



Update on the Focus on Severe Suffering initiative

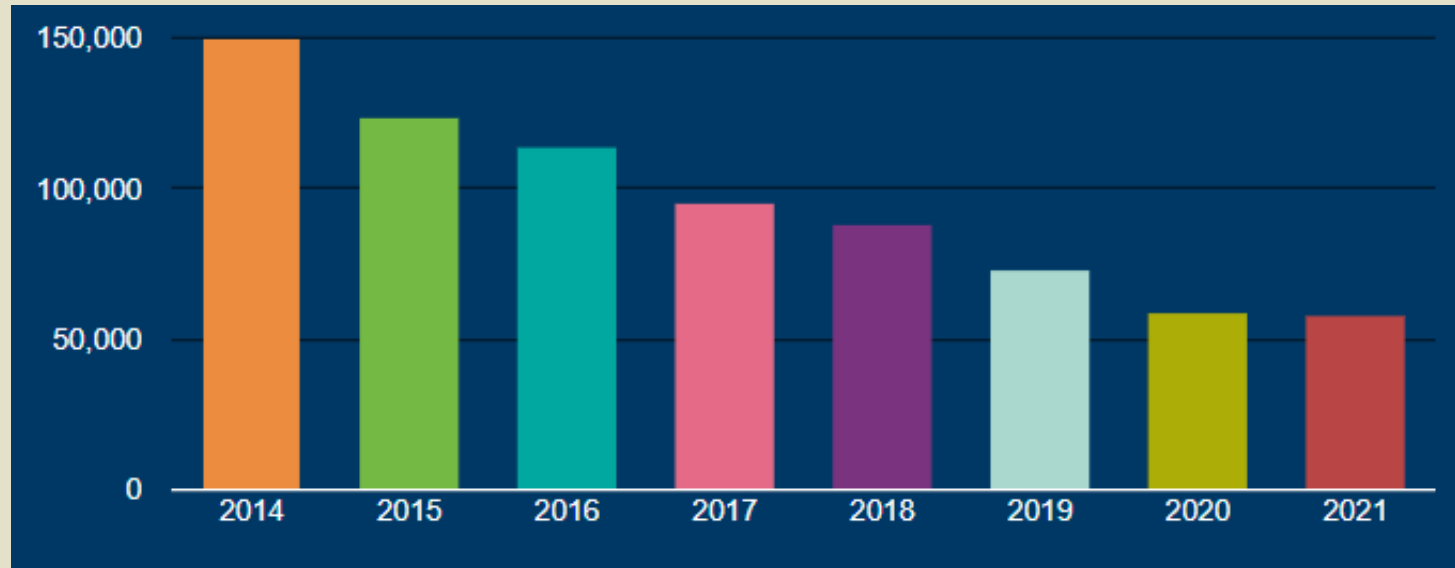


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ANIMALS IN SCIENCE DEPARTMENT

@RSPCA_LabAnimal

Progress so far ...



61%
reduction

in experimental procedures
causing severe suffering in the UK
since 2014

How was this achieved?

- Earlier **scientific and humane endpoints**
- Better **screening** of animals and **strain selection**
- Use of models at **earlier disease stages**
- **Avoiding severe tests/models**
- Better **husbandry and support**, e.g. rehydration
- Better **communication** within teams, more **project review meetings, analysis** of records
- More involvement of **animal technologists**, especially around identifying clinical signs
- Use of **technology**, e.g. temperature transponders
- AWB (**ethics committee**) involvement



THE ROADMAP TO REDUCING SEVERE SUFFERING



Causes of severe suffering

THREE MAIN REASONS

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'

ANALYSIS

Set up the group

Be clear about the purpose and outcomes

Gather relevant information

Severe disease models

Cumulative effects

Avoid mortality

Specific models

Review the animal's lifetime experiences

Scientific requirement?

Regulatory requirement?

Identify non-procedure effects

Problems predicting mortality

Effects of scientific procedures

EVALUATION

Implement the refinements

Welfare assessment

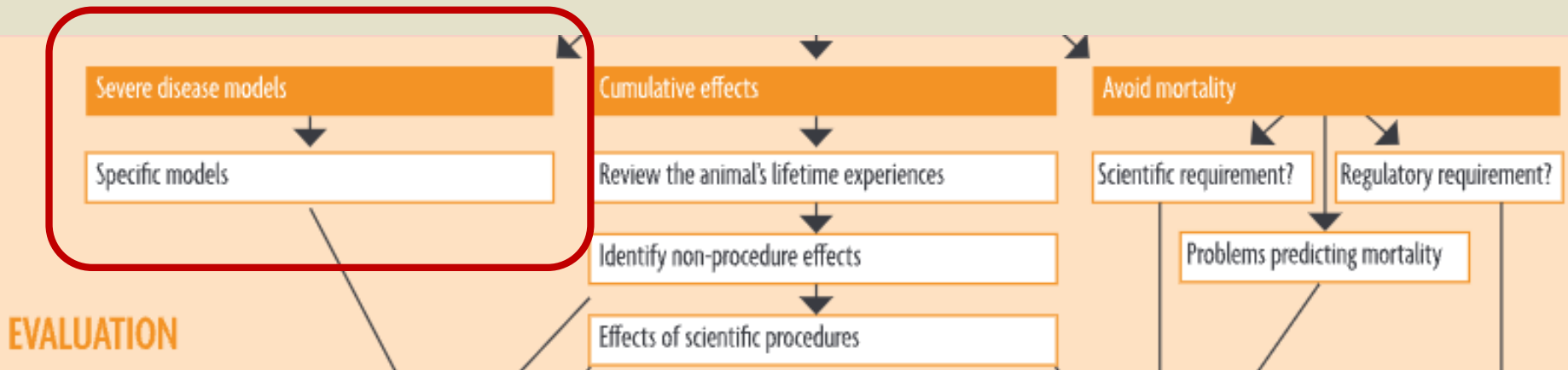
IDENTIFY ISSUES

Review your work

Next steps

OVERCOME OBSTACLES

Evaluation – three routes

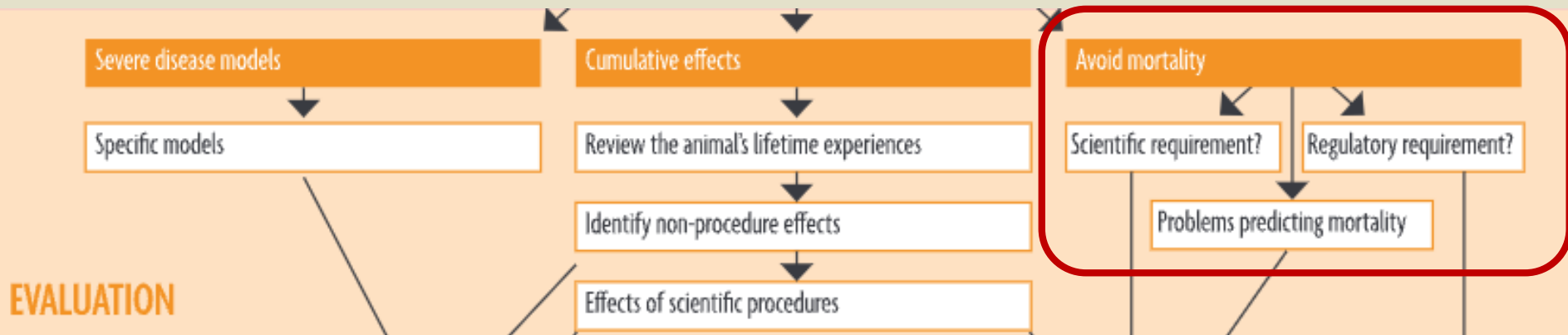


Potentially severe procedures

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



Evaluation – three routes



Avoiding mortality in animal research and testing

Report of two workshops held by the RSPCA, LASA, LAVA and the IAT
University of Cambridge, 19 September 2017 and 1 October 2018



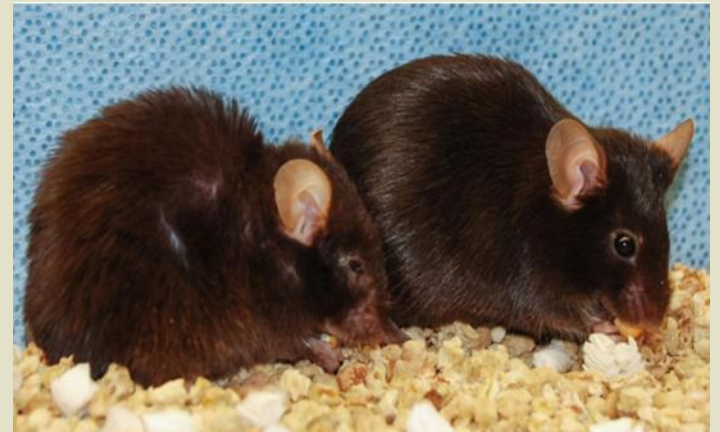
Penny Hawkins, Sharon Brookes,
James Bussell, Ngare Dennison,
Helmut Thal, Anne-Marie Farmer,
Theresa Langford, Chris Lelliott,
Elliot Lilley, Ian Ragan,
Kathy Ryder, Sara Wells

tinyurl.com/AvoidMort

Avoiding mortality

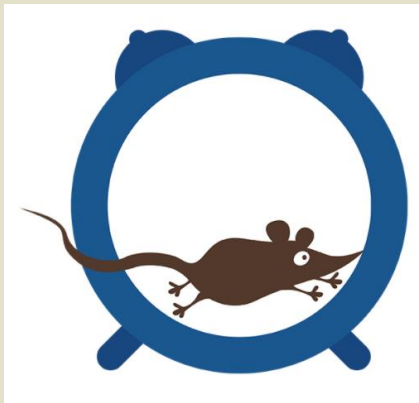
THREE KEY QUESTIONS

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?



A strategic approach to improving predictors of death

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



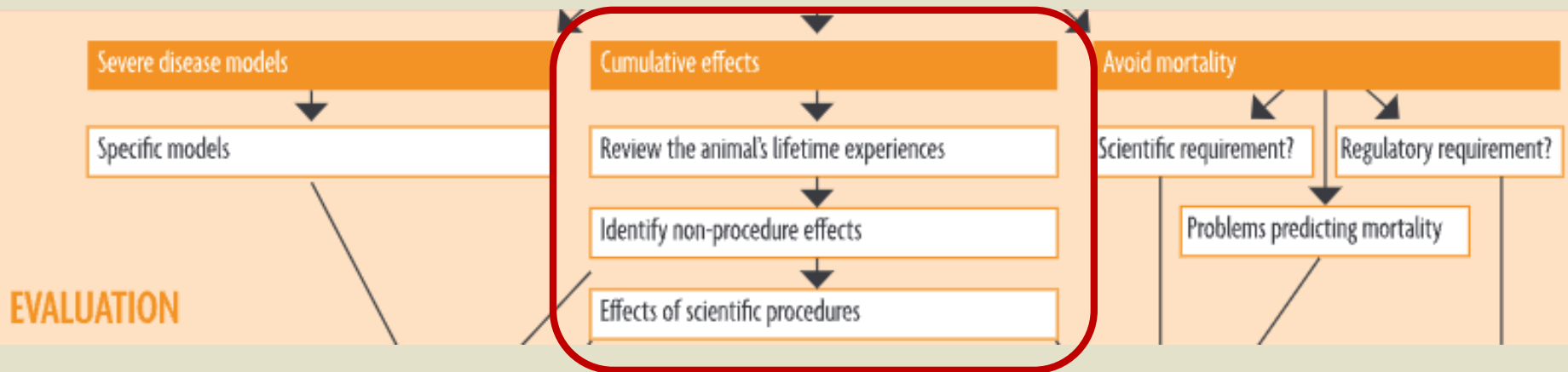
Regulatory requirements

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



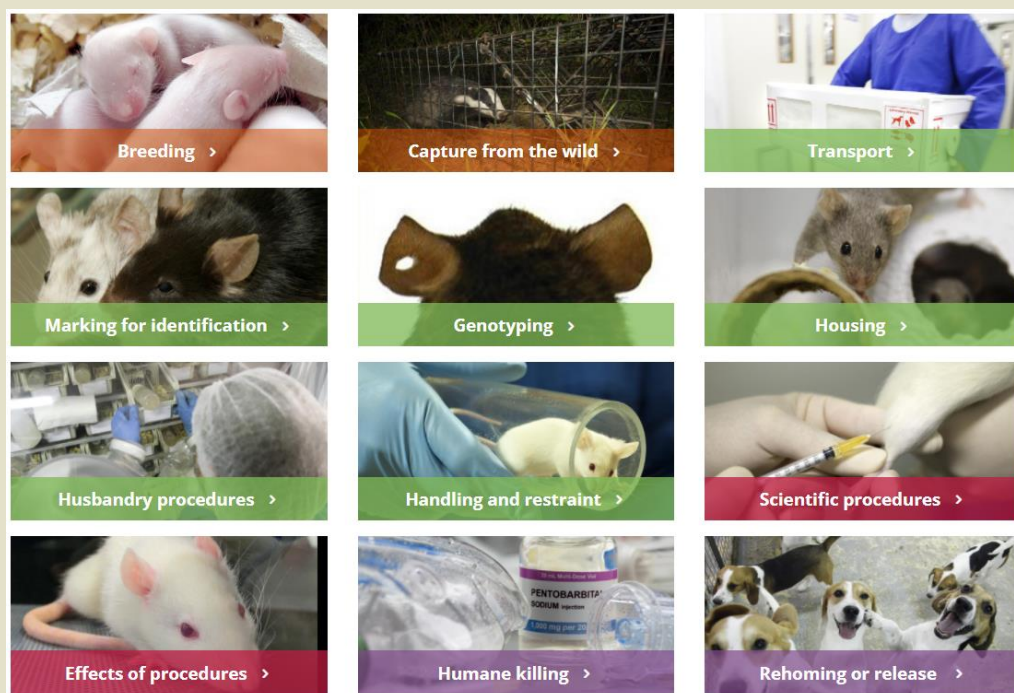
'with increasing knowledge and experience, investigators ... will be able to identify more specific, early humane endpoints in the form of clinical signs for impending death or severe pain and distress. This would permit international harmonisation of these humane endpoints' - OECD

Evaluation – three routes



Cumulative effects

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





Husbandry procedures ▾

Events such as cage cleaning, and feeding, are essential for health and welfare. But they can also cause anxiety and stress, e.g. by moving mice into clean cages with none of their scent markings, or involving noisy and disturbing practices such as filling food hoppers and cleaning the holding rooms.

Examples of actions: Ensure full cage changes are done at [appropriate intervals](#) and refined to reduce stress. Minimise noise and other disturbances in the animal facility that animals find aversive, e.g. ultrasound for mice. Think about the timing of noisy practices and how this fits with circadian patterns, lighting regimes and scientific procedures. Consider what food is provided, how it is presented to the animals, and how they might interact with it, e.g. will manipulating it ready for consumption provide physical or mental stimulation?



Handling and restraint ➤



Humane killing ➤



Scientific procedures ➤



Rehoming or release ➤

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"> - Ulceration that is painful, shows no signs of healing or becomes infected. - If an ulcer reaches >5 mm, the vet or senior animal technologist should be informed and consulted about treatment. Animal should be humanely killed if no signs of healing within 3 days.

The role of Animal Ethics Committees



Animal use for scientific purposes raises ethical issues, whatever the level and nature of any suffering involved. Procedures that can cause severe suffering are of particular concern and the justification for using these deserves special scrutiny.

Questions to ask

- Why is severe suffering needed?
- What is being done to reduce/avoid this?
- Are the benefits sufficiently high to justify the suffering?
- Can you demonstrate that the model is translatable?
- When do you envisage your research leading to new therapies in the clinic (for applicants with long series of published papers)?
- Could the protocol be run with a moderate severity limit?
- What if we said 'no'?

Local level actions

- **Commit to ending severe suffering**
- Use the Roadmap approach
- Use the PREPARE guidelines
- Challenge the justification and necessity for severe procedures
- Use the AW(ERB), IACUC or AEC
- Ensure good reporting: ARRIVE, Gold Standard Publication Checklist



Thank you

