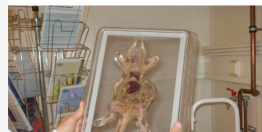
- The KOKEN-rat is useful for learning intubation and blood sampling. The tail is full of "blood" and makes the experience realistic. The Pro-Set rat model shows rat anatomy and is good for dissecting training.
- The Squeekums rat helps you to deal with any rat phobia, and to train on handling techniques and ear tagging.
- "Minor Skin Procedures" helps you to practice on some surgical techniques.
- In the MD-PVC-MODEL film you can see about 25 different surgery techniques like transplantation of veins and organs and injections.

The AltLab also works as a library for selected DVDs, like: Endotracheal Intubation, Laboratory Animal Anaesthesia, Surgery and Perioperative Care, Laboratory Animal Anaesthesia: Rat & Mouse, Experimental Design, Human Endpoint, and a few brochures on the subject alternatives to the use of laboratory animals.

We recommend the AltLab particularly to new technicians, PhDs and other students who have little experience with laboratory animals.

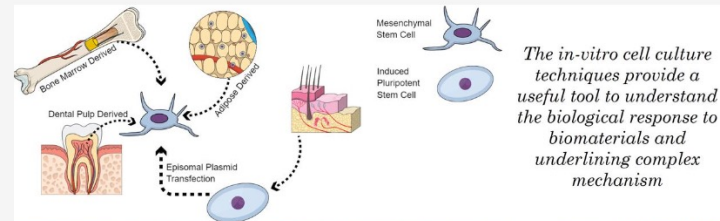


Photo: J.Stormark



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Cell culture labs



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Fergal O'Farrell studerer bananfluene som sannsynligvis utvikle kreft. Og de er forbausende lik mennesker.

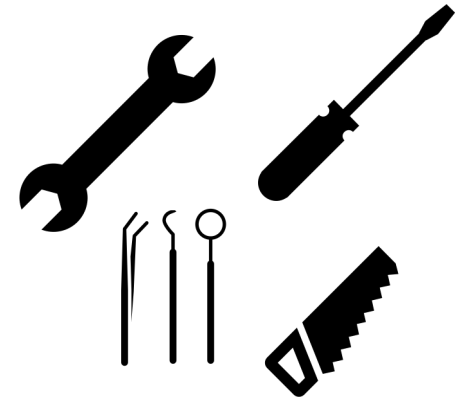
BT Magasinet | Fiskeolje

De har gitt svar på flere medisinske gåter. Her er Bergens nye forsøksdyr.



Av Kari Pedersen og
Rune Sævin (foto)

REFINEMENT HUMANE ENDPOINTS



TOOL TO DESIGN LESS SEVERE ANIMAL STUDIES

2nd international conference on the use of **Humane Endpoints** in animal experiments for biomedical research (Berlin 20-21 august 2005)



05.06.2024

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HEP CHAPTER

Chapter 8

Harm to research animals, severity categories, and humane endpoints

Aurora Brønstad

Department of Clinical Medicine, University of Bergen, Bergen, Norway

05.06.2024

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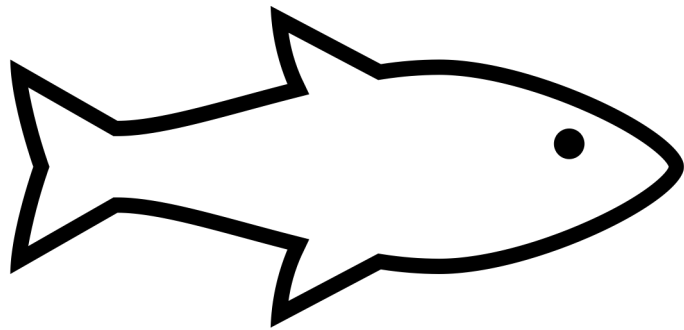
Practical Handbook on the 3Rs in the Context of the Directive 2010/63/EU

Edited by

Gianni Dal Negro

Silvia Sabbioni





Teaching HEP in Fish

PISCINE ENDPOINTS

[back for updates](#)

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SAGE

Working Party Report

Defining piscine endpoints: Towards score sheets for assessment of clinical signs in fish research

L Andersen¹, A Rønneseth², MD Powell³ and A Brønstad⁴

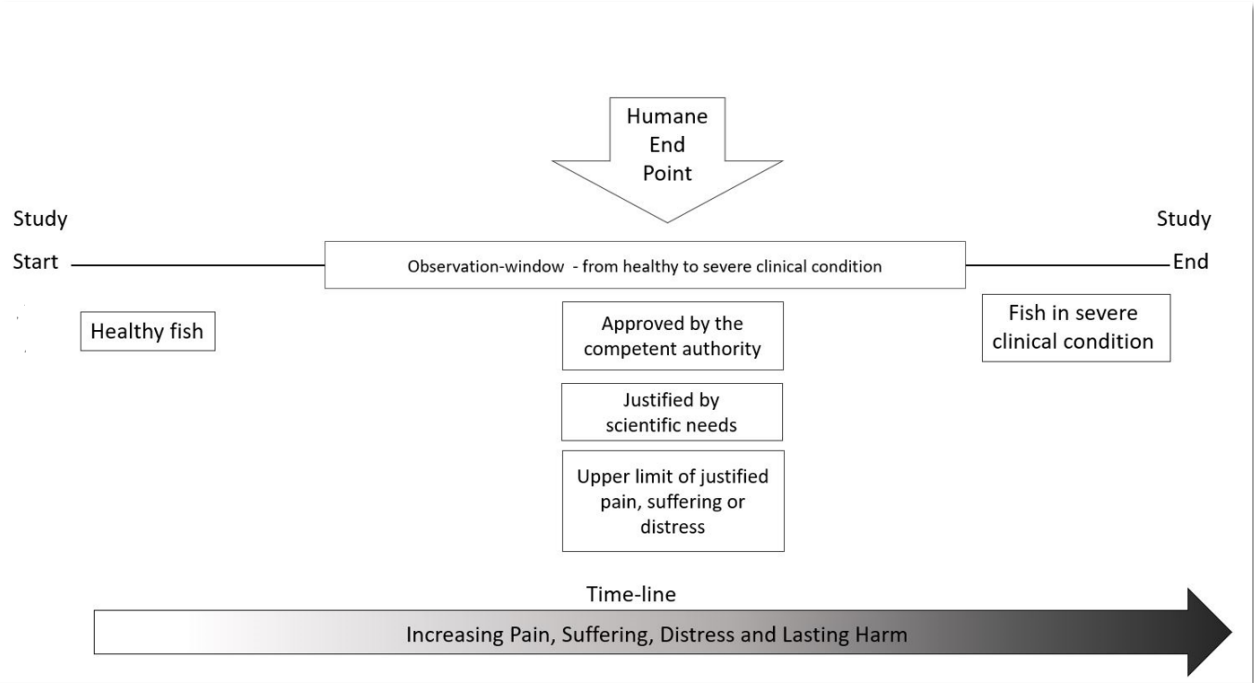
Abstract

The seminar 'Severity and humane endpoints in fish research' organized by the University of Bergen, the Industrial and Aquatic Laboratory, together with Fondazione Guido Bernadini, took place on 4 October 2019 in Bergen, Norway. The seminar was followed by a workshop, 'Establishing score sheets and defining endpoints in fish experiments', held on 28 January 2020, also in Bergen. The purpose of the seminar was to raise awareness about fish ethics together with severity classification and humane endpoints in fish studies, using examples from farmed fish, mainly salmonids and lumpfish. The overall aim of the workshop was to better define humane endpoints in fish experiments, as well as to discuss suggestions for development and use of score sheets for assessing clinical signs related to endpoints. Endpoints for fish should not only be based on what we know about fish diseases and the lesions they induce but should also take into consideration knowledge about fish species and life stage, fish anatomy, physiology and the general state and behaviour of the fish. For this reason, to reinforce that endpoints should come from the animal's perspective and needs, we renamed humane endpoints for fish to piscine endpoints. This paper reports the main messages from the workshop sessions including advice on development and use of score sheets.

Keywords

Moribund, categorization, scoring systems, severity assessment, humane endpoints, animal welfare, refinement

Date received: 12 September 2022; accepted: 4 January 2023



FISH-END

FishEnds-Dig

Project report for norecopa 2021

Evaluation of humane endpoints in fish

Aurora Brønstad¹, Anita Rønneseth², Mark Powell³, Svein Brekke⁴ og Linda Andersen⁵

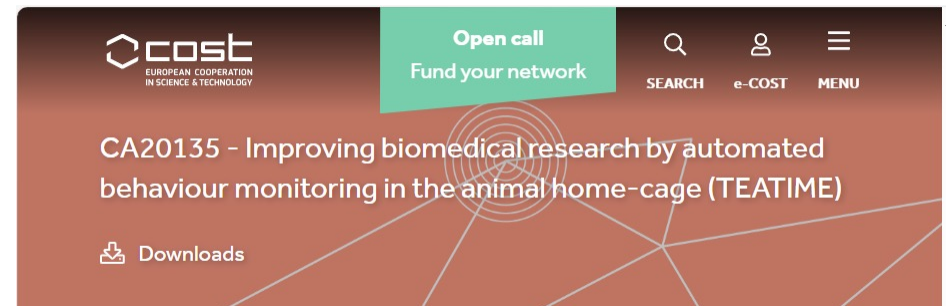
- Daily animal observation of live fish swimming in the tank without being disturbing
- Observing live fish gives an opportunity to timely apply mitigating actions to minimize or eliminate pain, suffering and distress.
- Necropsy of dead animals is important to understand disease mechanism. However, in a study we would like all study animals to survive the observation period to the study endpoint.



05.06.2024

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HOME CAGE MONITORING

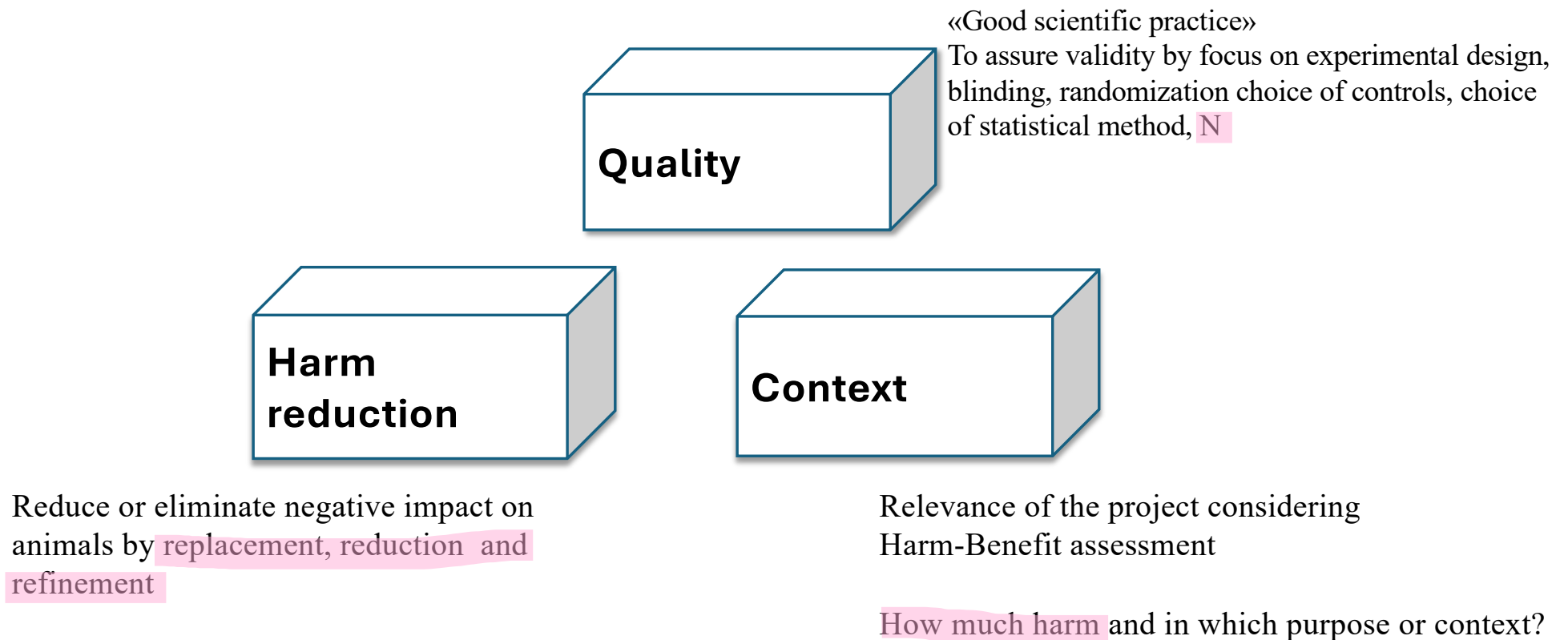


Description

Animal use for scientific purposes is guided by the principles of 3Rs (Reduction, Refinement and Replacement). Developing refined experimental conditions can substantially improve animal welfare and importantly, enhance the translational value and data reproducibility.

Novel and emerging technologies allow 24/7 collection of behavioural data in undisturbed mice, the most widely used species in biomedical research. These recently developed technologies minimize the impact of stressors, such as human interaction and testing in novel arenas, which are known to influence data collection and animal welfare. It is now possible to assess a more naturalistic behavioural profile in familiar environment, such as the animals' home-cage.

3Rs in the cornerstones in ethical behavior





3Rs

An intrinsic core
value or a concept
you need to learn?

PUBLIC OPINION IN SWEDEN ON THE USE OF ANIMALS IN RESEARCH



VETENSKAPSRÅDETS RAPPORTSERIE

Vetenskapsrådet

Animal experiments can be acceptable in the following context and conditions:

- *If there are no other options*
 - *(No replacements for animals)*
- *If the animals do not suffer*
 - *(refinements)*

Public opinion in Sweden on the use of animals in research, SwedishResearchCouncil, 2008

«3R culture»

The role of organizational culture in compliance with the principles of the 3Rs

Aurora Brønstad, DVM, PhD¹ & Anne-Grethe Trønsdal Berg, DVM²

In order for their research to be legitimate, scientists carrying out research using animals must comply with rules and regulations. The 3Rs (replacement, reduction and refinement) are one set of guidelines that help to promote the ethical use of animals for research. An important question is whether implementing the principles of the 3Rs in legal regulations, such as a Directive of the European Parliament and of the Council on the protection of animals used for scientific purposes, will increase compliance with the principles of the 3Rs in research organizations. Previous work suggests that organizational culture is just as important for directing behavior as are formalized rules and regulations. This article introduces the concepts of compliance and organizational culture and discusses their consequences on the implementation of the principles of the 3Rs.

Volume 40, No. 1 | JANUARY 2011

www.labanimal.com

“The important thing to understand is why and how humans, within defined conditions make their decisions and perform their actions”

Høivik, D. (2009). Health, safety and environment culture in the petroleum industry in Norway. University of Bergen.

3R culture

Pattern of **basic assumptions** within a group about how to best to comply with or adhere to the principles of the 3Rs

- **learned by a group** as it **solved its problems**
- **worked well enough** to be **considered as valid**
- **taught to new group members** as the **correct way to perceive, think and feel** about the 3Rs.

*Adapted from Edgar Schein
Organizational culture and leadership 2004*

- This way of thinking is conserved in the group, and can be difficult to change

3R Culture



- Tool to improve science
 - Faster
 - Cheaper
 - Better

Inspiration for continuous improvements



- “Bureaucratic exercise”
- Obstacle
 - research
 - progress

Least necessary actions to comply

Relationship and Compliance

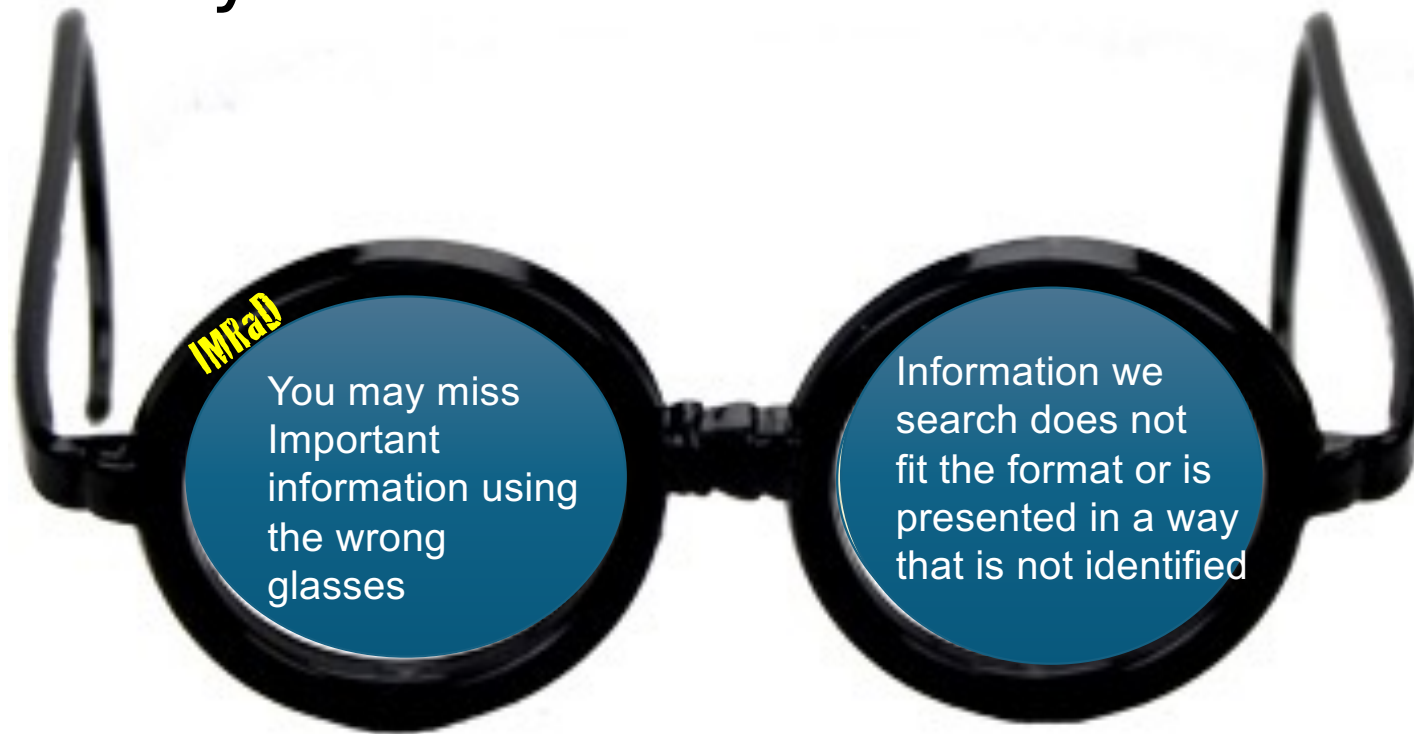
Paternalistic

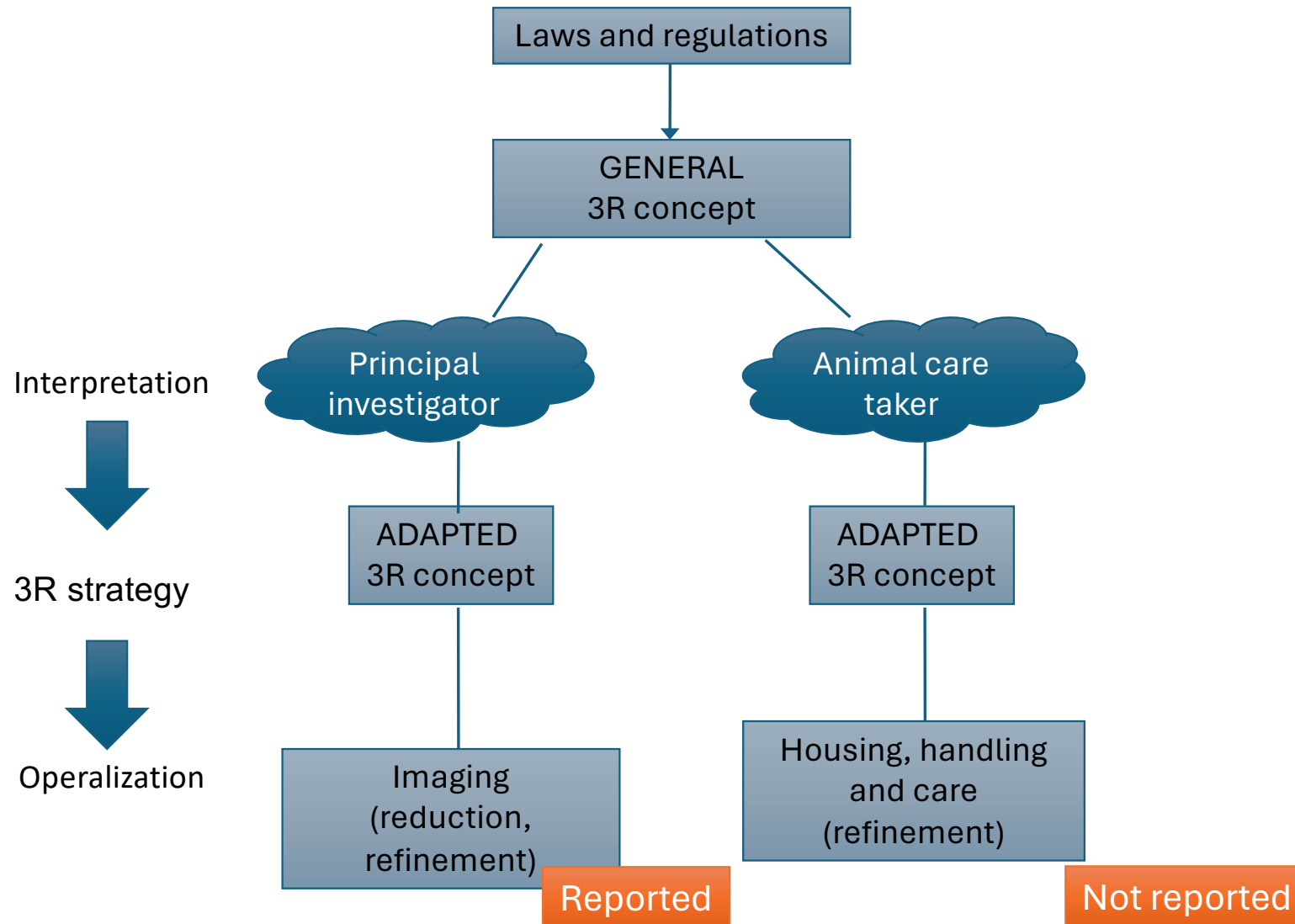


Partnership

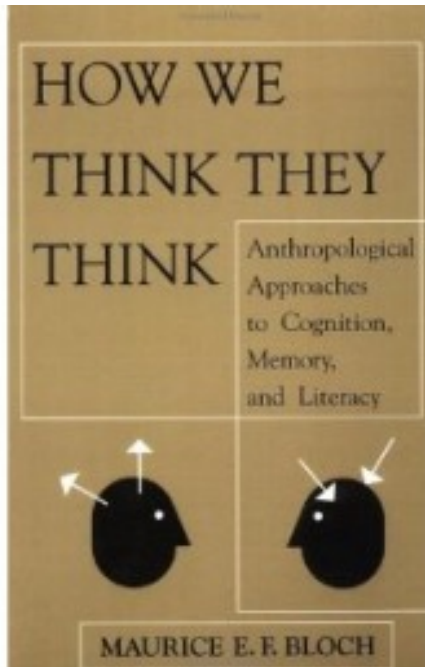


Why can 3R information be hard to find?





Studies of Culture – The limitation of language



*How do we know
how people make
decisions and
solve problems?*

- Qualitative methods
 - Interviews - open questions
 - Observations



Free access | Research article | First published online May 1, 2019

Examining compliance with ethical standards for animal research: is there a need for refinement? A qualitative study from northern Europe

[Aurora Brønstad](#) and [Peter Sandøe](#) [View all authors and affiliations](#)

[Volume 54, Issue 2](#) | <https://doi.org/10.1177/0023677219841080>

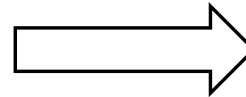
4 focus group
interviews

- **The informants expressed concerns which accord with the core-values of the 3Rs, but in only one group they explicitly referred to the 3Rs as a concept**
- Solving practical issues, the (refined) best way, and the importance of doing good science were dominant topics in the interviews
- Practical issues could not easily be separated from the goal of good science.
- Whereas policy makers seem to expect researchers to explicitly take ethical considerations into account, we found that their ethical thinking is mainly manifested as an implicit part of methodology and design, however not explicitly expressed.

Culture

«3R culture»

- **basic assumption that replace, reduce and refine is the preferred mode of action**



Culture of care.

- Respect
- Recognition
- Responsibility

HARM

BENEFIT



HARM TABLE

HARM-Freedoms Impacted

Pain/Injury: _____

Fear/Distress: _____

Hunger/Thirst: _____

Ability to express normal behavior: _____

Discomfort/Husbandry: _____

Modulating Factors for HARM	Description	Mitigating Effect	Aggravating Effect	Summary Color
Animal— Species	NHP		Sentient species	
Animal— Number	32	Statistically justified		
Animal— Suited to environment	F3 generation	Well trained for the task		
Animal— Health status				
Experimental— Intensity				
Experimental Duration				
Experimental Cumulative Experience				
Experimental— Endpoint				
Experimental Complication/Distribution Rate				
Experimental Genetic Modulation				
Environmental Housing/Husbandry				
Environmental Personnel competence/experience				

Refinement

Need to be refined

Working Group Report

Recommendations for Addressing Harm-Benefit Analysis and Implementation in Ethical Evaluation – Report from the AALAS-FELASA Working Group on Harm-Benefit Analysis – Part 2

Kathy Laber¹, Christian E Newcomer², Thierry Decelle³,
Jeffrey I Everitt⁴, Javier Guillen⁵ and Aurora Brønstad⁶

Laboratory Animals
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Be kind

Don't harm



THANK YOU FOR YOUR ATTENTION