




# A walk through the Roadmap



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FOCUS ON  
SEVERE SUFFERING



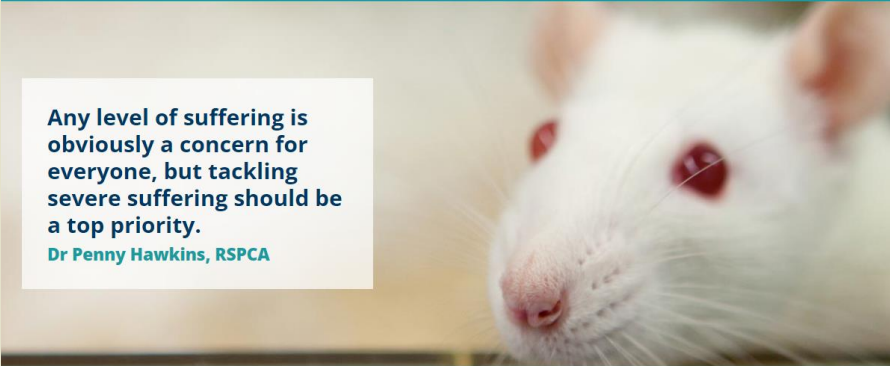
CAUSES

AVOIDING & REDUCING


Events Reports Latest

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

Dr Penny Hawkins, RSPCA



Can we end 'severe' suffering?



WHAT IS 'SEVERE' SUFFERING?

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

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

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# Causes of severe suffering

## THREE MAIN REASONS

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



## THE ROADMAP TO REDUCING SEVERE SUFFERING



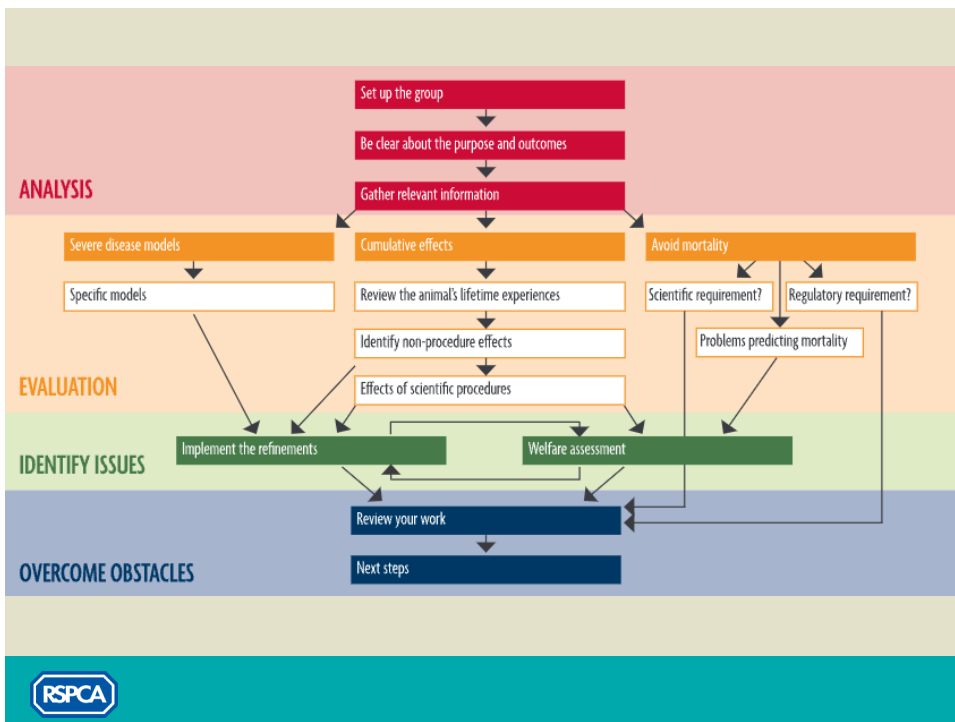
FOCUS ON  
SEVERE SUFFERING



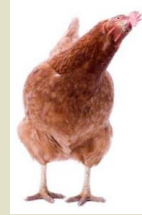
[FOCUSONSEVERESUFFERING.CO.UK/ROADMAP](https://focusonseveresuffering.co.uk/roadmap)

## A commitment to address severe suffering

- Agreement that ending severe suffering is desirable and achievable
- Part of the 'Culture of Care'



## Analysis



- The 'group' could be the ethics committee, a 3Rs sub-group or a specific committee
- Clear purpose and outcomes, e.g. records and actions
- Information includes the protocol, EC WG on severity assessment and downloadable forms



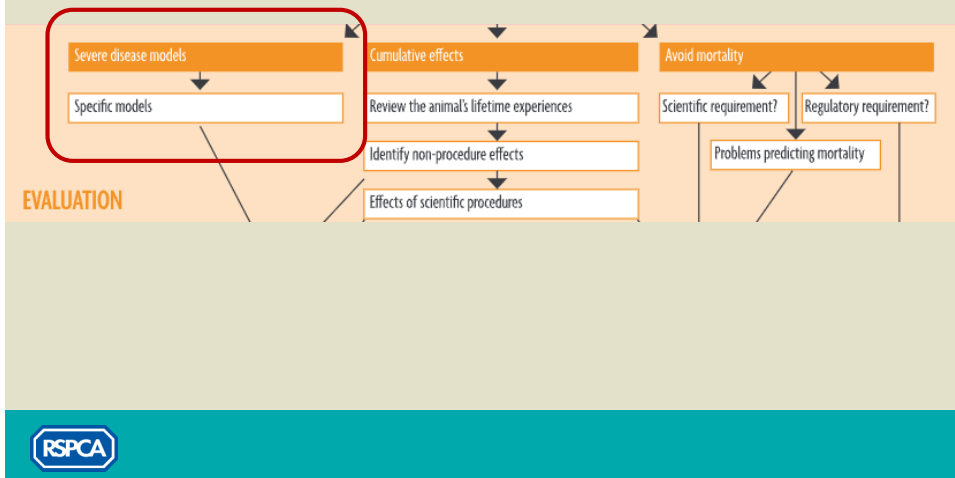
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## Aims and outcomes

- **Focus on 'severe' procedures, identify contributing factors and find ways of avoiding or refining these**
- Record of key points, with clear actions for specific individuals – could be shared with others (e.g. AWERB, Home Office Inspector) as appropriate
- Possible edits to project licence application, or amendments
- Most importantly - reduced severity, with positive welfare impacts for animals; good records and follow-up are essential



## Evaluation – three routes



## Potentially severe procedures

- Batch potency testing of vaccines and other biologics
- Infectious disease models with severe symptoms, e.g. some vaccine development
- Studies of diseases causing severe suffering in humans, e.g. rheumatoid arthritis, sepsis, spinal cord injury
- Some regulatory toxicology tests, e.g. acute toxicology, ecotoxicity
- Animal diseases and disorders

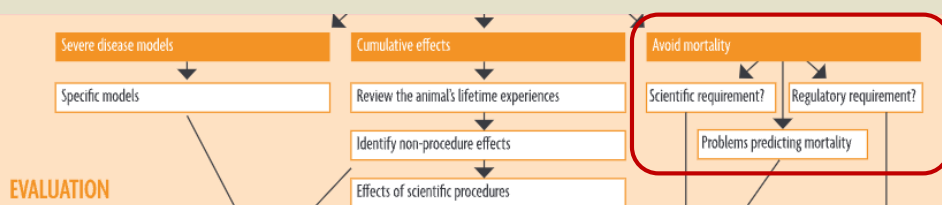


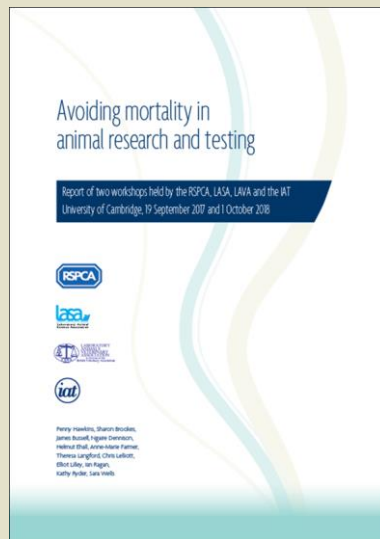
## Specific models

- Guidance on how to search for refinements in the literature
- Suggestions for other information sources and discussion forums
- Action points:
  - Plan (with deadlines) to retrieve further information about refinement
  - Task individuals with (i) searching the literature, (ii) consulting colleagues and (iii) consulting discussion forums



## Evaluation – three routes





[tinyurl.com/AvoidMort](https://tinyurl.com/AvoidMort)



## Avoiding mortality

### THREE KEY QUESTIONS

1. Is there a scientific requirement for death as an endpoint?
2. Is there a regulatory requirement for mortality?
3. Is mortality difficult to predict in the strain or model?

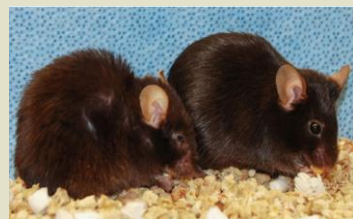


Photo: RSPCA

## Regulatory requirements

- Any perceived, or actual, regulatory requirements for death as an endpoint should be rigorously examined and critically challenged

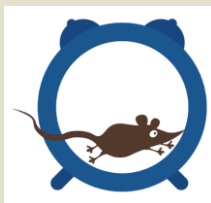


*'with increasing knowledge and experience, investigators ... will be able to identify more specific, early humane endpoints in the form of clinical signs for impending death or severe pain and distress. This would permit international harmonisation of these humane endpoints' - OECD*



## Welfare assessment

- Is an indicator of mortality being missed?
  - Could observation and monitoring be made more effective and timely?
- Literature on assessing pain, suffering, distress
  - Welfare assessment records

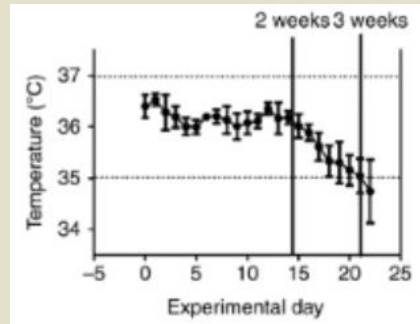


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## Frequently occurring indicators

- Body temperature
- Body weight
- Difficulty in rising or moving



[doi.org/10.1038/bjc.2013.818](https://doi.org/10.1038/bjc.2013.818)

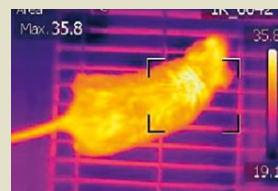


## Animal monitoring

- Rapid developments in software and hardware
- Can require a harm-benefit analysis
  - single housing social animals
  - device/chip implantation
- New developments
  - home cage systems for group housed animals
  - non-contact thermography



[actualanalytics.com/](http://actualanalytics.com/)



[nc3rs.org.uk](http://nc3rs.org.uk)



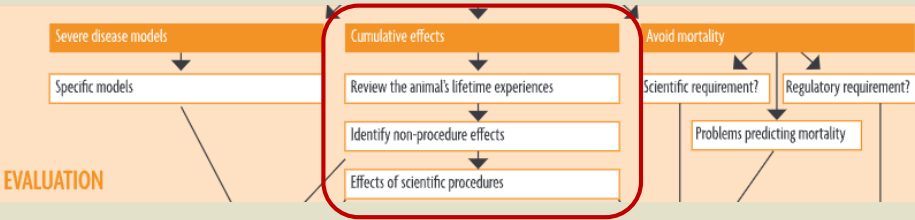
# Data/record mining

- Review by the AWERB
- Structured review of assessment records
  - Add useful predictors, remove those that do not help
- Informatics approaches

Examples of factors
Age range
Background strain (GA)
Sex of animals
Temperature in room/cage
Genetic status
Dam's litter history
For neonates/juveniles: presence of sire, age of dam
Diet
Whether breeding, stock, on procedures
Room in facility



# Evaluation – three routes



## Cumulative effects

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



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## Effects of standard housing on morbidity and mortality

- Over 214 studies using over 6000 rodents
- Conventional housing (CH) consistently increases severity in cancer, cardiovascular, stroke, anxiety and depression studies
- CH increases risk of death at any time point by 50%
- Research rodents are typically CRAMPED (cold, rotund, abnormal, male-biased, poorly surviving, enclosed and distressed)




[doi.org/10.1186/s12915-021-01184-0](https://doi.org/10.1186/s12915-021-01184-0)




 [norecopa.no/PREPARE](https://norecopa.no/PREPARE) will help predict welfare impacts

Factor	Experience of the animal	Welfare issues	Ways of mitigating these
Sourcing	Mice are bred in-house. Supply and demand are carefully matched and animals provided with litter, nest boxes and nesting material. Cages are cleaned weekly.	Distress due to separation of dam and pups at weaning.	Ensure removal from dam is appropriately timed and keep litters together wherever possible. Review frequency of cage change (e.g. fortnightly?) to ensure cage is sufficiently clean but with minimal disturbance.
Transport	Once, between rooms within the same building before procedures begin.	Stress and anxiety due to movement.	Move in home cages, minimise distance, think about timing, ensure sufficient time to recover before any other interventions or procedures.
Marking for identification	Animals are identified using microchips, which involves capture and restraint for insertion.	Distress due to restraint, short term pain of chip insertion.	Trial less aversive capture techniques (see below). Research pros and cons of sedating or anaesthetising mice. Ensure adequate checks in case of longer term discomfort.

What does this study involve doing to the animals?	What will the animals experience? How much suffering might it cause? What might make it worse?	How will suffering be reduced to a minimum?	
	Adverse effects and indicators of these	Methodology and interventions	Humane endpoints
Administration of rheumatoid arthritis inducer	<p>Capture and restraint – distress. Aggression, vocalisation, unwilling to be caught.</p> <p>Administration i.d. or s.o. – pain. Flinching, vocalisation, aggression.</p> <p>Pain or ulceration around injection site. Attention to site, reduction in nest quality, body weight/food intake reduction.</p>	<p>Competent, empathetic capture (e.g. not by tail) and handling, habituate to handling and restraint.</p> <p>Use gaseous anaesthesia for i.d.; inject into rump, not tail base (if tail base is painful, restraint by the tail will hurt). Minimise volumes and doses, use multiple sites if large volumes. Ensure injectate formulated to minimise adverse effects</p> <p>Inject into rump (less risk of ulceration); never inject into the foot; if attention paid to site apply topical anaesthesia and review</p>	<p>Humane endpoints with respect to administration of inducer in general:</p> <ul style="list-style-type: none"><li>- Ulceration that is painful, shows no signs of healing or becomes infected.</li><li>- If an ulcer reaches &gt;5 mm, the vet or senior animal technologist should be informed and consulted about treatment.</li></ul> <p>Animal should be humanely killed if no signs of healing within 3 days.</p>





IDENTIFY ISSUES

OVERCOME OBSTACLES

Implement the refinements


Welfare assessment

Review your work


Next steps

- **Tailored welfare indicators**
- Relevant to the study, species and strain
- Readily and reliably recognisable
- Effective and robust
- Practical
- Consistent

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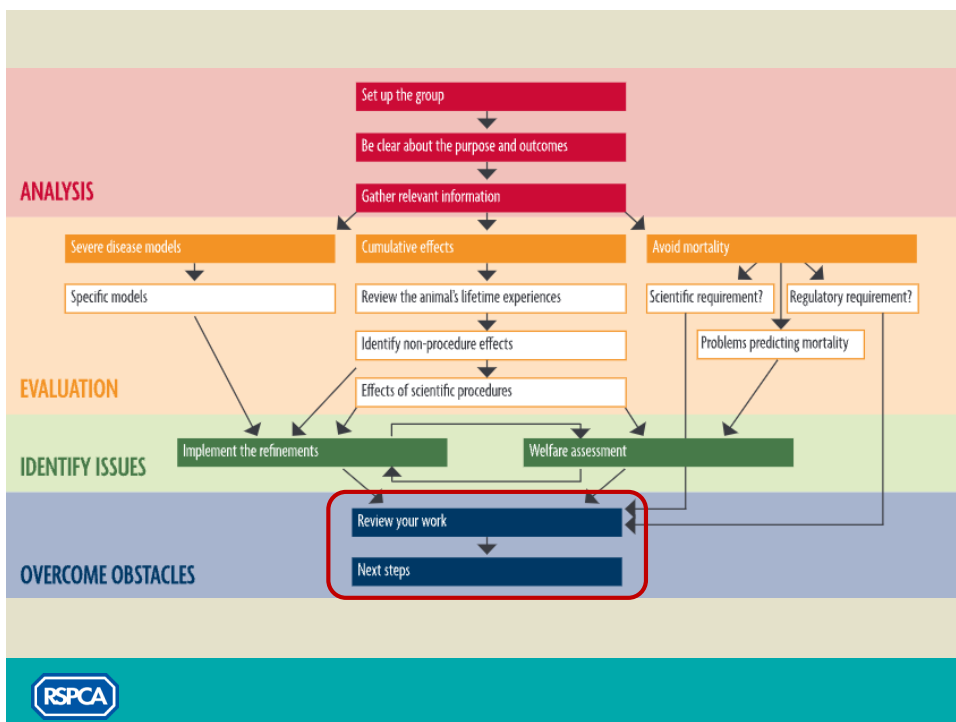


[nc3rs.org.uk/3rs-resources/evaluating-environmental-enrichment](https://nc3rs.org.uk/3rs-resources/evaluating-environmental-enrichment)



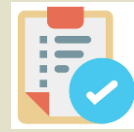
## EC document on a severity assessment framework

- Six high level categories: Appearance, Body Functions, Environment, Behaviours, Procedure-specific Indicators, Free observations
- 'Areas to focus on' e.g. coat and skin condition, enclosure environment, social interaction
- 'Specific indicators to monitor' e.g. lack of grooming, whether using enrichment, temperament change



## Reviewing your work

YOU WILL HAVE ...



- Set out a plan to retrieve information on refining inherently severe protocols
- Reviewed lifetime experiences and the potential impact on the animals
- Worked through the protocol sheet
- Identified likely adverse effects, possible refinements, humane endpoints, welfare indicators
- Set out a plan to review and optimise the welfare assessment and recording system
- Decided on outputs, e.g. reports, edits to the project proposal form



## Thank you



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