

FOCUS ON **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:

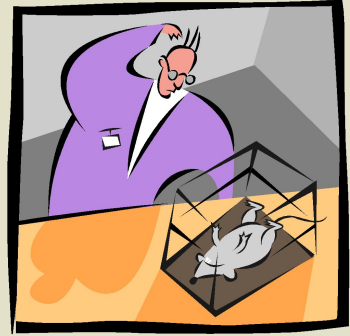
- severe pain, suffering or distress
- long-lasting moderate pain, suffering or distress, or
- severe impairment to their wellbeing or general condition

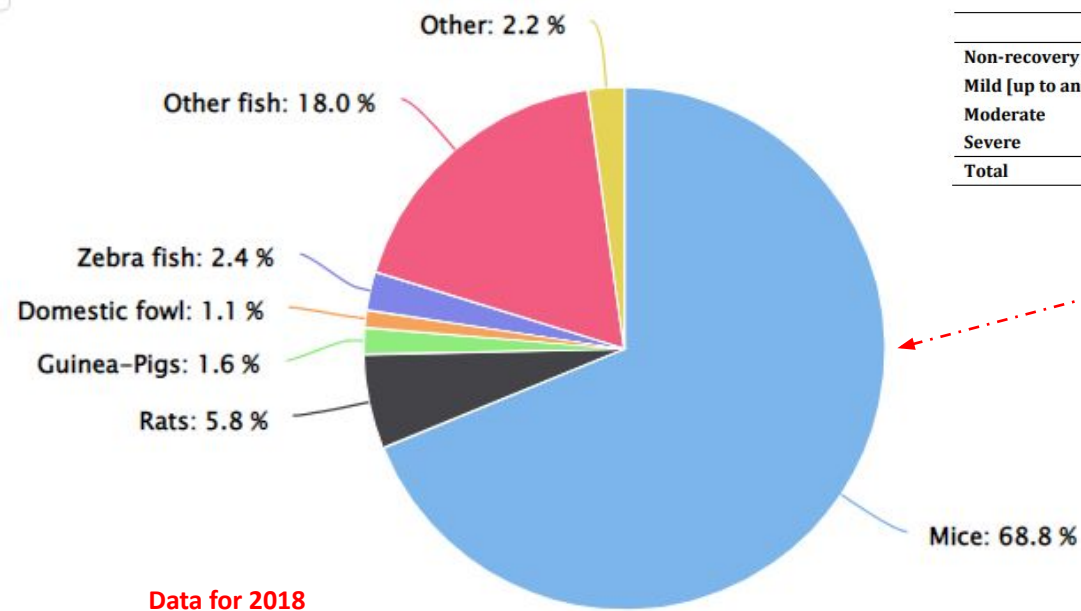


Causes of severe suffering

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 as an **'endpoint'** of the study





	2017	2018 (EU)	2018 (EU-28 incl. NO)
Non-recovery	6% (621,054)	6% (534,999)	6% (612,094)
Mild [up to and including]	51% (4,865,721)	49% (4,522,747)	50% (5,469,214)
Moderate	32% (3,071,828)	34% (3,096,460)	34% (3,658,621)
Severe	11% (1,023,138)	11% (983,237)	10% (1,064,925)
Total	100% (9,581,741)	100% (9,137,443)	100% (10,804,854)

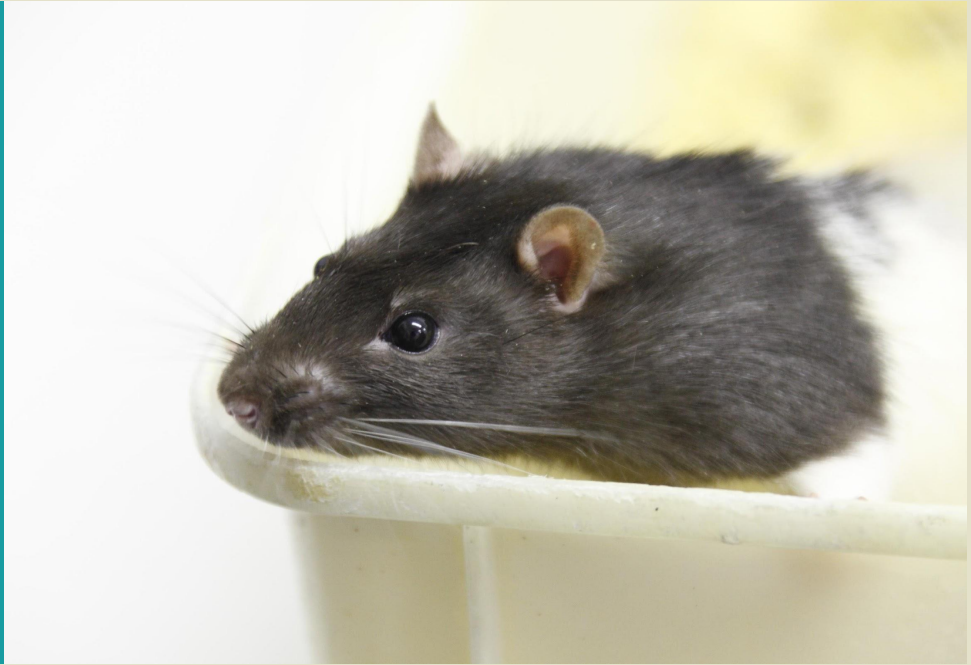


10M

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



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.

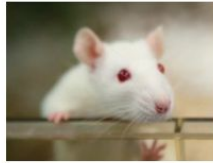


61% reduction

in experimental procedures causing severe suffering in the **UK** since 2014

NEW DATA PUBLISHED ON 'SEVERE' SUFFERING IN THE UK AND EU

15th July 2021



The most up-to-date data currently available on the use of animals in research and testing in the UK, and the EU, was published on 15 July 2021. 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 relating to the number of animals reported to have experienced 'severe' suffering, and in which areas of science.

The mouse is the species most likely to experience 'severe' pain, suffering, distress or lasting harm. In both the UK and EU, batch potency testing of vaccines and other substances (such as botulinum toxin) for quality control purposes is the category responsible for the most uses of animals reported as 'severe'.

UK

Data for 2020

Source: Home Office. See Tables 3.1 and 3.2 of the [Data Tables](#) associated with the [Statistics of scientific procedures on living animals, Great Britain 2020](#) – published 15 July 2021.

Summary

58,499 experimental procedures using animals (4% of the total) were reported as causing 'severe' pain, suffering, distress or lasting harm.

44,093 – for regulatory purposes (9% of all use for regulatory purposes was 'severe')

10,867 – in basic research

3,511 – in applied research

Main categories of research and testing involving severe suffering

(data shown represent the number of 'procedures' undertaken that were reported as causing 'severe' suffering)

35,997 – Batch potency testing (represents 61.5% of all experimental procedures involving animals that were 'severe')

2,592 – Nervous system

2,567 – Immune system

1,512 – Human infectious disorders

1,479 – Batch safety testing

1,303 – Oncology

Which animals experienced the most 'severe' suffering?

(data shown represent the number of 'procedures' undertaken involving those animals)

55,155 – Mice (94.3% of all 'severe' suffering)



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



Expert Working Groups

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



Events

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



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

Website

PERCEIVED OR ACTUAL REGULATORY REQUIREMENTS

The OECD recognises that "with increasing knowledge and experience, investigators in animal research 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". Researchers and establishments should challenge regulatory bodies to accept evidence that death can be predicted and to accept data from tests in which humane endpoints have been defined and implemented.



PREDICTING ANIMAL DEATHS

There is always scope to better predict mortality, and to challenge any assumptions that a proportion of deaths is 'inevitable' or that endpoints cannot be refined. Perceptions about the ability to predict death often change: for example, telemetered body temperature using microchips has improved the ability to define humane endpoints and avoid severe suffering in a number of fields. It is good practice to keep up with the literature and to identify any new approaches that may be suitable for trialling at the facility.



ACTIONS FOR THE AWBER (OR EQUIVALENT BODY)

The AWBER, AWL, IACUC or AEC should ask for explanations of humane endpoints, including how they are defined, refined and implemented. They can also ask to see, and discuss, animal 'fate' data, including a breakdown of animals humanely killed as part of the experiment, found dead, killed because they are close to a humane endpoint, or because they are not needed (surplus). This will allow the institution to monitor wastage, identify where endpoints may need to be revised and see where additional welfare monitoring should be applied.



For further information about humane endpoints, see www.humane-endpoints.info and www.acfr.org.uk/humane-endpoints.



Avoiding mortality

Avoiding mortality in animal research and testing.
ISBN: 978-0-901093-17-9



Experimental Autoimmune Encephalomyelitis (EAE)

Wolffensohn et al. (2013)
Reducing suffering in experimental autoimmune encephalomyelitis (EAE).
Journal of Pharmacological & Toxicological Methods 67, 169-176



Rheumatoid arthritis

Hawkins et al. (2015)
Applying refinement to the use of mice and rats in rheumatoid arthritis research.
Inflammopharmacology 23, 131-150



Seizures, convulsions and epilepsy

Wolffensohn et al. (2013)
Reducing suffering in animal models and procedures involving seizures, convulsions and epilepsy.
Journal of Pharmacological & Toxicological Methods 67, 9-15



Sepsis

Lilley et al. (2015)
Refinement of animal models of sepsis and septic shock.
Shock 45, 304-316



Spinal cord injury

Lilley et al. (2015)
Refining rodent models of spinal cord injury.
Experimental Neurology 328, 113273

CUMULATIVE SEVERITY

Apart from experimental procedures and their impacts, each animal experiences many other **events during their lifetime** – including transport, marking for identification, capture, handling, restraint, laboratory housing and husbandry, and humane killing. Some of these events can be anxiety-inducing, painful or distressing, and may affect the animal's ability to cope with experimental procedures.

It is important to consider how the effects of all these events may interact with one another. The term 'cumulative severity' is often used, but harms do not 'accumulate' or simply add up – although animals may become sensitised to certain procedures (e.g. repeated injections), so the distress associated with each one is increased. As another example, if recovery time is not sufficient following stressful events (such as cage cleaning and changes) before conducting a procedure, then the severity of the procedure may increase. The cumulative impact of some procedures (e.g. surgery without the most effective perioperative analgesia regime) may be long-lasting or permanent.

Alternatively, animals may habituate (become used) to repeated procedures, which can reduce suffering, especially if they can be trained using positive reinforcement techniques to avoid restraint.

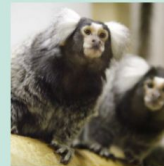
It is critically important not to make subjective assumptions about cumulative severity either increasing or decreasing – expert input and monitoring systems are both necessary to ensure that the animal's **lifetime experiences** are understood and that welfare issues, and refinements, are identified.

Regarding severe suffering, two key questions are:

Might a procedure that does not prospectively appear to be severe, actually end up being severe in practice, because of cumulative effects?

Can we use the concept of cumulative severity to make multiple refinements (or 'marginal gains'), which will combine to significantly reduce severity?

For more information, see section 3.3 of the UK Animals in Science Committee **review of harm-benefit analysis**



• SEVERE PROCEDURES

MORTALITY •

focusonseveresuffering.co.uk





Breeding >



Capture from the wild >



Transport >



Marking for identification >



Genotyping >



Housing >



Husbandry procedures >



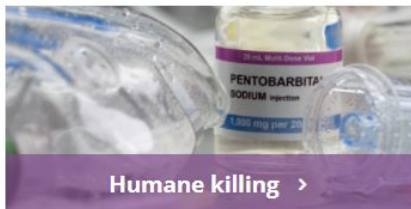
Handling and restraint >



Scientific procedures >



Effects of procedures >



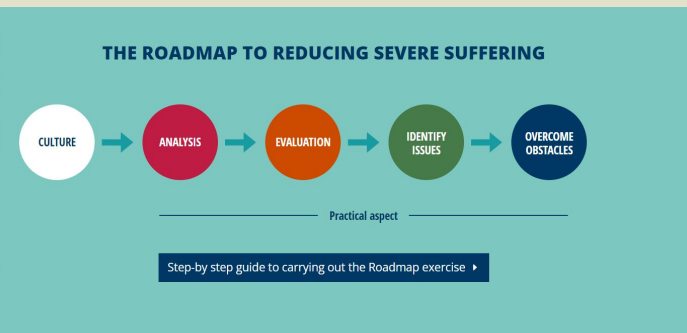
Humane killing >



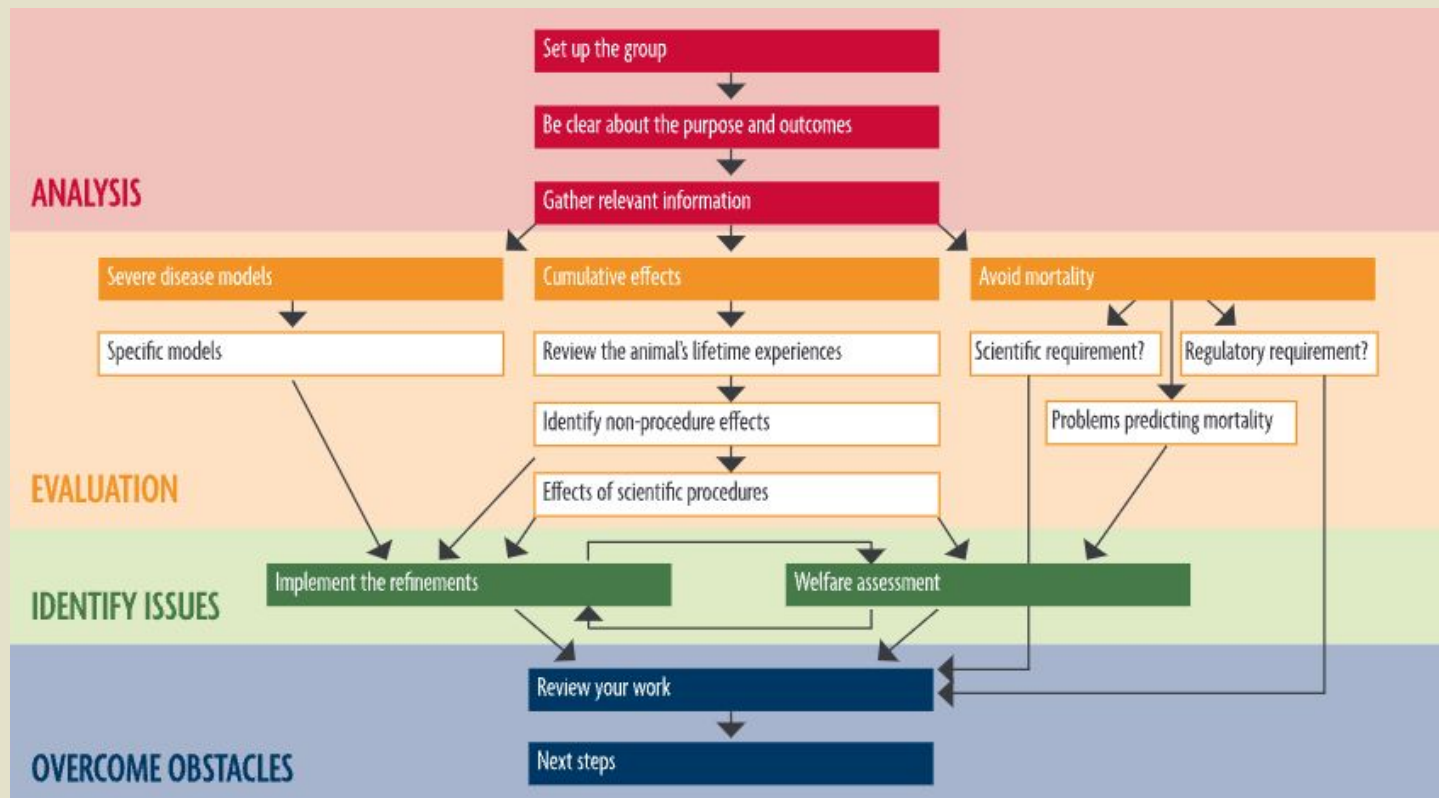
Rehoming or release >

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’



Examples of questions to consider

- Why is severe suffering needed? Is there a robust scientific justification?
- Is the 'model' translatable? How significant are the proposed benefits of the work?
- Could the protocol be run with a moderate severity limit?
- 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?

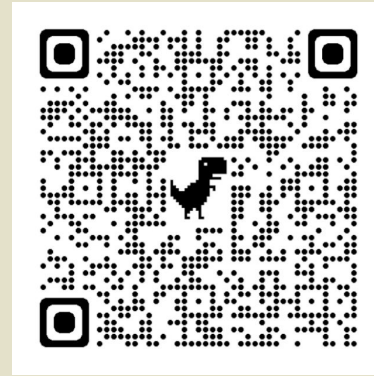
Refining severe disease models and procedures

24-25 August 2022

Stockholm, Sweden



**Karolinska
Institutet**



focusonseveresuffering.co.uk/events