

Assessing Welfare

How, Why and When

Research Animals Department

- Principal goal = replacement of animals with humane alternatives
- **ROBUST ETHICAL REVIEW OF ANIMAL USE**
 - Challenging necessity and justification
- **EFFECTIVE IMPLEMENTATION OF THE THREE RS**

RAD part of
RSPCA Science Group
CAD FAD WLD
Science driven policy



Penny



Barney



Elliot



Juliet



Research Animals Department

Our approach

- Long history of working with the scientific community
 - Researchers, regulators, animal care staff
- Challenge from 'within'
 - Ethical review, actual severity reporting, training & competency
- Highlighting problems *and* finding practical solutions

Our key **areas of work**

- Challenging the use of animals - ethically and scientifically
- Ensuring effective, well enforced regulation of animal experiments
- Raising standards internationally
- Promoting debate which is open and honest
- Promoting animal welfare in tertiary education
- Reducing the use and suffering of lab animals

Assessing Welfare

Why?

Ethical and legal implications

Article 4

Principle of replacement, reduction and refinement

1. Member States shall ensure that, wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure.

2. Member States shall ensure that the number of animals used in projects is reduced to a minimum without compromising the objectives of the project.

3. Member States shall ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals.

- Level

benefit

- Re

- Pr

- Legal

suffering under Directive 2010/03/ED

harm-

minimise

Assessing suffering is a necessary step towards reducing it

- Earlier detection leads to more effective alleviation
 - Animal spends less time suffering
 - More severe levels of suffering can be prevented
 - Ideally, suffering could be avoided altogether for animals in future studies

There are also scientific benefits

- Responses to suffering (physiological, immunological or behavioural) can affect data quality
- Can also affect scientific validity
 - Humans with cancer pain receive pain relief; providing equivalent pain relief to an animal 'model' could improve validity in cancer research

Assessing Welfare

When?

Project Planning

Appendix I
High level categories as the basis for the development of project and procedure specific scoring sheets

Develop project, species and strain specific severity assessment

Decide on monitoring tools, frequency & types of scoring

Agree on actions when signs of pain, distress or suffering are observed

Ensure personnel with all necessary skills are included in the process

Appendix II
Reference material for the development of project and procedure specific scoring sheets

During The Project

Consistency in observations/trained staff

Effective day-to-day monitoring

Good communication among all involved

Ongoing assessment protocol as necessary

Appendix II
Reference material for the assessment and scoring

After The Project

Assessment and scoring of *actual severity*

→ Statistical information

→ Retrospective project assessment

→ Feedback for future studies

→ Reflect on further opportunities to implement the 3Rs

→ Input to thematic reviews

Assessing Welfare

How?

A continuous process of assessment

1. Observe animals during procedures, using effective protocols for assessing indicators
2. Use the observations to make a judgement on the nature and level of suffering
3. Extract an overall judgement on suffering (mild, moderate, severe) for statistical reporting
4. Take the opportunity to reflect upon how effectively the Three Rs were implemented and whether improvements could be made

Four factors for good monitoring

1. Understand good welfare and the 'normal' animal
2. Recognise all potential causes of suffering
3. Select appropriate indicators of suffering
4. Use appropriate recording systems, that enable welfare problems to be dealt with at the time and are compatible with severity reporting requirements

What would the individual animal's experience be?

National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes

Working document on a severity assessment framework

Brussels, 11-12 July 2012

The Commission established an Expert Working Group (EWG) for the assessment of severity of procedures to facilitate the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes. All Member States and main stakeholder organisations were invited to nominate experts to participate in the work.

The EWG for the assessment of severity met twice: in December 2011 with the focus on genetically altered animals, and in May 2012 discussing a general framework for assessing the actual severity experienced by animals in procedures.

This document is the result of the work of the two EWG meetings, discussions with the Member States as well as legal input from the Commission on the understanding of a severity assessment framework, its components, participants and working tools and methods. It was endorsed by the National Competent Authorities for the implementation of Directive 2010/63/EU at their meeting of 11-12 July 2012.

Examples to illustrate the process of severity classification, day-to-day assessment and actual severity assessment

Brussels, 11 January 2013

The *Working Document on a Severity Assessment Framework*¹ produced by the European Commission Expert Working Group and endorsed by the National Competent Authorities for the implementation of Directive 2010/63/EU on the protection of animals used for scientific purposes at their meeting of July 2012 recommended that examples be developed to illustrate the "process of severity classification, day-to-day assessment and final, actual severity assessment" and that these should be made available to the scientific community.

Following on from this, the Expert Working Group produced a range of examples to show how the process described in the *Working Document* might be applied to different procedures. These are intended to help Competent Authorities, users, animal technologists, veterinarians and all other relevant staff to ensure that pain, suffering and distress are effectively predicted, recognised, ameliorated, where possible, and consistently assessed during procedures. This document was endorsed by the National Competent Authorities for the implementation of Directive 2010/63/EU at their meeting of 23-24 January 2013.

It is crucial that a number of important factors are taken into account when using these examples:

- It is assumed that **good practice is implemented** throughout with respect to housing, husbandry and care; refining procedures; education and training; assessing competence; retrieving and applying current information on replacement, reduction and refinement; and experimental design.
- The kind of score sheets included within the examples are intended to **complement – not substitute for – the judgement of trained, competent, empathetic staff**. The aim is to enable more systematic and objective observation, record keeping and assessment of suffering, but not to over-ride professional judgement.

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_Severity_Assessment.pdf

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/examples.pdf



Recording systems - EAE

PHYSICAL

Weight loss
Food/water consumption
Coat maintenance
Piloerection
Noticeable attention to area of body, e.g. scratching, licking
Posture, e.g. belly pressing
Convulsions
Abnormal gait/impaired mobility
Skin lesions
Tumours
Impaired sight or hearing
Impaired balance
Nasal or ocular discharge

PHYSIOLOGICAL

Respiration
Poor ability to thermoregulate
Physiological parameters where available
Increased susceptibility to disease

PSYCHOLOGICAL STATE

Provoked behaviours
Interaction with other animals
Aggression towards other animals
Undesirable behaviours such as stereotypy or barbering
Anxiety, assessed using elevated-plus maze or other relevant paradigm
Use of enrichment items e.g. on or in refuges, gnaw blocks, making nests
Mismothering

OTHER

Specific indicators relevant to disease model, e.g. neurodegeneration, hyperalgesia, psychiatric disorders

Recording systems - EAE

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OTHER

Specific indicators relevant to disease model, e.g. neurodegeneration, hyperalgesia, psychiatric disorders
Bladder control, tail tone

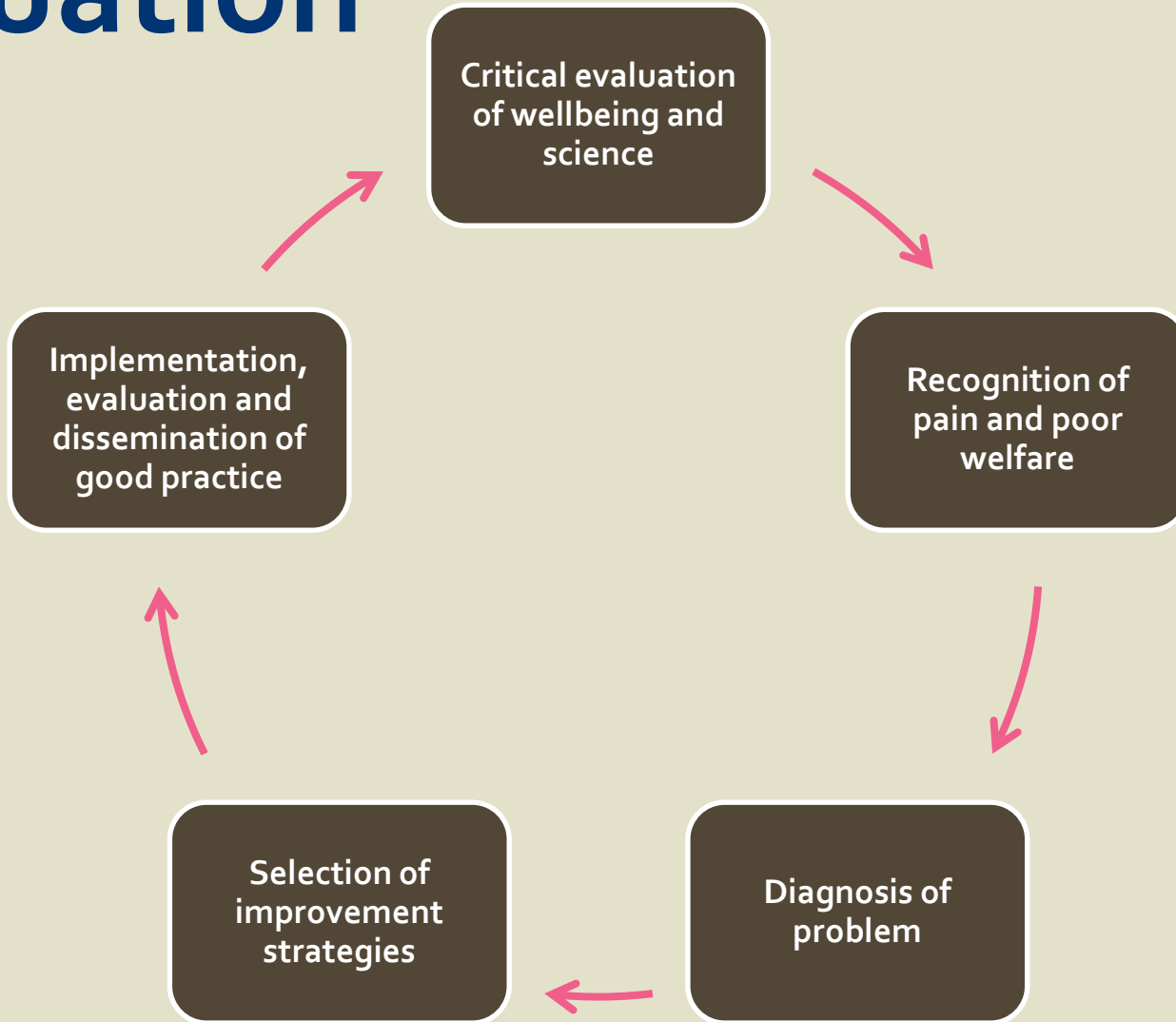
EAE record sheet for cage-side monitoring – technologist/researcher

Date:					
Appearance					
Weight					
Reduced grooming					
Body function					
Reduced bladder control					
Reduced tail tone					
Rapid, slow or deep breathing					
Environment					
Poorly constructed nest					
Behaviour					
Reduced social behaviour					
Altered gait					
Procedure-specific indicators					
Side resting position					
Increased righting time					
Near-complete plegia					
Paresis					
Other observations					

ASSESSMENT SYSTEM FOR INDICATORS IN SCORE SHEET

Score:	1 = Mild	2 = Moderate	3 = Severe
Weight loss	Up to 10 %	10 to 20 %	20 to 35 %
Fur condition	Slightly unkempt	Slight piloerection	Marked piloerection
Bladder control	Evidence of some loss of control, e.g. small amount of urination in nest	More pronounced 'leaking' of urine	Incontinence
Tail tone	Diminished lifting or curling of tail	Loss of tone in distal half of tail	Loss of tone in entire tail
Rapid, slow or deep breathing	Slight	Moderate	Marked
Nest condition	Slightly disorganised	Some attempt at nest but disorganised	No nest
Social behaviour	-	Reduced interaction with other animals	Significantly reduced interaction; passive
Gait	Clumsy	Dragging one hindlimb	Dragging two hindlimbs
Side resting position	-	-	Present
Righting	Slow to right when placed on back	Marked difficulty in righting	Inability to right within 5 seconds after placing on back
Near complete or complete plegia	-	-	Present
Paresis	Slow forelimb abduction when placed on back	Reduced range of forelimb abduction when placed on back	No forelimb abduction

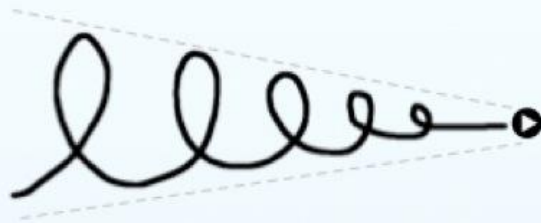
Evaluation



(Lloyd *et al* 2008)

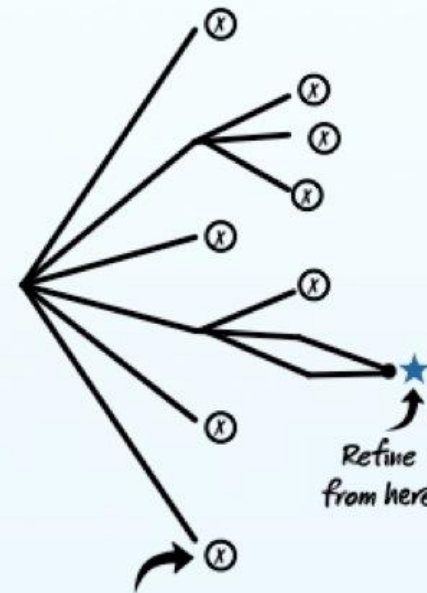
Refinement, pause for thought....

Refinement



Best solution
is missed

Exploration



Refine
from here

Many alternate
solutions explored

Refinement

AGGREGATION OF MARGINAL GAINS?

- Single large change
 - Boardman bike
 - Robo-athlete
 - Add a motor!
- Series of small changes
 - Better front forks
 - More aerodynamic wheels
 - More aerodynamic helmets
 - Heat pads to warm muscles between races
 - Better suit design
 - Better physiotherapy
 - Psychological support

Refinement

AGGREGATION OF MARGINAL GAINS?

- Single large change
 - Replace all procedures with alternatives
 - Choose not to perform the experiment
- Series of small changes
 - Improve housing and care
 - Improve welfare assessment
 - Implementation of humane endpoints
 - Rigorous ethical review
 - Better experimental design



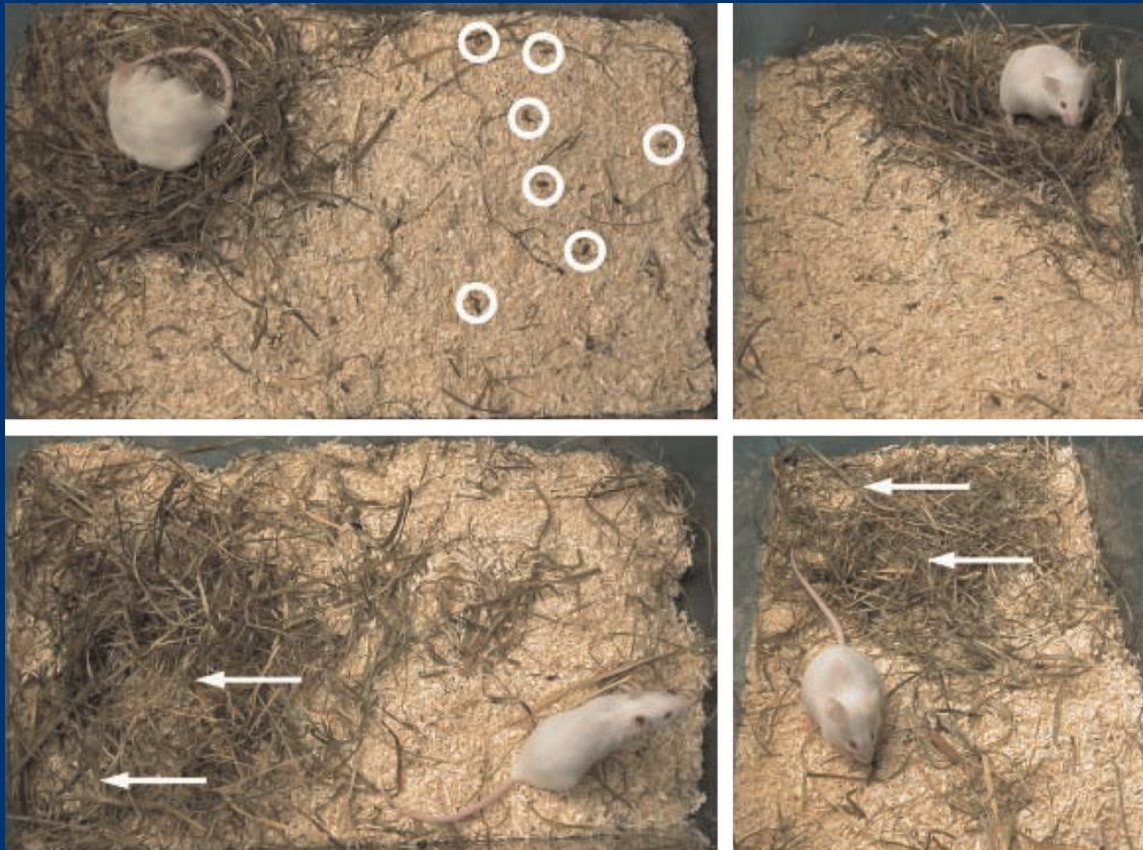
End Suffering



Suffering reduced,
can be applied
broadly

More subtle signs:

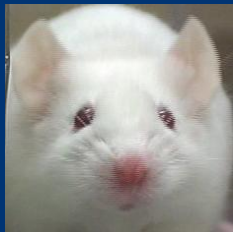
E.G. NEST BUILDING BEHAVIOUR



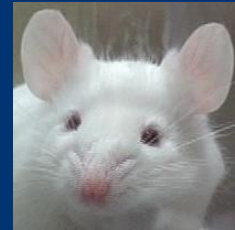
Normal



Increasing evidence of pain



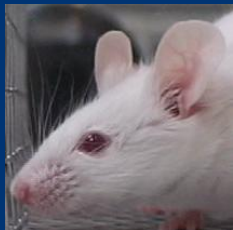
Orbital tightening



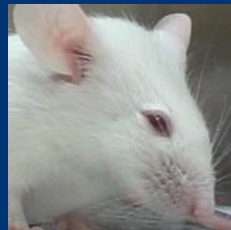
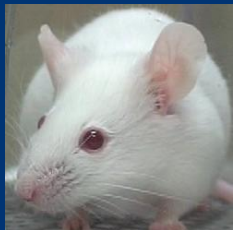
Nose bulge



Cheek bulge



Ear position



Whisker change

Rats*

Mice*

Rabbits*

Horses*

Sheep

Pigs

Rhesus macaques

Koalas



Grimace scales

GREAT TOOL

BUT.....



16 | CORRESPONDENCE

VETERINARY PRACTICE AUGUST 2015

Use of 'grimace scales' to assess pain in animals

The article acknowledges that grimace scales should be used alongside other rating scales, and we would agree and suggest that they should also be accompanied by good clinical judgement, part of which is the presumption that a procedure or condition considered likely to be painful probably is, even if a grimace is not detected.

The perceived or actual absence of a pain face should never be used to withhold treatment where it would otherwise have been given.

Yours faithfully,
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<http://www.nc3rs.org.uk>

<http://www.nc3rs.org.uk>

[Grimace%20Manual.pdf](#)

[Grimace%20Manual.pdf](#)

Important points to note about reducing suffering

REFINEMENTS NEED TO BE EVALUATED

It can be obvious when a refinement will reduce suffering

– **but this is not always the case**

There has to be a system in place for evaluating refinements so that an informed decision can be made about their value, or they can be further developed

This can be done as part of welfare assessment during the procedure

Welfare as a continuum?

Good welfare

A good life

Mainly positive experiences & emotions

Adequate Welfare

A life worth living

Minimal suffering

Poor welfare

A life not worth living

All suffering



Positive welfare

Encouraging a good Quality of Life

What does a 'happy' animal look like, and how do you make animals happy?

Good self-care

Normal activity budget, including sleep

Interacting with humans

Interest in pleasurable things, *e.g.* treats

Play

“Anticipatory” behaviour (looking forward to pleasurable events)



A stretch objective

- Could we eliminate severe suffering?
- What would we have to do to make this happen?
 - What issues would prevent this from being possible?
 - How would we address these issues?

Why are some models severe?

- 'Understanding and treating diseases that cause high levels of suffering in patients requires animal models of disease that cause similar suffering'
- Regulatory requirements
- 'Pressure' from peer review

- Can any of these be challenged?

Yes!

- Animal can never be 1:1 model for human disease
- What information is needed?

- Understanding mechanism
- Efficacy (does treatment work?)
- Dose (what is the plasma concentration ?)

- A model of mechanism is more relevant than a disease model

- Model the mechanism, not the disease
- Less severe endpoints

- Both regulators and journal editors should be challenged about requiring data from severe models

Goal: to **end** severe suffering



- Convincing the scientific community that ending severe suffering is both desirable and achievable
- Multiple work streams
 - Producing guidance to promote and facilitate ending severe suffering
 - Challenging necessity and justification
 - Forming expert working groups to refine procedures and models

**Challenge
people to
think
differently!**

Comment

A 'Road Map' Toward Ending Severe Suffering of Animals Used in Research and Testing

Elliot Lilley, Penny Hawkins and Maggy Jennings

Ending severe suffering is a desirable goal for both ethical and scientific reasons. The RSPCA has pledged to work toward the end of such suffering for laboratory animals, and in this article we outline a practical approach that establishments can follow to achieve this aim

Introduction

The introduction of *EU Directive 2010/63/EU*¹ controlling experiments on animals, and the associated updating of the *UK Animals (Scientific Procedures) Act 1986 (ASP)*,² have focused attention on the need to reduce animal suffering in scientific procedures. Classification of levels of suffering into mild, moderate and severe, and the need to report actual levels of severity, have provided added impetus to the drive to refine the most severe models and procedures, and have resulted in greater recognition that high levels of suffering impact on an animal's physiological responses, increasing the variability of experimental data. So ending severe suffering is a desirable goal for scientific, ethical and legal reasons.

Clearly, the responsibility to end severe suffering falls on the whole scientific community, who need to accept this as a worthwhile goal and commit to achieving it. There needs to be a coordinated effort from researchers, industry and academia, regulatory authorities, funding bodies and scientific journals. But animal welfare organisations also have a key role, and even before revision of the *ASP*, the RSPCA had pledged to work toward ending severe suffering. Since 2011, the Society has been developing a programme of work with the scientific community, aimed at producing innovative, challenging and feasible approaches to the achievement of this goal. This article focuses on the role of research establishments, and outlines some practical steps that can be taken to create a 'road map' to end severe suffering.

There are currently no data on the proportion of the approximately four million procedures carried out on animals in 2013 in the UK that caused severe suffering — or indeed, for any previous year. This will change from 2014, because the *EU Directive* and the *ASP* will require research establishments to assess and report the actual level of suffering experienced by individual animals undergoing regulated procedures. This is good news for three reasons. Firstly, it will give the public a clear indication of the levels of suffering that laboratory animals experience, which will be an important step toward open and honest reporting of animal use in research. Secondly, it will give establishments an opportunity to evaluate how successful their *refinement* programmes are in reducing suffering, and highlight areas where more work is needed. Finally, these new data will allow regulators, welfare organisations and research funding bodies to focus resources on areas of research where suffering is the most severe and/or *refinement* is lacking, and to track progress

of Three Rs-related programmes targeted at reducing suffering.

Clearly, the responsibility to end severe suffering falls on the whole scientific community, who need to accept this as a worthwhile goal and commit to achieving it. There needs to be a coordinated effort from researchers, industry and academia, regulatory authorities, funding bodies and scientific journals. But animal welfare organisations also have a key role, and even before revision of the *ASP*, the RSPCA had pledged to work toward ending severe suffering. Since 2011, the Society has been developing a programme of work with the scientific community, aimed at producing innovative, challenging and feasible approaches to the achievement of this goal. This article focuses on the role of research establishments, and outlines some practical steps that can be taken to create a 'road map' to end severe suffering.

Stages on the Road

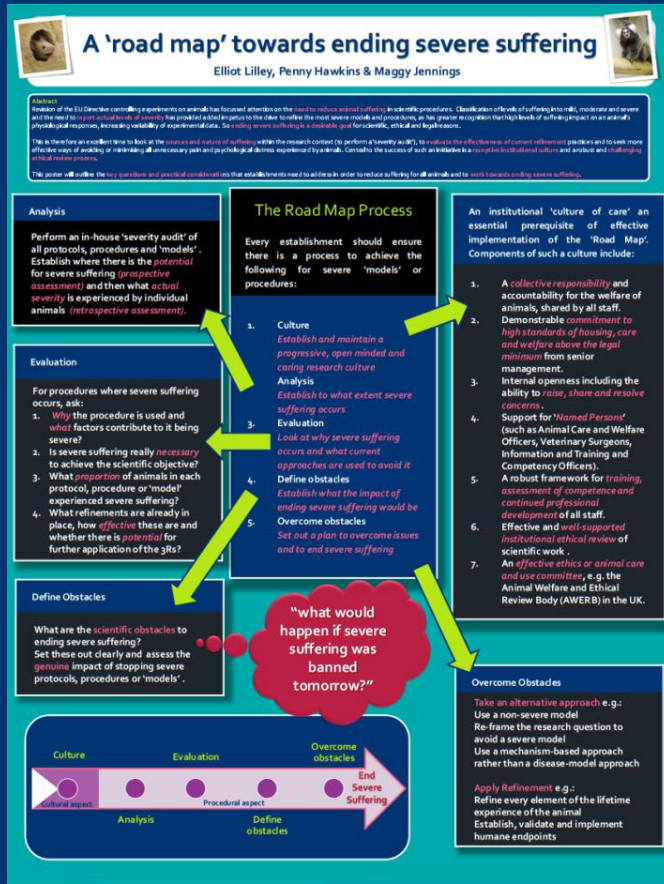
There are two complementary aspects to the 'road map' approach (Figure 1):

1. The *cultural* aspect — developing an environment that will support and encourage positive attitudes toward change; and
2. The *procedural* aspect — developing the activities and initiatives that will end severe suffering.

The cultural aspect — establishing the culture of care

Fundamental to ending severe suffering is the belief that this is both desirable and possible —

Road map RESOURCES



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Website

RESOURCES



Focus on severe suffering

My RSPCA Login/Register

Search

Who we are What we do Implementing the 3Rs Ethical review Reports and resources

Home / Research animals / Focus on severe suffering

Share this page



Focus on severe suffering

Welcome to the RSPCA/LASA/LAVA/IAT Severe Suffering web resource.



Institute of
Animal Technology

These web pages provide information and resources that will help you to avoid severe suffering. All of the material can be used by anyone involved with the use of animals in research, but you may wish to follow one of the three different routes for (1) researchers, (2) animal technologists or veterinarians and (3) members of ethics or animal care and use committees, such as Animal Welfare and Ethical Review Bodies (AWERBs) in the UK and Animal Welfare Bodies (AWBs) in the rest of the European Union.

The RSPCA is a scientific animal welfare organisation that works to progress the 3Rs and encourage effective **ethical review** of research and testing using animals. We have partnered with LASA, LAVA and IAT to create this resource as part of our ongoing **work with respect to animal use**, which has a special focus on severe suffering. With a positive approach and good communication, much can be done to reduce suffering – and animal welfare and science will both benefit.

This is the first version of this resource and we will be adding much more. The content has been reviewed by a diverse panel of individuals from industry, academia, regulatory authorities, learned societies and organisations. The authors of this material are indebted to these reviewers for their contributions. Please visit regularly and send us your feedback at research.animals@rspca.org.uk

Focus on severe suffering

Scientists	V
Animal technologists and veterinarians	V
AWERB members	V
Resources	V

Why focus on severe suffering?: Scientists



Specific information for research staff on the need to reduce severe suffering. >>

Why focus on severe suffering?: Animal technologists and vets



Specific information for animal technologists and vets on the need to reduce severe suffering. >>

Why focus on severe suffering?: AWERB members




Specific information for members of AWERBs or AWBs on the need to reduce severe suffering. >>



www.rspca.org.uk/severesuffering


Road Map

RESOURCES



Progress towards ending severe suffering working together to achieve positive change


Elliot Lilley, Barney Reed & Penny Hawkins




All laboratory animal suffering is a concern, but the RSPCA believes that ending severe suffering should be a top priority. There are a number of reasons to do this: (i) the ethical benefit of reducing suffering, (ii) the legal requirement to minimise suffering set out in Directive 2010/63/EU and (iii) the scientific benefits – good science goes hand in hand with good welfare.

...iated a number of parallel activities including:
 ...up' towards ending severe suffering, outlining the generic
 ...s and practical considerations that establishments can
 ...duce suffering for all animals and work towards ending
 ...ing.
 ...nsive web resource for the research community,
 ...idance and resources to help end severe suffering.
 ...Expert Working Groups' of scientists, vets, animal

Resources





Divisions
Epilepsy

EAE

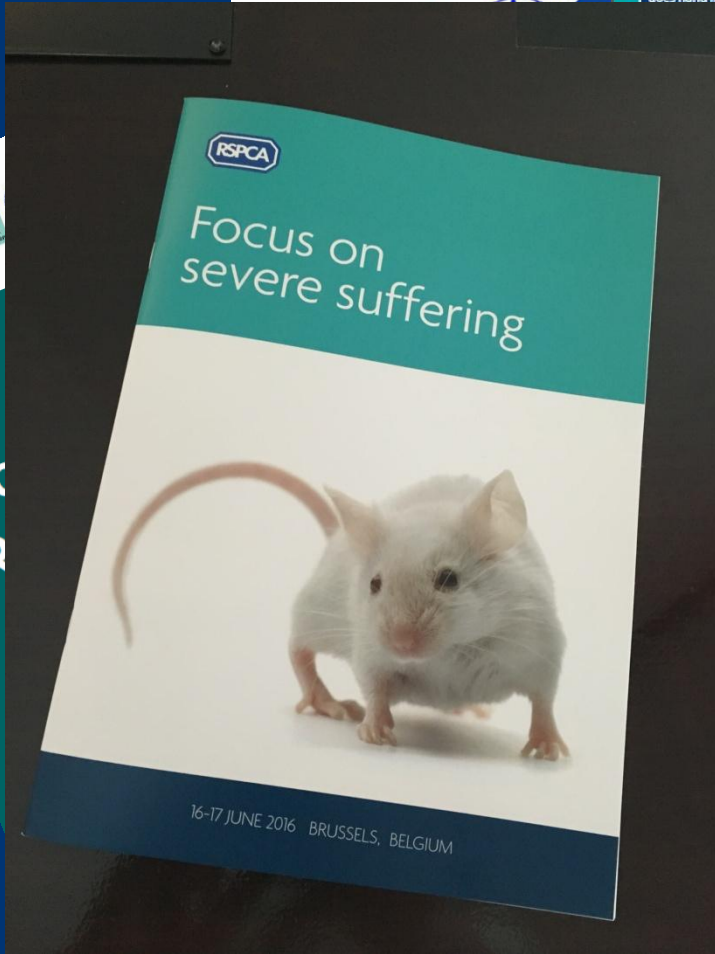
Sepsis

Rheumatoid arthritis

Working with.... You?

If you think you may be able to help us to tackle severe suffering, get in touch.

Organisations
UK Home Office, LASA
IAT, LAVA



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Institute of
Animal Techno

k

EWG approach

WORKING WITH THE SCIENTIFIC COMMUNITY

- RSPCA chaired and convened groups
 - Researchers (academic, industry & CRO)
 - Animal technologists
 - Veterinarians
 - Regulator (UK Home Office – ASRU)
- Establish **why** severe suffering occurs and set out **practical** solutions

EWG publications

RESOURCES

Journal of Pharmacological and Toxicological Methods 67 (2013) 9–15



Contents lists available at SciVerse ScienceDirect

Journal of Pharmacological and Toxicological Methods

journal homepage: www.elsevier.com/locate/jpharmtox



Appraisal of state-of-the-art

Reducing suffering in animal models and procedures involving seizures, convulsions and epilepsy

Sarah Wolfensohn ^a, Penny Hawkins ^b, Elliot Lilley ^{b,*}, Daniel Anthony ^c, Charles Chambers ^d, Sarah Lane ^e, Martin Lawton ^f, Sally Robinson ^g, Hanna-Marja Voipio ^h, Gavin Woodhall ⁱ

Journal of Pharmacological and Toxicological Methods 67 (2013) 169–176



Contents lists available at SciVerse ScienceDirect

Journal of Pharmacological and Toxicological Methods

journal homepage: www.elsevier.com/locate/jpharmtox



Appraisal of state-of-the-art

Reducing suffering in experimental autoimmune encephalomyelitis (EAE)

Sarah Wolfensohn ^a, Penny Hawkins ^b, Elliot Lilley ^{b,*}, Daniel Anthony ^c, Charles Chambers ^d, Sarah Lane ^e, Martin Lawton ^f, Hanna-Marja Voipio ^g, Gavin Woodhall ^h

SHOCK, Vol. 43, No. 4, pp. 304–316, 2015

REFINEMENT OF ANIMAL MODELS OF SEPSIS AND SEPTIC SHOCK

Elliot Lilley ^{1,*}, Rachel Armstrong [†], Nicole Clark [‡], Peter Gray [§], Penny Hawkins ^{*}, Karen Mason [§], Noelia López-Salesansky [¶], Anne-Katrien Stark ^{||}, Simon K. Jackson ^{**}, Christoph Thiemermann ^{††} and Manasi Nandi ^{††}

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Inflammopharmacol (2015) 23:131–150
DOI 10.1007/s10787-015-0241-4

REVIEW

Inflammopharmacology



Applying refinement to the use of mice and rats in rheumatoid arthritis research

Penny Hawkins ¹, Rachel Armstrong ², Tania Boden ³, Paul Garside ⁴, Katherine Knight ⁵, Elliot Lilley ¹, Michael Seed ⁶, Michael Wilkinson ⁷, Richard O. Williams ⁸

UK HO using sepsis report for first **thematic review** of sepsis research in the UK



Expert working groups

Future groups

Spinal cord injury

Pancreatitis

Tamoxifen

Bone marrow irradiation

Predicting mortality

Thank you



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