



# Understanding cumulative severity

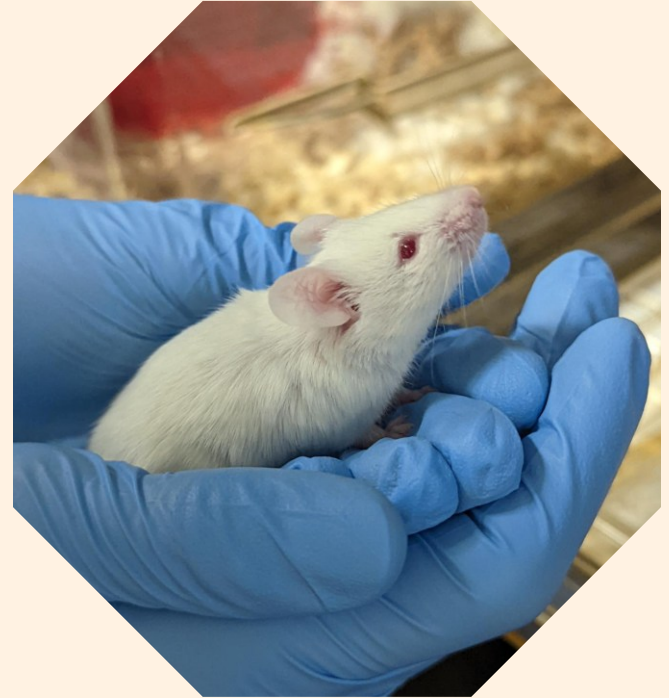
*TALAS International Conference*

*July 22, 2026*

Registered charity in England and Wales. Charity no. 219099.

Replacing lab animal use with  
humane alternatives  
globally is our **primary goal**

Aim: to reach a point where important  
science is done without causing harms to  
animals



# Definitions in different countries

- South Korea/USA: Category E - Experiments that may involve pain or suffering that is not alleviated through anaesthetics and/or analgesics
- Canada: Category D - experiments which cause moderate to severe distress or discomfort'; Category E - procedures which cause severe pain near, at, or above the pain tolerance threshold of unanesthetised conscious animals



[freepik.com](https://www.freepik.com)

# Severe procedures

Within the UK and the European Union, 'severe' procedures are those where animals used in science are likely to experience the highest level of harm:

- severe pain, suffering or distress
- long-lasting moderate pain, suffering or distress, or
- severe impairment to their wellbeing or general condition



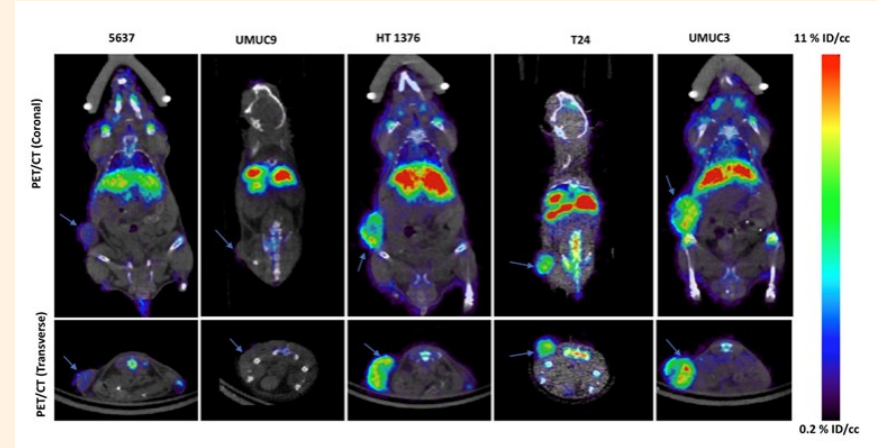
# Severe pain, suffering or distress

- Toxicity testing where **death is the end-point**, e.g. single dose acute toxicity testing
- Testing of a device where failure may cause severe pain, distress or death, e.g. **cardiac assist devices**
- Surgery under general anaesthesia expected to result in severe postoperative pain, e.g. **unstable fractures**
- Use of metabolic cages involving **severe restriction of movement** over a prolonged period
- Inescapable electric shock (e.g. to produce **learned helplessness**)
- **Complete isolation** for prolonged periods of social species e.g. dogs and non-human primates
- **Immobilisation stress** to induce gastric ulcers or cardiac failure in rats
- Forced swim or exercise tests with **exhaustion** as the end-point



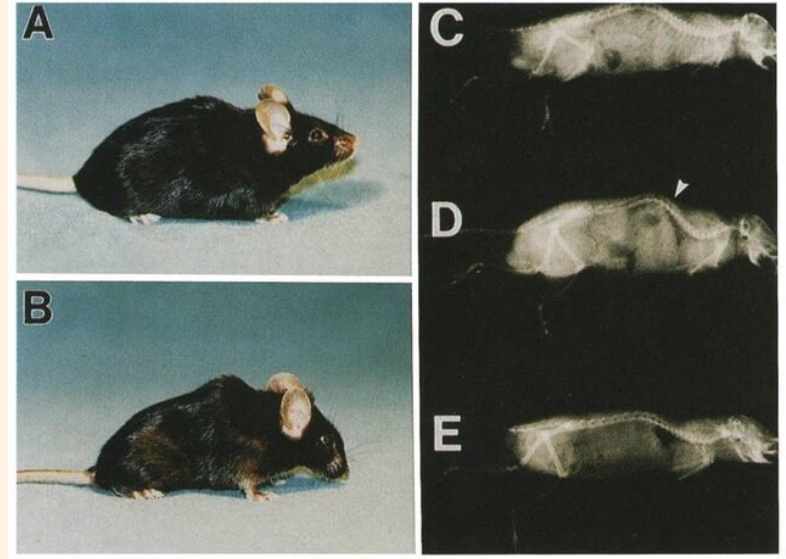
# Long-lasting moderate pain, suffering or distress

- Tumours that cause **progressive lethal disease** with long-lasting moderate pain, distress or suffering. For example metastatic spread, or tumours that are allowed to ulcerate
- Surgery under general anaesthesia expected to result in **severe or persistent moderate postoperative pain, suffering or distress** or severe and persistent impairment of the general condition of the animals



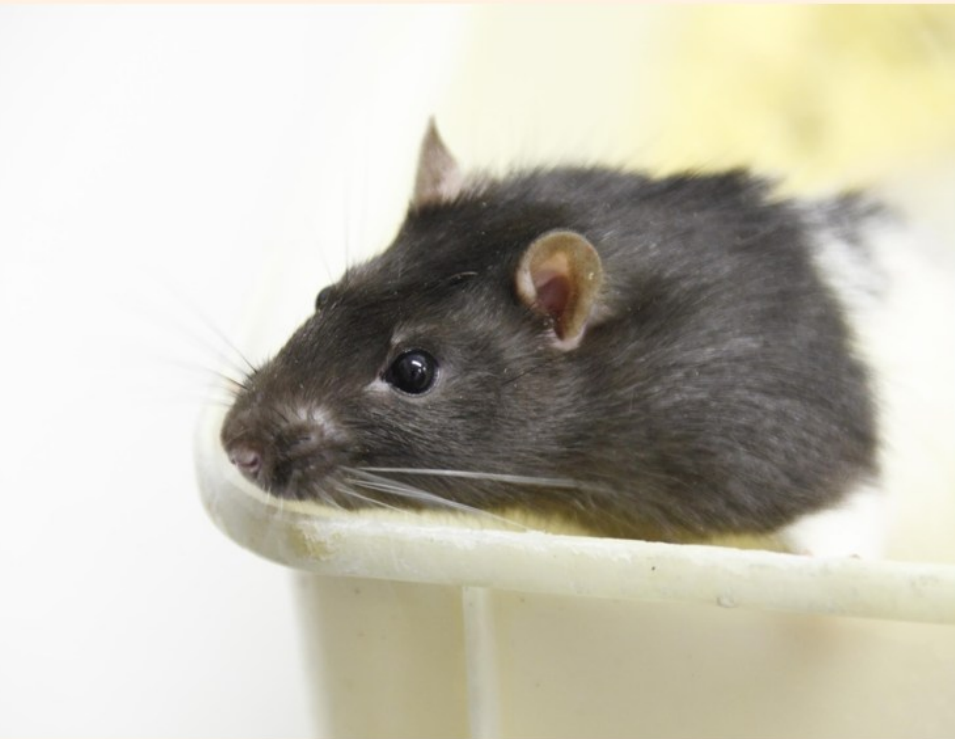
# Severe impairment to wellbeing or general condition

- **Breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington's disease, Muscular dystrophy, chronic relapsing neuritis models**
- **Organ transplantation where organ rejection is likely to lead to severe distress or impairment of the general condition of the animals, e.g. xenotransplantation**
- **Vaccine potency testing characterised by persistent impairment of the animal's condition, progressive disease leading to death, associated with long-lasting moderate pain, distress or suffering**



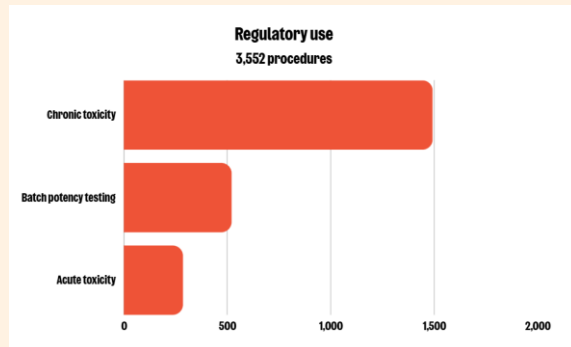
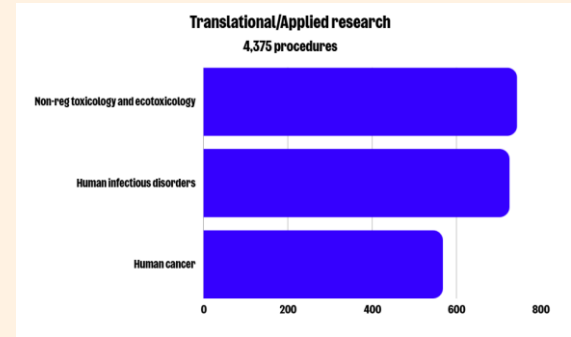
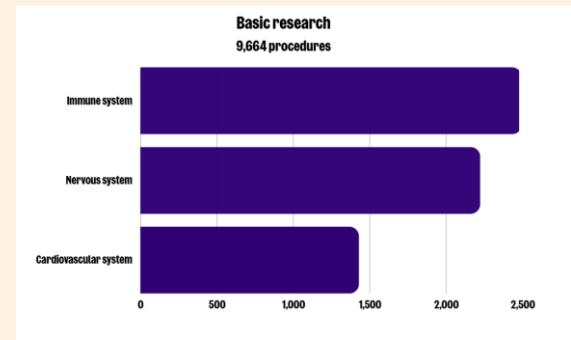
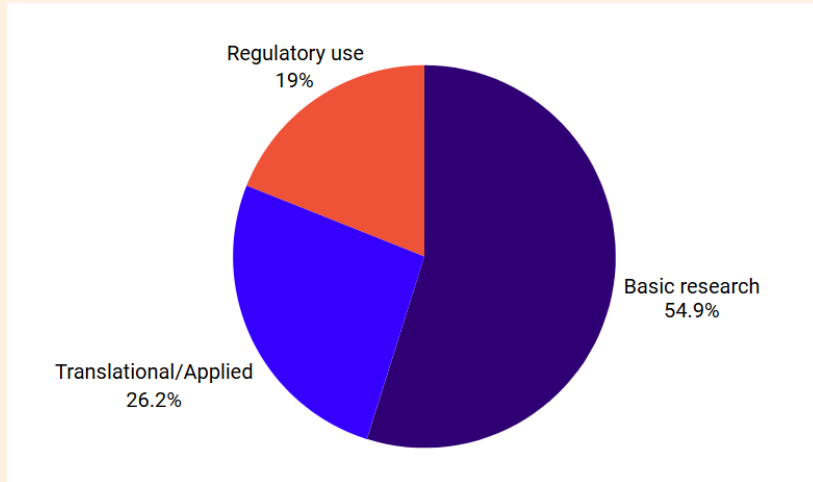
# 10 million

**ANIMALS ACROSS THE WORLD  
EXPERIENCE SEVERE SUFFERING EACH  
YEAR\***



1.3% of all procedures are severe

## Severe experimental procedures by purpose



## Focus on Severe Suffering initiative

Since 2012, the RSPCA has been **working collaboratively** with the scientific community in the UK and internationally, to initiate and promote a range of activities aimed at identifying and promoting **practical steps** which will help people to **reduce** or, ideally, **avoid** 'severe' suffering.

Main emphasis: identify **innovative** and **practical** ways to **refine** **severe procedures**.

# Causes of severe suffering

1. Some procedures or 'models' are likely to cause severe suffering
2. A combination of less severe factors can lead to increased overall suffering: 'cumulative severity'
3. Where animals die, this may involve severe suffering - including both unexpected mortality, and 'death as an endpoint'



# Reasons to act on severe suffering

- **Legal**
  - Many laws require severity to be minimised and refinement to be implemented
- **Ethical**
  - Reducing and avoiding harms to animals is the right thing to do
- **Scientific**
  - If animals are struggling with avoidable suffering, data quality can be affected
- **Human welfare**
  - Staff can be distressed by animal suffering, especially if this is severe

## FOCUS ON SEVERE SUFFERING

"Any level of suffering is obviously a concern for everyone, but tackling severe suffering should be a top priority."

Dr Penny Hawkins, RSPCA



# Everyone has a part to play

- Scientists
- Animal technicians
- Vets
- IACUCs
- Competent authorities
- National Committees
- National 3Rs centres
- NGOs



# The role of researchers

What can researchers do to reduce suffering?

- Literature searches for refinements (both procedural and also housing and husbandry related)
- Discussing with colleagues in relevant fields
- Being open-minded about the link between better welfare and better science



# The role of the animal technologist

What can an animal technologist do to reduce severe suffering?

- Practicing refined handling, husbandry, and habituation
- Communication with colleagues (including vets and users)
- Advocate for the animals in your care and voice any concerns
- Bring in information and skills from meetings (e.g. these slides)



# The role of IACUC members

What can the IACUC do to reduce severe suffering?

- Ask 'animal centric' questions - how will the animal feel?
- Asking the establishment to set itself a goal to end severe suffering
- Facilitate a good "culture of care" in the establishment



# What can IACUCs do?

1. Support better predictions of *prospective* severity by enabling better understanding of animals' experiences
2. Enable reductions in suffering and improvements in welfare
3. Make sure special attention is paid to severe protocols in Post Approval Monitoring, which should include assessing *actual* severity
4. Set establishment goals to reduce and avoid severe suffering

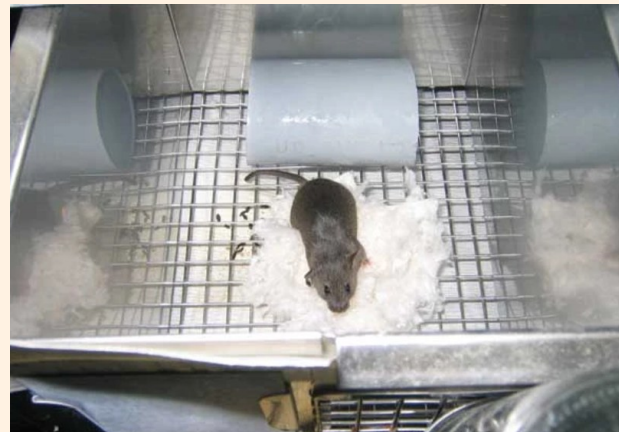


# Prospective severity assessment - first classification

Directive 2010/63/EU

Factors relating to the procedure:

- Pain, suffering, distress or lasting harm caused by the protocol - its nature, intensity, duration and frequency
- Number of times that techniques are applied
- Cumulative suffering
- Prevention from expressing natural behaviour including restrictions on the housing, husbandry and care standards



[nature.com/articles/lab0205-30](https://www.nature.com/articles/lab0205-30)

# Prospective severity assessment - first classification

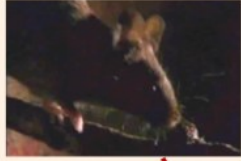
Directive 2010/63/EU

Additional factors:

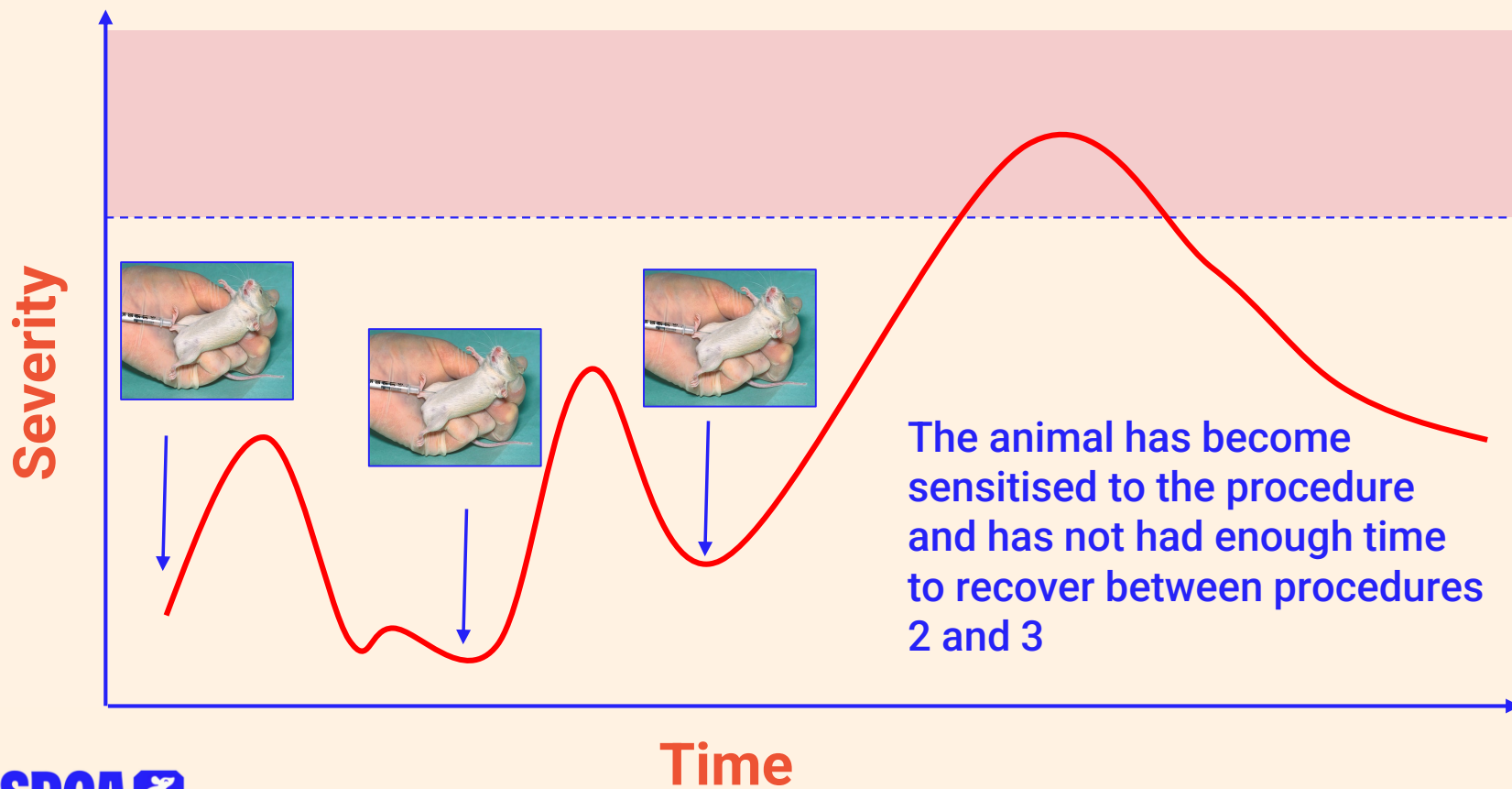
- Type of species and genotype
- Stage of development and sex of the animal
- Whether the animal can be trained to cooperate with the procedure, or habituated to it
- The methods used to reduce or eliminate pain, suffering and distress, including refinement of housing, husbandry and care conditions
- Humane end-points



[3hs-initiative.co.uk](http://3hs-initiative.co.uk)

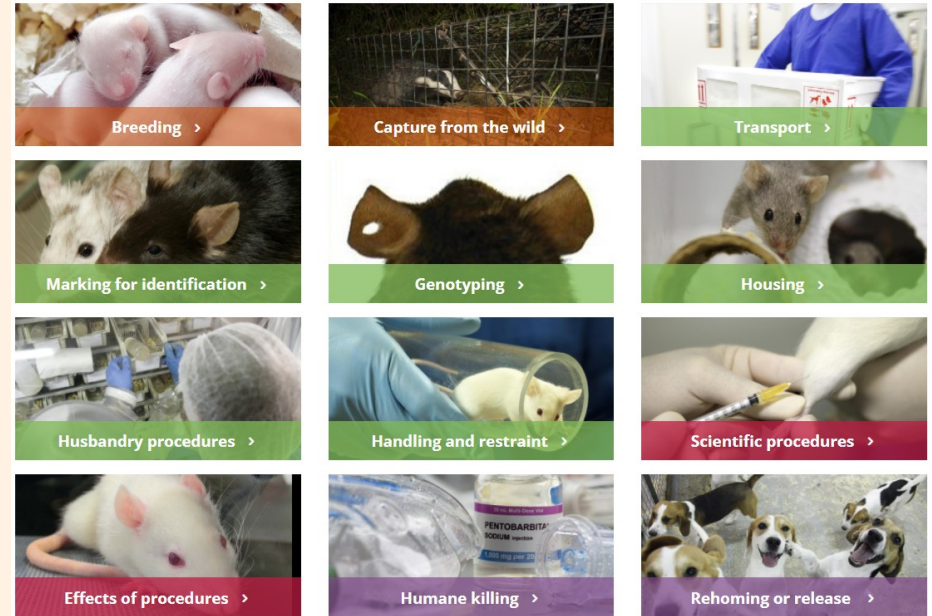






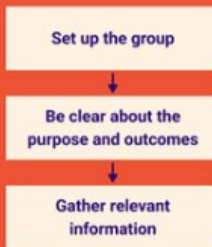
# Cumulative severity

- Consider animals' entire lifetimes
- Habituation or sensitisation – never assume
- Understanding harms to animals is essential

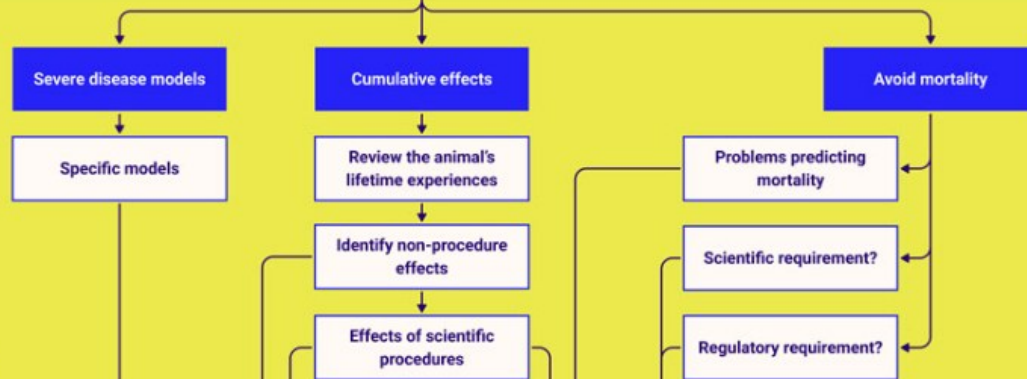




## Analysis



## Evaluation



## Identify issues



## Overcome obstacles



Set up the group

Be clear about the  
purpose and outcomes

Severe disease models

Specific models

Cumulative effects

Review the animal's  
lifetime experiences

Identify non-procedure  
effects

Effects of scientific  
procedures

Avoid mortality

Problems predicting  
mortality

Scientific requirement?

Regulatory requirement?

Evaluation

Implement the  
refinements

Welfare assessment

Identify issues

Review your work

Next steps

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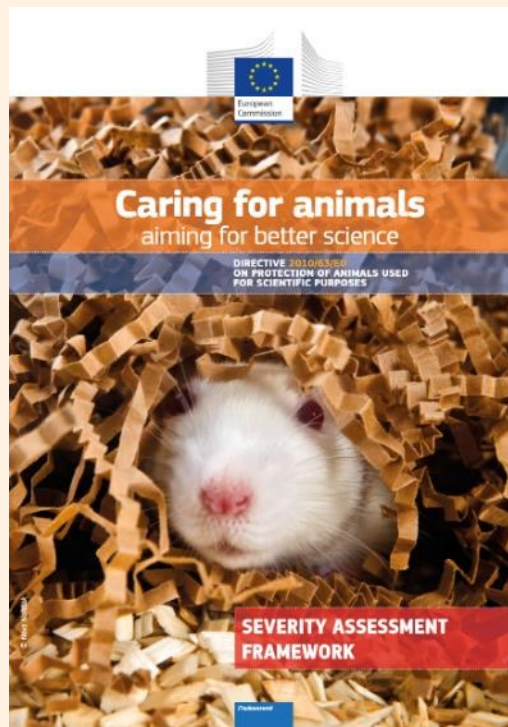
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Review your work

Next steps

Overcome obstacles

# Severity assessment framework



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# Glossary of clinical observations

Appearance / Body Functions / Environment / Behaviours / Procedure-specific indicators / Free observations

| High level categories | Areas to focus on when observing animals                                        | Specific indicators to monitor                                                                                                                                             |
|-----------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Body functions        | Respiration                                                                     | Accelerated breathing (tachypnoea)                                                                                                                                         |
|                       |                                                                                 | Laboured breathing (hyperpnoea)                                                                                                                                            |
|                       |                                                                                 | Very laboured breathing (dyspnoea)                                                                                                                                         |
|                       |                                                                                 | Wheezing or other sound when breathing                                                                                                                                     |
|                       | Food/water intake                                                               | Increased/decreased                                                                                                                                                        |
|                       | Body temperature                                                                | Increased/decreased; measured body temperature if available (e.g. via microchip or telemetry device, contact or non-contact thermometry); colour of extremities in rodents |
|                       | Senses                                                                          | Impaired sight, hearing or balance                                                                                                                                         |
| Environment           | Enclosure environment, including any litter, nesting material, enrichment items | Presence and consistency of faeces                                                                                                                                         |
|                       |                                                                                 | Wet bedding, e.g. due to polyuria                                                                                                                                          |
|                       |                                                                                 | Presence of vomit or blood                                                                                                                                                 |
|                       |                                                                                 | Whether animal is using enrichment items e.g. nesting material, chew blocks                                                                                                |
| Behaviours            | Social interaction                                                              | Change from normal temperament - apprehensive/aggressive interactions with other animals; anxiety (e.g. marked escape responses, hiding)                                   |
|                       |                                                                                 | Isolated or withdrawn from other animals in social group                                                                                                                   |

# Welfare assessment example

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

| High level category | Areas to focus on when observing animals                                        | Specific indicators to monitor                                                                                          |
|---------------------|---------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------|
| Appearance          | Body condition                                                                  | Weight loss and/or loss of body condition                                                                               |
|                     | Coat and skin condition                                                         | Ulceration                                                                                                              |
|                     |                                                                                 | Faecal or urine staining                                                                                                |
|                     |                                                                                 | Unkempt or greasy coat                                                                                                  |
|                     |                                                                                 | Scabbing, <b>ulceration</b> , <b>infection</b> at injection site associated with adjuvant                               |
|                     |                                                                                 | Skin tenting (dehydration)                                                                                              |
|                     |                                                                                 | In adjuvant arthritis, crusting or lesions around eyes, ears, paws, tail; tail 'ribbing' (changes in connective tissue) |
| Body functions      |                                                                                 | <b>Paw ulceration</b>                                                                                                   |
|                     | Discharge                                                                       | Ocular discharge                                                                                                        |
|                     | Other                                                                           | 'Pain face', e.g., semi-closed eyes and nose bulge in mice                                                              |
|                     |                                                                                 |                                                                                                                         |
| Body functions      | Respiration                                                                     | Dyspnoea or tachypnoea                                                                                                  |
|                     | Food/water intake                                                               | Reduced                                                                                                                 |
|                     | Body temperature                                                                | Decreased temperature, indicated by observing shivering or use of thermography                                          |
| Environment         | Enclosure environment, including any litter, nesting material, enrichment items | Soft faeces or diarrhoea; or lack of faeces (constipation)                                                              |
|                     |                                                                                 | Poor quality nest                                                                                                       |
|                     |                                                                                 | Reduced use of enrichment items such as chew blocks                                                                     |

# Creating welfare assessment records

|                                       |     |                                                                                   |                                                                                    |                                                                                     |   |
|---------------------------------------|-----|-----------------------------------------------------------------------------------|------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|---|
| Initial body weight (g)               |     |                                                                                   |                                                                                    |                                                                                     |   |
| Minimum weight (g)<br>= 0.8 × initial |     |                                                                                   |                                                                                    |                                                                                     |   |
|                                       | Day | 1                                                                                 | 2                                                                                  | 3                                                                                   | 4 |
| Body weight                           |     |                                                                                   |                                                                                    |                                                                                     |   |
| 0 – 5 %                               | 0   |                                                                                   |                                                                                    |                                                                                     |   |
| 5 – 10 %                              | 1   |  |                                                                                    |                                                                                     |   |
| 10 – 15 %                             | 2   |                                                                                   |  |                                                                                     |   |
| ≥15 % for up to 5 days <sup>a</sup>   | 4   |                                                                                   |                                                                                    |                                                                                     |   |
| 20 %                                  | HEP |                                                                                   |                                                                                    |  |   |
| Coat condition                        |     |                                                                                   |                                                                                    |                                                                                     |   |
| Normal                                | 0   |                                                                                   |                                                                                    |                                                                                     |   |
| Lack of grooming                      | 1   |  |  |                                                                                     |   |
| Staring coat                          | 2   |                                                                                   |                                                                                    |  |   |

# Post Approval Monitoring should involve ...

- Continuous monitoring of ongoing protocols
- Observation of selected procedures and animals
- Retrospective review at the end of a protocol
- Inspections and visits to the animal facility – preferably every 6 months

Guide for the Care and Use of Laboratory Animals:  
Eighth Edition (2011). Washington, DC: The National  
Academies Press [doi.org/10.17226/12910](https://doi.org/10.17226/12910)



Photo: IAT

# Actual severity assessment

- What the animal *actually experienced*
- Good welfare assessment records are essential
- Reviewing these records is essential to see:
  - the level and nature of actual severity; when effects occurred
  - which refinements worked well (or not)
  - which techniques or protocols caused more suffering (and should be the focus of refinements)
  - if animals died, whether this could be predicted and prevented



# Other elements of retrospective review



- Were the expected scientific advances obtained? If not, why?
  - e.g. unrealistic, technical problems, approach abandoned as unlikely to justify further use of animals etc
- How will the results/data be reported or disseminated? (even if the hypothesis is not proven; to help maximise the benefits)
- Are there opportunities to share 3Rs advances with other researchers - especially refinement, for severe protocols?
- What lessons could be learnt to guide future protocols?
- Was the 'harm-benefit analysis' accurate?

## Action points

- Assume that there is always more than can be done to reduce and avoid severe suffering
- Seek advice from the IACUC
- Review how prospective suffering is predicted - is it consistent and accurate?
  - Focus on understanding animals' experiences instead of what will be done to them
  - Consider the whole life experience of each animal and identify opportunities for refinement at each step
- Improve processes for welfare assessment and retrospective review
- Make sure special attention is paid to severe protocols in Post Approval Monitoring
- Set establishment goals to work together to reduce and avoid severe suffering

See: [focusonseveresuffering.co.uk](https://focusonseveresuffering.co.uk)



# Thank you

