Working together to end ‘severe’ suffering

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ANIMALS IN SCIENCE DEPARTMENT

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

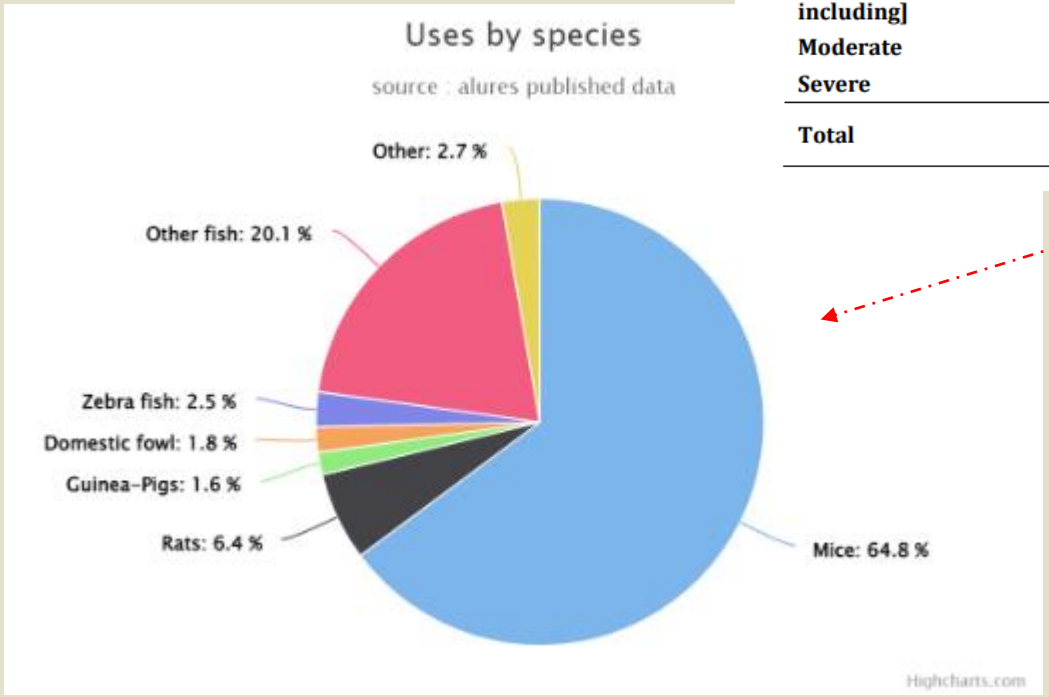
- severe pain, suffering or distress
- long-lasting moderate pain, suffering or distress, or
- severe impairment to their wellbeing or general condition

e.g. Annex VIII of EU Directive 2010/63

Causes of severe suffering

THREE MAIN REASONS

- Animals may be used in studies of **diseases or conditions** that by their nature can cause severe suffering
- A **combination** or series of less severe factors can combine to lead to an increase in overall suffering
- Where animals **die unexpectedly**, or where the **death** of an animal is used an **‘endpoint’** of the study



	2017	2018 (EU-28 incl. NO)	2019 (EU-28 incl. NO)
Non-recovery	6% (621,054)	6% (612,094)	**6% (586,373)**
Mild [up to and including]	51% (4,865,721)	50% (5,469,214)	**52% (5,512,134)**
Moderate	32% (3,071,828)	34% (3,658,621)	**33% (3,510,993)**
Severe	11% (1,023,138)	10% (1,064,925)	**9% (999,264)**
Total	**100% (9,581,741)**	**100% (10,804,854)**	**100% (10,608,764)**

https://ec.europa.eu/environment/chemicals/lab_animals/reports_en.htm

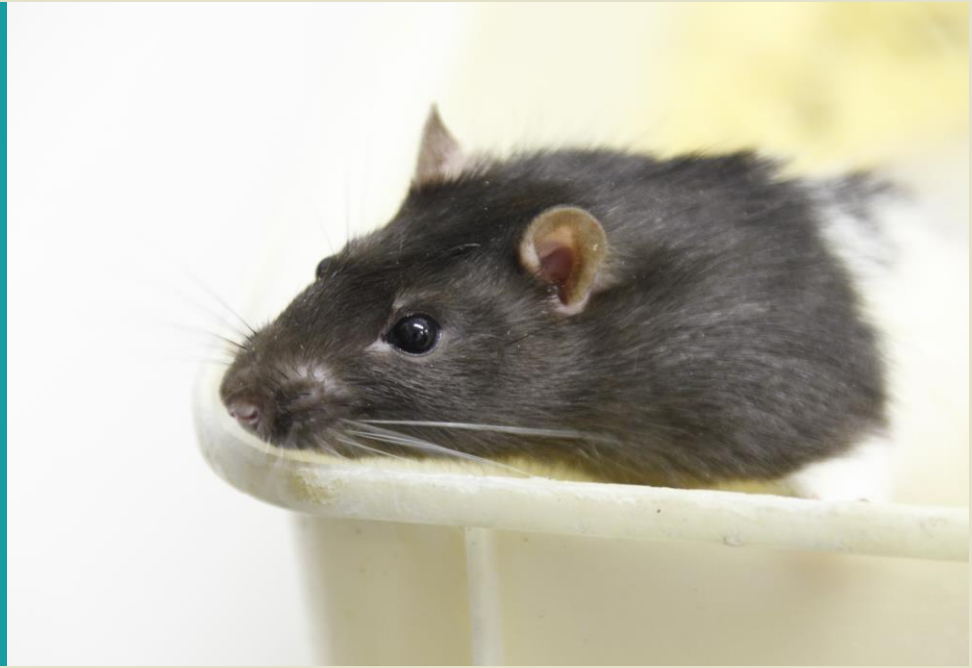
Member State	Uses of animals causing 'severe' suffering	% of total use
AUSTRIA	20245	9.24
BELGIUM	63134	14.20
CROATIA	2253	8.07
CYPRUS	0	0.00
CZECHIA	30653	12.98
DENMARK	4112	1.65
ESTONIA	0	0.00
FINLAND	6368	6.86
FRANCE	258440	14.55
GERMANY	97024	5.23
GREECE	12817	26.78
HUNGARY	19831	14.64
IRELAND	18543	13.39
ITALY	112087	20.37
LATVIA	82	1.93
LITHUANIA	0	0.00
LUXEMBOURG	344	3.08
MALTA	0	0.00
NETHERLANDS	4811	1.26
POLAND	83626	29.57
PORTUGAL	11170	14.82
ROMANIA	1055	7.75
SLOVAKIA	952	5.31
SLOVENIA	57	1.07
SPAIN	60119	7.94
SWEDEN	26842	11.39
NORWAY	91434	7.20
UK (GB+NI)	73265	4.18
EU + Norway total	999264	9.42

https://ec.europa.eu/environment/chemicals/lab_animals/reports_en.htm

10M

animals across the world experience severe suffering each year

*estimate



All laboratory animal suffering is a concern, but reducing and avoiding 'severe' suffering should be a top priority

- ✓ **Ethical** and animal welfare benefits
- ✓ **Legal** requirements to minimise suffering
- ✓ **Societal** concerns about harms to animals
- ✓ **Scientific** benefits - better welfare means better science

Everyone has a part to play

- Scientists
- Animal technologists
- Persons with responsibilities under Articles 24 and 25 (attending veterinarians, staff responsible for ensuring information access, training and competency etc)
- Animal Welfare Bodies
- Competent authorities
- National Committees
- National 3Rs centres
- NGOs

Our initiative

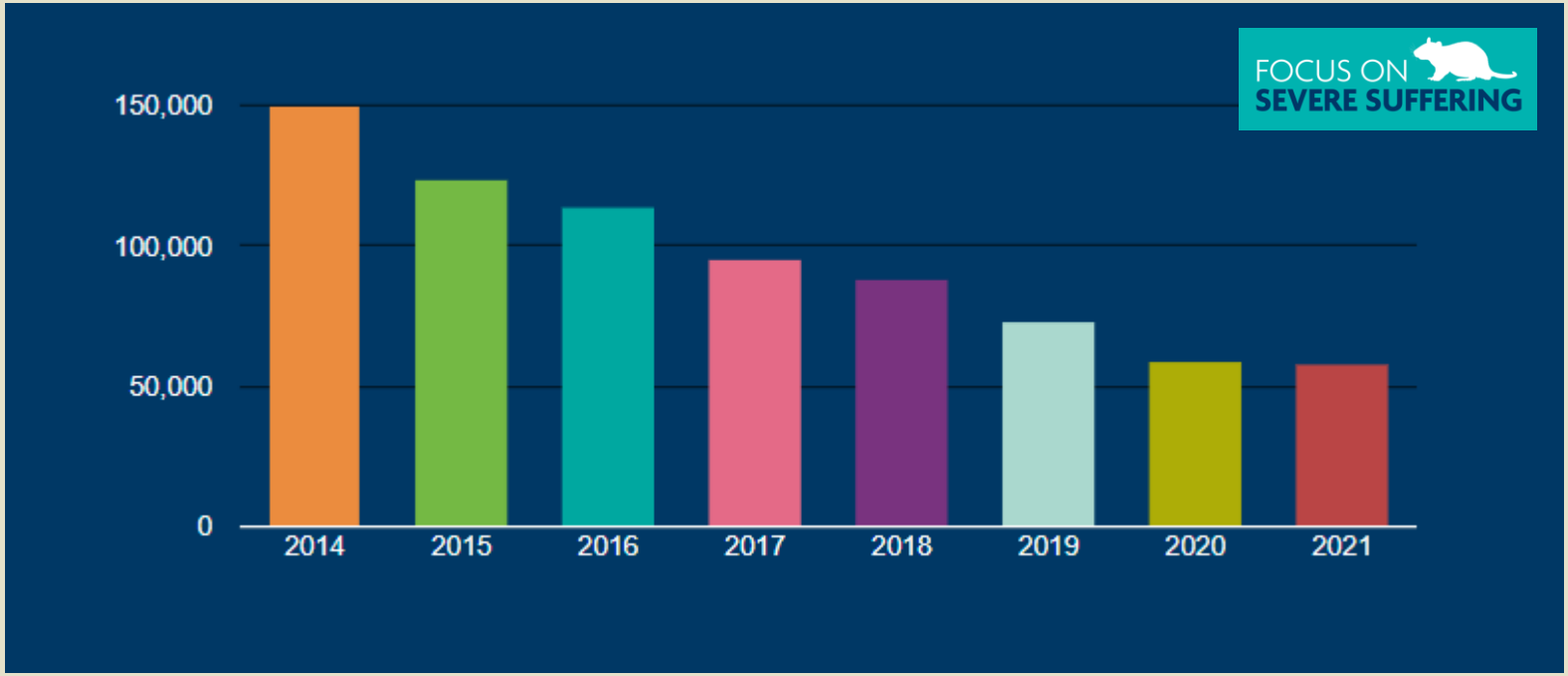
Since 2012, the RSPCA has been **working collaboratively** with the scientific community in the UK, EU and internationally, to initiate and promote a range of activities aimed at identifying and promoting **practical steps** which will help people to **reduce** or, ideally, **avoid** ‘severe’ suffering.

Key objectives

- Refine models to bring them to **a lower severity** limit where possible

  - applies to other levels of suffering too

- Ensure there has been **robust discussion** and a rationale that justifies the need for ‘severe’ limits, where they still exist



61% reduction in experimental procedures causing severe suffering in the **UK** since 2014

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EXAMPLES OF POTENTIALLY 'SEVERE' PROCEDURES

Batch potency testing of vaccines (where control animals experience 'severe' disease symptoms) **and other biologics** e.g. botulinum toxin, for regulatory purposes

Studies involving infectious disease models, including the development of vaccines or other treatments, where animals may experience 'severe' disease symptoms

Various tests involved in regulatory toxicology, including ecotoxicology, especially where animals may become moribund or die

Monoclonal antibody production using the mouse ascites method – NB this method has not been used in the UK since 2012 but is still used elsewhere in the world

Some cancer models – involving large tumours, resection, bone metastasis, brain tumours, pancreatic tumours

Some heart disease models – myocardial infarction induction; monocrotaline (MCT)-induced pulmonary arterial hypertension; transverse aortic constriction/banding

Multi-organ failure models

Demyelination of the central nervous system (CNS)

Models of motor neurone disease (MND)

Spinal cord injury models

Neuroscience studies using non-human primates, involving the cumulative effects of numerous surgeries, regular and long periods of restraint, and/or fluid or food control

Tamoxifen as an inducer of gene function

Irradiation with reconstitution of bone marrow

Cerebral malaria in rodents

Pancreatitis models

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NEW DATA ON 'SEVERE' SUFFERING IN THE EU AND NORWAY

1st August 2022

The most up-to-date data currently available on the use of animals in research and testing in the European Union (EU), and Norway, was published by the European Commission on 15 July 2022. This information is important for openness and transparency and can also help to focus 3Rs efforts more effectively. Below is a summary of the data, which is for 2019, setting out the number of animals reported to have experienced 'severe' suffering, and in which areas of science.

As in previous years, the mouse is the species most likely to experience 'severe' suffering, and batch potency testing of vaccines and other substances (such as botulinum toxin) is the category responsible for the largest proportion of 'severe' animal uses.

But on a positive note, the number of 'severe' animal uses fell by 65,661 in comparison with the 2018 data. This means that the percentage of 'severe' uses decreased from 10% to 9%, which is a small step in the right direction.

999,264 uses of animals (9% of the total) were reported as causing 'severe' pain, suffering, distress or lasting harm. This included:

- 344,582 in basic research *(7.2% of all uses for basic research involved severe suffering)*
- 310,367 in applied research *(10.9% of all uses for applied research involved severe suffering)*
- 291,166 for regulatory purposes *(12.2% of all uses for 'regulatory' purposes involved severe suffering)*

Main categories of use causing severe suffering

- 215,735 – Batch potency testing *(represents 21.6% of all uses of animals that were 'severe')*
- 132,695 – Studies of animal diseases and disorders *(represents 13.3% of all uses of animals that were 'severe')*
- 104,164 – Nervous system *(represents 10.4% of all uses of animals that were 'severe')*
- 77,654 – Immune system *(represents 7.8% of all uses of animals that were 'severe')*
- 52,574 – Oncology *(represents 5.3% of all uses of animals that were 'severe')*

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Expert Working Groups

- Seizures, convulsions and epilepsy
- Experimental autoimmune encephalomyelitis (EAE)
- Rheumatoid arthritis
- Sepsis
- Spinal cord injury
- Bone marrow ablation and reconstitution

- Avoiding mortality

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Events

- **Brussels**, Belgium - 2016
- **Berlin**, Germany - 2017
- **Stevenage**, UK - 2019
- **Athens**, Greece - 2019
- **Manchester**, UK - 2022
- **Stockholm**, Sweden - 2022
- Netherlands - 2023

100s of participants: regulators, scientists, veterinarians, animal technologists and care staff, members of Animal Welfare Bodies and National Committees etc.

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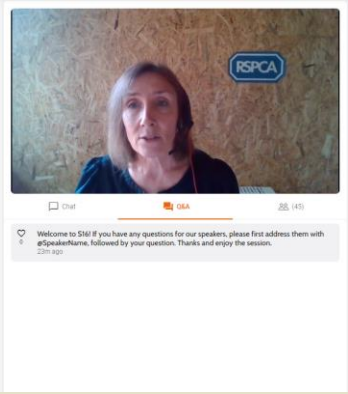
Potentially severe procedures
2021
• Batch potency testing of vaccines and other biologics
• Infectious disease models with severe symptoms, e.g. some vaccine development
• Studies of diseases that cause severe suffering in humans, e.g. rheumatoid arthritis, sepsis, spinal cord injury
• Some regulatory toxicology tests, e.g. acute toxicology, ecotoxicity
A
B
C


RSPCA
Chat
Q&A
(45)
Welcome to Stitl! If you have any questions for our speakers, please first address them with @SpeakerName, followed by your question. Thanks and enjoy the session.
23m ago


efpia
RSPCA
How the pharmaceutical industry is tackling 'severe' suffering in animals used in science
An online event co-organised by EFPIA and the RSPCA
Wednesday 26 January 2022: 14:30 - 16.00 CET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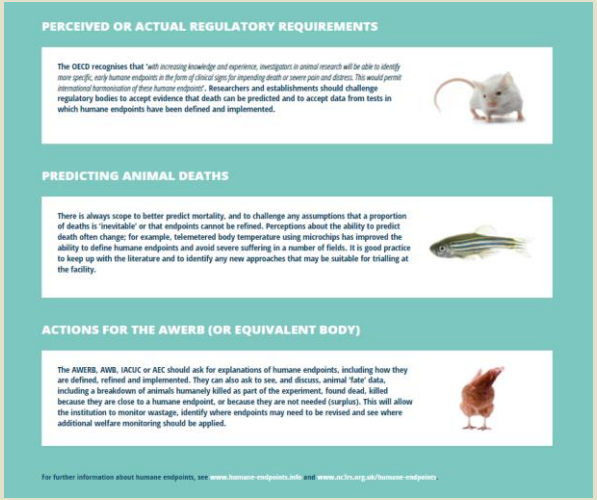
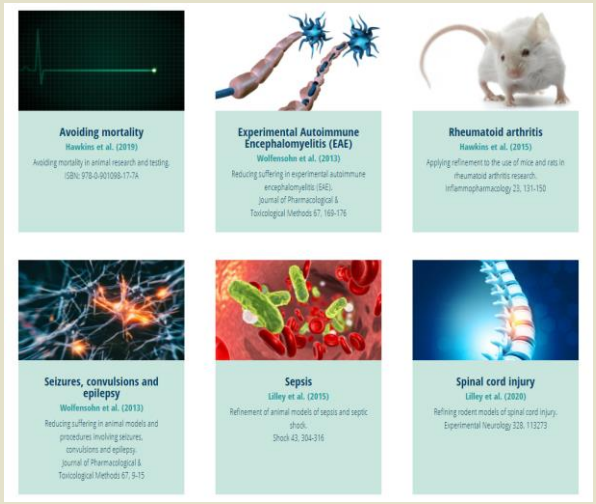
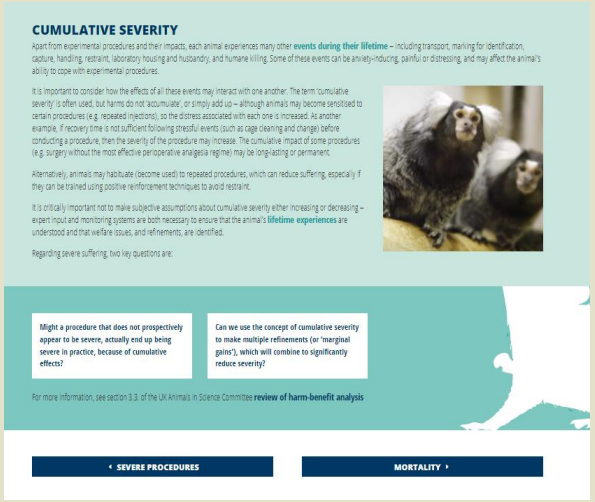
14th felasa congress 2019
Prague, Czech Republic

Website







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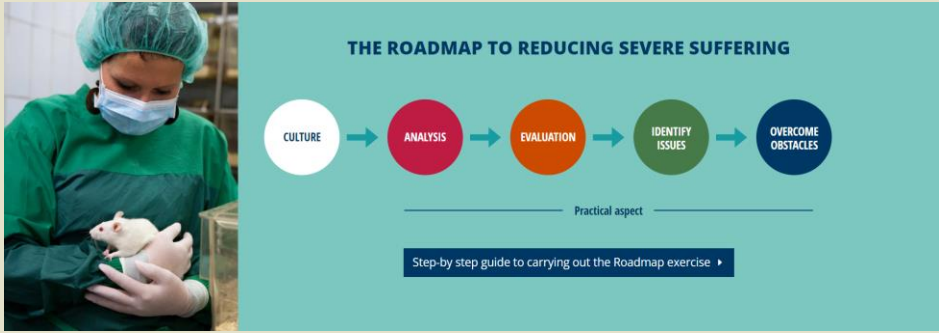
A commitment to address severe suffering

- Agreement as a priority area for attention and action
- Institutional strategy and responsibilities
- Setting of clear objectives



Consider as part of the ‘Culture of Care’

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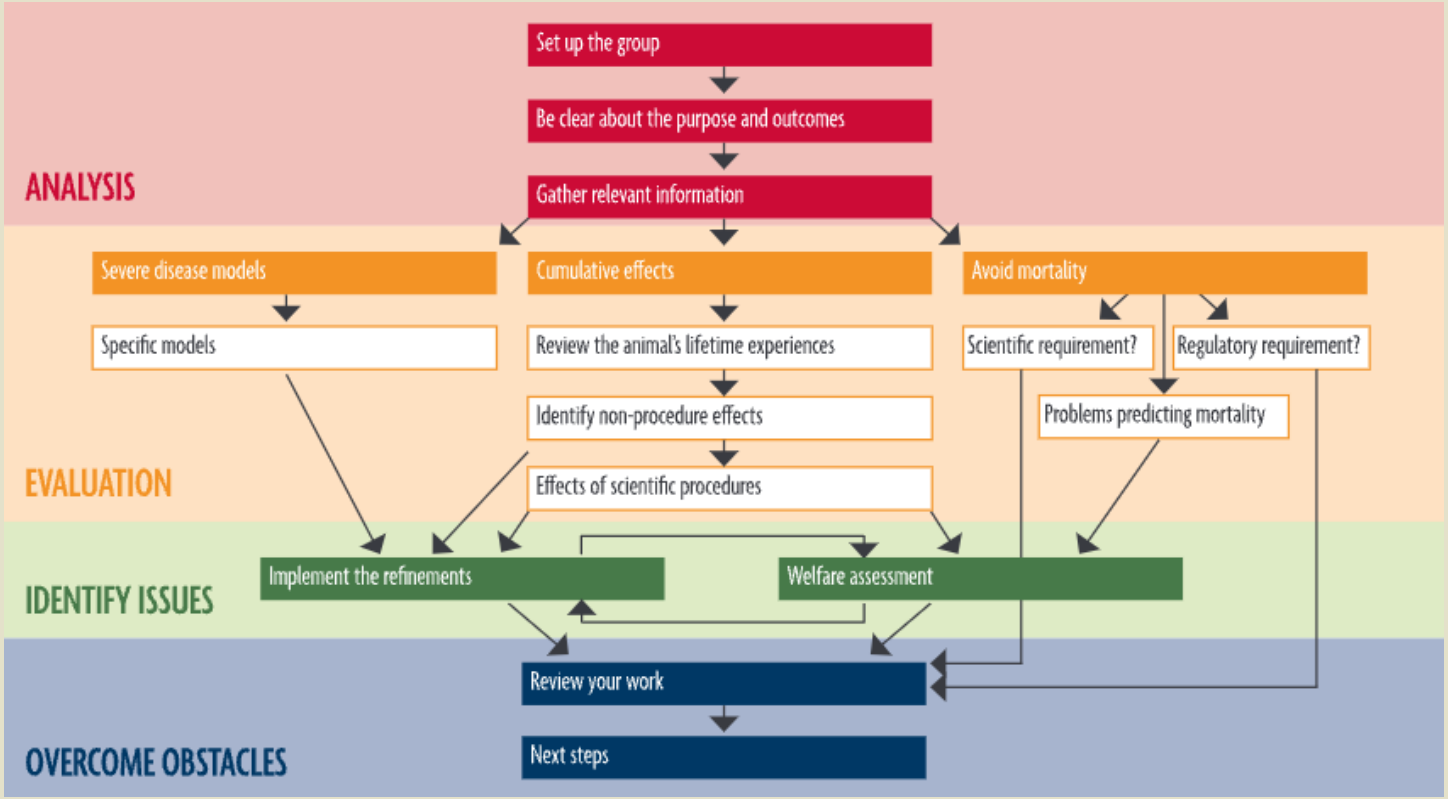

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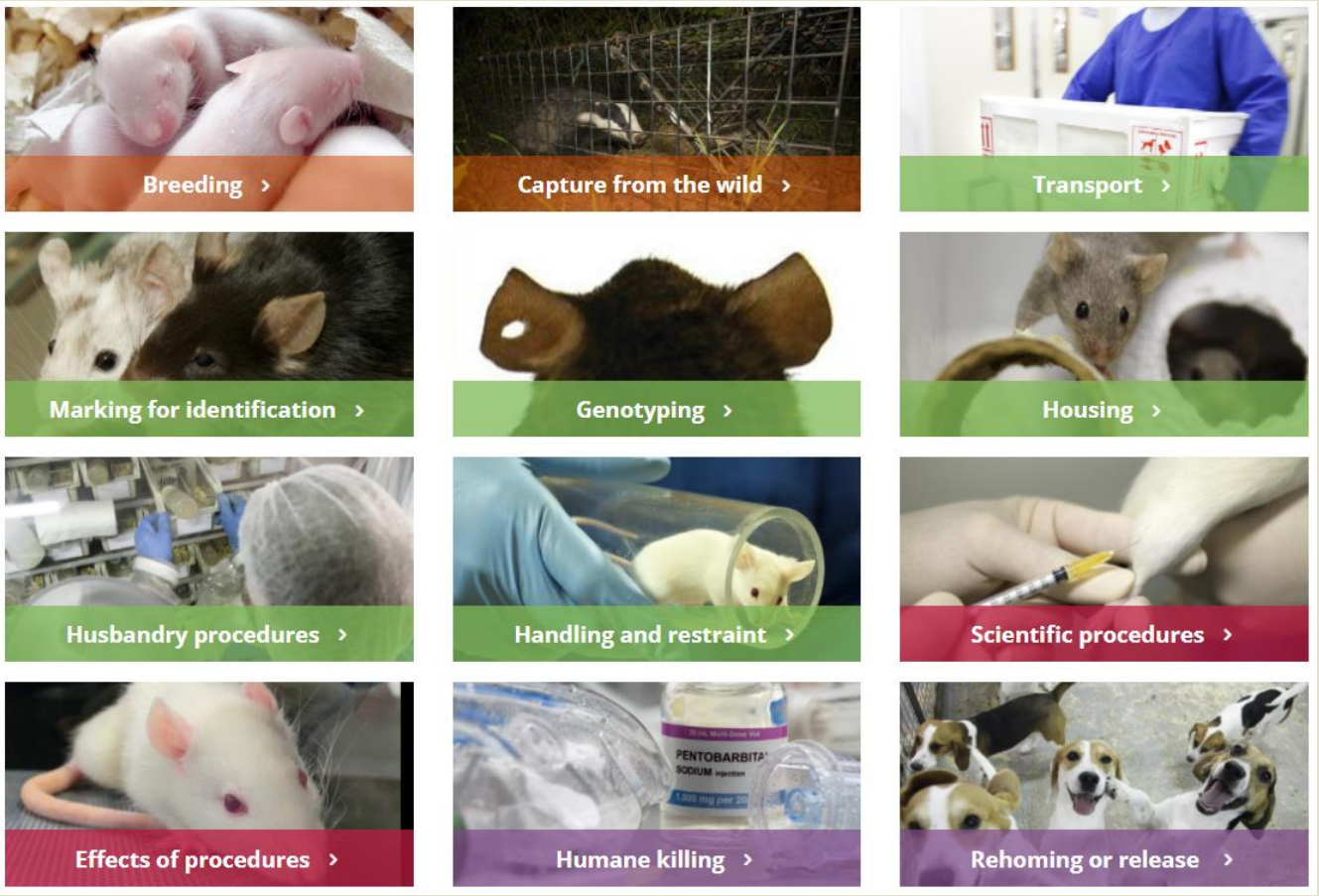

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Factor	Experience of the animal	Welfare issues	Ways of mitigating these
Sourcing	Mice are bred in-house. Supply and demand are carefully matched and animals provided with litter, nest boxes and nesting material. Cages are cleaned weekly.	Distress due 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	Capture and restraint – distress. Aggression, vocalisation, unwilling to be caught. Administration i.d. or s.c. – pain. Flinching, vocalisation, aggression. Pain or ulceration around injection site. Attention to site, reduction in nest quality, body weight/food intake reduction,	Competent, empathetic capture (e.g. not by tail) and handling, habituate to handling and restraint. 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 Inject into rump (less risk of ulceration); never inject into the foot; if attention paid to site apply topical anaesthesia and review	Humane endpoints with respect to administration of inducer in general: - 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.

Examples of questions to consider

- Why is severe suffering needed? Is there a robust scientific justification?
- Could the protocol be run with a moderate severity limit?
- Is the ‘model’ translatable? How significant are the proposed benefits of the work?
- Is there a regulatory requirement for the experimental design and ‘endpoint’? Can this be challenged?
- Are welfare assessment and monitoring protocols optimised?
- What more could be done to mitigate impacts on animals?

Applying the roadmap at Novo Nordisk

Prospectively

- Identify as many sources of harm as possible
  - Related to the (disease) model
  - Related to procedures
  - Related to housing, husbandry and care
- Agree on Humane Endpoints
  - General
  - Model specific
- Agree on procedures for welfare assessment

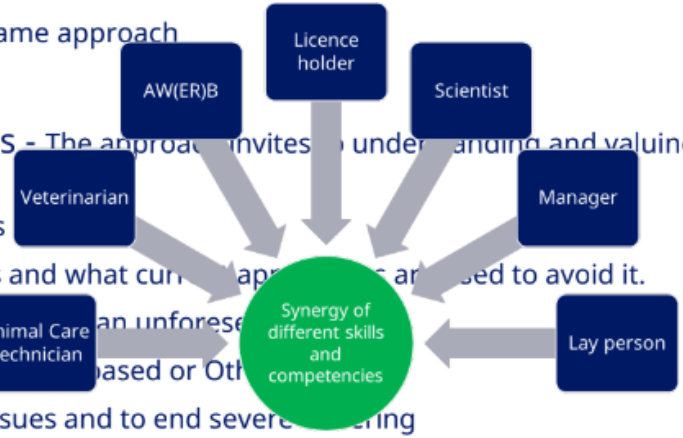
Retrospectively

- Assess actual severity
  - Identify when and why severe harm was experienced by the animal
  - Identify if avoidable harm unintentionally occurred
  - Evaluate the effectiveness of the implemented Humane Endpoints
  - Evaluate the effectiveness of how animal welfare was assessed
- Agree on revisions
- Agree on how learnings are captured and communicated to all relevant people

From presentation at ‘Refining severe disease models and procedures’ international meeting- August 2022

Why the roadmap works

- The RSPCA approach facilitates a **cooperative response** from licence holders and scientists, because:
  - Objective, data driven, systematic and no blame-game approach
- Dialogue with licence holders and scientists - The approach invites to understanding and valuing the roles of different people within an establishment
  - Data check: Is the scoring as 'severe' for all animals
  - Evaluation: Looking at why severe suffering occurs and what current approaches are used to avoid it.
  - Is the harm prospective or does severe suffering an unforeseen
  - Define obstacles: Are the obstacles, - Scientific, R based or Oth
  - Overcome obstacles: Set out a plan to overcome issues and to end severe ering
  - Action plan
  - Evaluate



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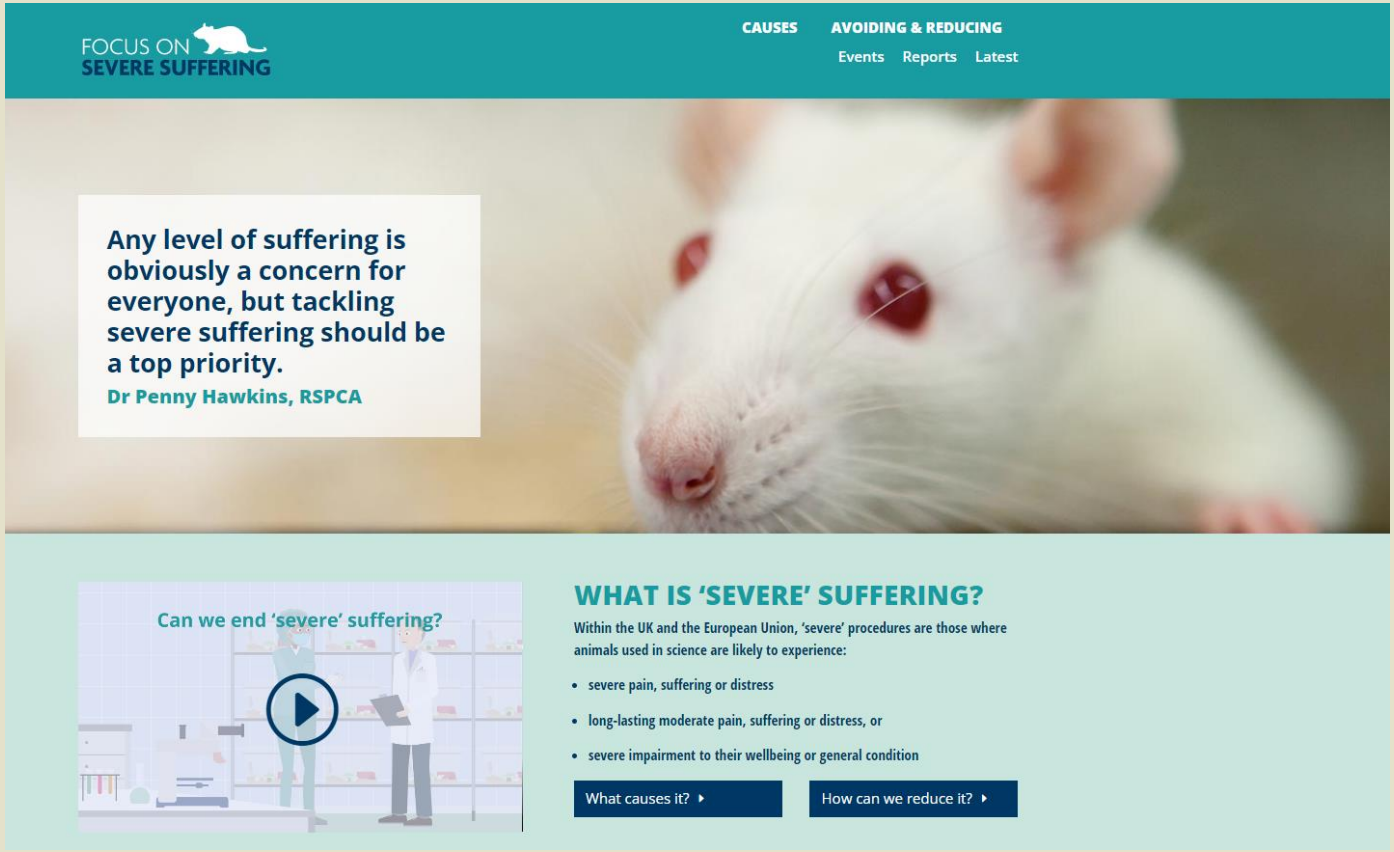

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