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

- Level of suffering has a bearing on harm-benefit assessment, when:
  - Reviewing projects
  - Predicting suffering in future projects

- Legal requirement to predict and minimise suffering under Directive 2010/63/EU

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

Appendix II
Reference material for the assessment and scoring of actual severity

Project Planning
- 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

During The Project
- Consistency in observations/trained staff
- Effective day-to-day monitoring
- Good communication among all involved
- Ongoing assessment protocol as necessary

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

Severity Assessment – A Continuous Process

http://ec.europa.eu/environment/chemicals/lab_animals/pdf/Endorsed_Severity_Assessment.pdf
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 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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- Bladder control, tail tone

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- Poor ability to thermoregulate
- Physiological parameters where available
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<table>
<thead>
<tr>
<th>Date:</th>
<th>Appearance</th>
<th>Weight</th>
<th>Reduced grooming</th>
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<table>
<thead>
<tr>
<th>Body function</th>
<th>Reduced bladder control</th>
<th>Reduced tail tone</th>
<th>Reduced bladder control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<table>
<thead>
<tr>
<th>Environment</th>
<th>Poorly constructed nest</th>
<th></th>
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<tbody>
<tr>
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<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Behaviour</th>
<th>Reduced social behaviour</th>
<th>Altered gait</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure-specific indicators</th>
<th>Side resting position</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Procedure-specific indicators</th>
<th>Increased righting time</th>
<th>Near-complete plegia</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Procedure-specific indicators</th>
<th>Paresis</th>
<th>Other observations</th>
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[Logo: RSPCA]
### ASSESSMENT SYSTEM FOR INDICATORS IN SCORE SHEET

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

Critical evaluation of wellbeing and science

Recognition of pain and poor welfare

Diagnosis of problem

Selection of improvement strategies

Implementation, evaluation and dissemination of good practice

(Lloyd et al 2008)
Refinement, pause for thought....
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

http://pilas.org.uk/refinement-lessons-from-the-2012-olympics/
More subtle signs:

E.G. NEST BUILDING BEHAVIOUR

Photo: Arras M et al. 2007; http://www.biomedcentral.com/1746-6148/3/16
Orbital tightening

Nose bulge

Cheek bulge

Ear position

Whisker change

Rats*
Mice*
Rabbits*
Horses*
Sheep
Pigs
Rhesus macaques
Koalas

Grimace scales

GREAT TOOL

BUT......

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.

Yours faithfully,

HUW D.R. GOLLEDGE, BSc, PhD, Senior Scientific Programme Manager, Universities Federation for Animal Welfare, The Old School, Brewhouse Hill, Wheathampstead, Herts. AL4 8AN

golledge@ufaw.org.uk and AURELIE A. THOMAS, DVM, MSc, MRCVS, 23 Henry Jackson Road, London, SW15 1DL

The perceived or actual absence of a pain face should never be used to withhold treatment where it would otherwise have been given.
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!
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 controlling experiments on animals, and the associated Animals Scientific Procedures Act 1986 (ASPA), 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 ensure that 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 reasons, as well as ethical and legal ones.

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 ASPA 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 openness 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 those RSPCA 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 co-ordinated 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 ASPA, 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 promoting 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 —
Focus on severe suffering

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

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.animal@rspca.org.uk

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
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
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,c, Daniel Anthony c, Charles Chambers c, Sarah Lane e, Martin Lawton f, Sally Robinson g, Hanna-Marja Voipio h, Gavin Woodhall i

REFINEMENT OF ANIMAL MODELS OF SEPSIS AND SEPTIC SHOCK
Elliott Lilley,* Rachel Armstrong,† Nicole Clark,‡ Peter Gray,§ Penny Hawkins,‡ Karen Mason,¶ Noelia López-Salesiansky,‖ Anne-Katrien Stark,‡ Simon K. Jackson,** Christoph Thiemermann,†† and Manasi Nandi‡‡
*Research Animals Department, RSPCA, Southwater; †Huntington Life Sciences, Huntington; ‡University College London, London; §Animals in Science Regulation Unit, Home Office, London; ‖Royal Veterinary College, London; ¶The Babraham Institute, Cambridge; ||Centre for Biomedical Research, Plymouth University Peninsula Schools of Medicine and Dentistry, Plymouth; ‡‡The William Harvey Research Institute, Queen Mary University of London, London; and ††Institute of Pharmaceutical Science, Kings College London, United Kingdom

Applying refinement to the use of mice and rats in rheumatoid arthritis research
Penny Hawkins a, Rachel Armstrong b, Tania Boden c, Paul Garside d, Katherine Knight f, Elliot Lilley e, Michael Seed g, Michael Wilkinson h, Richard O. Williams i

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