

7th International Focus on Severe Suffering meeting report

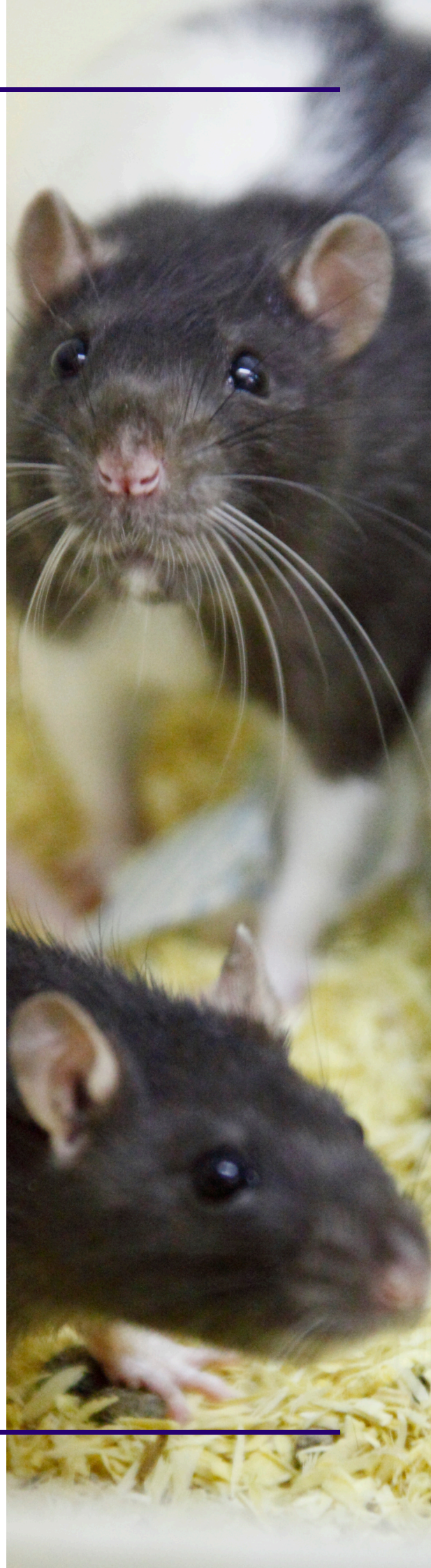
Madrid, Spain



**Animals in Science Department
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Summary



The 7th International Focus on Severe Suffering meeting was delivered in collaboration with the Network of Bodies Responsible for Animal Welfare (ROEBA), the Spanish Society for Laboratory Animal Science ([SECAL](#)) and the Official College of Veterinarians of Madrid ([COLVEMA](#)).

This was the latest in our series of international events promoting

knowledge about, and approaches to, avoiding and educing severe suffering, and improving the welfare of animals used in research and testing. The two-day meeting featured case studies of refinements in different research areas, talks on compassion fatigue (which is strongly associated with severe suffering), and guidance on how to use the RSPCA's Roadmap to reduce severe suffering.

Day One

Introduction

After a welcome and introduction from José Orellana from COLVEMA, the first session opened with an **update on the Focus on Severe Suffering initiative** by Lorena Sordo from the RSPCA. Alberto Pastor Campos, president of SECAL, followed with an **overview of severe suffering within Spain**. His presentation revealed that despite a 19% reduction in overall animal use since 2023, the number of severe procedures increased from 67,574 (5.91%) to 69,503 (7.83%) in 2024, possibly driven by greater use of fish models in vaccine research. He further noted that severe classifications persist because 1) severe suffering may be inherent to the scientific question, 2) many procedures are dictated by production and regulatory requirements, such as aquaculture vaccine development, and 3) when available refinements are already implemented, further progress can be challenging. He concluded by highlighting that any severe classification should trigger a higher scrutiny through rigorous harm–benefit analysis, using prospective severity to

evaluate and challenge study designs, ensuring continuous real-time animal monitoring, and implementing targeted 3Rs initiatives.

Case studies in oncology

This session opened with a presentation by Alfonso Mora, from the Spanish National Cancer Research Centre, on the **mouse model of hepatocellular carcinoma as a case study**. He highlighted that the level of suffering is not always proportional to the size of the tumour and is rarely caused by the tumour alone, but by accompanying factors. These include the duration (e.g. chronic models) and slow progression of the disease, repetitive manipulations, cumulative events, and inadequate processes for monitoring animals (e.g. defining late clinical endpoints, infrequent monitoring, not listening to animal caretakers, etc.). He then shared refinement strategies based on a whole-animal approach, such as designing a robust welfare assessment protocol and improving predictive monitoring that can be used not only to monitor the tumours but also to understand the impact on the animals and their welfare. It is also important to provide preventive supportive care and implement early humane endpoints.

In the next talk, Rita Silva-Reis from the University of Trás-os-Montes and Alto Douro discussed the **refinement of humane endpoints for mouse models of chemically-induced colorectal cancer**. Her team identified that current guidelines, such as those from the Canadian Council on Animal Care, were insufficient for predicting mortality in this specific research area. Consequently, they integrated model-specific indicators to define more early and effective endpoint triggers. Their observations indicated a clear progression of clinical signs including weight gain, abdominal swelling, diarrhoea, and priapism, which occur in sequence, weeks prior to death. They proposed including rapid increases in body weight ($\geq 6\%$), the presence of priapism, and elevated abdominal thermography as novel criteria for implementing humane endpoints in these studies.

In the following presentation, Rebecca Marlow from AstraZeneca described the **development of a comprehensive welfare scoring system for graft versus host disease (GvHD) in humanised mouse models**. She highlighted that the development of such scoring systems must be a collaborative effort involving veterinarians, researchers, and animal care staff. Moreover, she underlined that performing pilot studies and reviewing the literature are crucial for selecting appropriate clinical indicators. Her team successfully identified seven key indicators that effectively captured GvHD at the earliest

and most severe stages: activity, posture, weight loss, inflammation (including yellowing of the tumour and surrounding skin), fur condition, breathing abnormalities, and diarrhoea. Once the indicators were identified, they developed and refined the scoring system using a traffic light system (Figure 1) to guide timely interventions and establish humane endpoints. Further **refinements in bone marrow ablation and reconstitution in mice** have been published elsewhere¹.

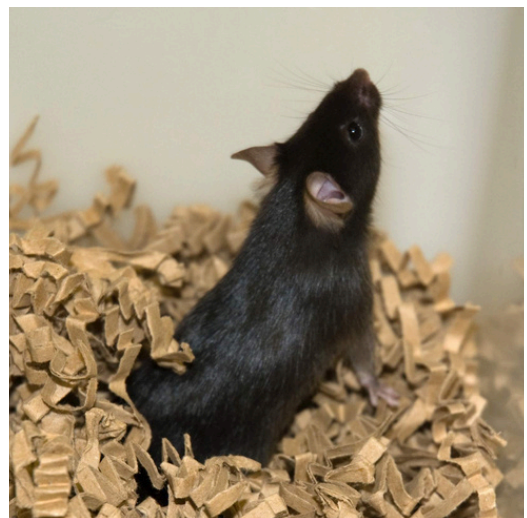
Total score	Class description	Action
0 to 3	Minimal clinical signs	Continue to monitor mice for clinical signs (3x week)
4 to 6	Mild clinical signs	- Monitor closely for clinical signs (every day) and consult with a senior animal technologist, or the attending veterinarian, about scoring if any signs are unclear. YELLOW: Any animal in this range will be monitored for up to 14 days and humanely killed at day 14. - Worsening of clinical condition at any point during the 14 days observation will be categorised as ORANGE.
7 or 8	Moderate clinical signs	Monitor closely (everyday) and consult with a senior animal technologist, or the attending veterinarian, about scoring if any signs are unclear. ORANGE: Animals in ORANGE category (score of 7 or higher) will be monitored for up to 5 days and humanely killed on Day 5. *MOVE YELLOW TO ORANGE* Animal is only kept for 5 days after moving from yellow to orange and will be humanely killed on day 5 in orange. Maximum monitoring in yellow/orange is 14 days.
≥ 9	Risk of exceeding moderate severity	Humanely kill animals immediately. Take endpoint samples.

Figure 1. Traffic light system used to guide interventions and humane endpoints in humanised mouse models of cancer. Note that this system was developed to monitor additional, tailored clinical signs; hence, it is important to continue monitoring animals routinely, every day, for other clinical signs. It is included in this report as an example approach; all welfare assessment protocols should be tailored to the species, strain and project.

In the final presentation of the session, Simone Kumstel from the University Medical Center Rostock discussed **identifying early humane endpoints within a mouse model of pancreatic cancer**. Her team incorporated standard clinical signs like apathy, ascites and loss of body weight; however, they also identified that monitoring burrowing behavior (by measuring the amount of burrowed pellets, in grams, after 2 and 17 hours) provided significant predictive value for establishing humane endpoints. Their findings showed that burrowing is a highly effective parameter for predicting endpoints, with a reduction in burrowed pellets of over 44% observed two days before, and over 75% one day before the humane endpoint was reached. In the final part of her talk, she discussed refinements in pain management, specifically noting that tramadol significantly improved welfare in the mouse model of acute lymphatic leukemia, when compared to metamizole. Furthermore, in her experience, buprenorphine was identified as the best analgesic for improving animal welfare during the humane endpoint phase of colorectal cancer studies.

Case studies in neuroscience

The session in neuroscience began with a presentation by Laura Calvillo from the IRCCS Istituto Auxologico Italiano. She explained how pain and stress can cause changes in gene expression and vagal nerve dysfunction, and trigger neuroinflammation, highlighting the importance of having a robust **pain management strategy** in place. Through the integration of systematic manual behavioural analysis, the Mouse Grimace Scale, and video monitoring via infrared thermography, her team identified that whole-body twitching served as the most reliable clinical indicator of pain in a mouse model of spinal cord injury. Furthermore, they demonstrated that a multi-modal analgesia approach combining buprenorphine and carprofen reduced observed pain signs by 80%. Notably, her findings also revealed that elevated temperatures in brown adipose tissue were closely correlated with pain levels. She concluded by emphasizing the critical role of smart monitoring, noting that standard smartphones offer a convenient and non-invasive method for detecting pain and stress in these studies.



Next, Zoe Windsor from University College London discussed **husbandry challenges associated with the use of exteriorised cranial devices in mice**, including nesting restrictions due to tangling potential. She then shared how her team assessed various materials, such as paper pulp, facial tissue, short fibre rolls, and short paper shavings, to determine which one is most suitable in these studies. They developed a tangling severity score to evaluate whether materials tangled on the device, and monitored the quality of both individual (either nestlet or paper pulp) and composite (made from nestlet and paper pulp combined) nests. Their findings revealed that tangling incidents were exclusively associated with the use of facial tissue as it tends to become long and string-like. Regarding nesting performance, paper pulp was identified as the superior material for maintaining nest quality and lack of tangling risk. She concluded by stressing the importance of tailoring environmental enrichment for both safety and quality, noting that failing to provide such enrichment is not an acceptable practice.

In the following presentation, Andrew Emberton from the University of Oxford discussed strategies for **mitigating stress and anxiety in non-human primates within neuroscience research**. He explained that specific procedures, including fMRI, electrophysiology and transcranial ultrasound stimulation, require animals to perform complex tasks for long periods, frequently involving head movement restrictions, which can be stressful for the animals. To reduce animals' stress and anxiety, his team established a training programme where animals learn to voluntarily cooperate. He underlined the value of using high-motivation positive reinforcers, such as raisins, which are strictly reserved for training sessions, and highlighted the importance of keeping the animals engaged and minimising periods of inactivity. Since introducing the training programme, they have seen that animals learn new tasks faster, display fewer stereotypic behaviours, and maintain better physical and coat conditions.

In the final presentation of the session, Visila Moiche from the Biobide Zebrafish facility discussed **refining severity limits within zebrafish models of amyotrophic lateral sclerosis and Dravet syndrome**. Her team developed a comprehensive welfare assessment that incorporates a detailed body condition score alongside evaluations of general appearance, movement and behaviour, bone development, and the condition of the body, the scales and fins. To ensure timely intervention, they also established a regular disease monitoring protocol. Specific refinement strategies included allowing a two-week spawning period to prevent egg-binding and prioritising the use of heterozygous over homozygous lines where feasible. Furthermore, the implementation

of a cryopreservation and in vitro fertilisation programme enabled them to reduce the number of animals kept in stock by 75%.

Keynote

The keynote talk was delivered by Javier Guillén from [AAALAC International](#), who discussed **the role of ethics committees and other oversight bodies in animal research**. Although ethics committees and oversight bodies across the world have some differences, they all serve as key mechanisms for ethical review, regulatory compliance, and effective oversight of animal care and use programmes. During his talk, he provided an overview of how these committees/bodies function across different regions, while highlighting common elements between them. Moreover, based on observations from AAALAC International's global accreditation programme, he shared frequently identified findings related to the committee's performance and outlined AAALAC International's expectations for their effective functioning. He highlighted that using a performance-based approach is useful to evaluate the outcome of the ethical review and oversight process. Finally, he emphasised the committee's role in fostering a Culture of Care, promoting ethical reflection, and supporting researchers in implementing best practices.



Day Two

Case studies in infectious diseases

The session started with a presentation by Cristina Jurado from the Animal Health Research Centre, who shared **refinement strategies to minimise severe suffering within infectious disease studies**. During her presentation, she shared several refinements implemented at her facility, including providing species-specific environmental enrichment for all species, the implementation of refined anaesthetic and analgesic protocols, conducting daily assessments using species-specific scoring sheets, and implementing predefined early humane endpoints. She highlighted the importance of reviewing and implementing dynamic welfare refinements (i.e. adapting these in response to the condition of the animal) particularly with respect to monitoring and humane endpoints. She concluded by demonstrating that significant improvements in welfare are achievable even in high-containment environments, sharing examples such as maintaining social contact through the use of pen separators in pig infection models.

In the following talk, Rachel Tanner from the University of Oxford provided an overview of **refinement strategies in tuberculosis vaccine research**. One of these refinements involved implementing early humane endpoints instead of conducting survival studies, allowing for intervention or termination before the onset of severe disease. Moreover, using low- and ultra-low-dose challenges mimics natural exposure more closely and results in less severe disease, while still allowing the assessment of vaccine performance. Additionally, challenging animals with attenuated *Mycobacterium bovis* BCG as a surrogate for virulent *Mycobacterium tuberculosis* also reduces disease severity and biosafety requirements, while enabling the assessment of vaccine-induced protection. She then shared that ex vivo functional assays offer a valuable alternative to in vivo challenge models. By collecting blood samples from animals and assessing them in vitro, these highly sensitive assays are useful to evaluate disease control while significantly reducing the need for live animal infection.

The next presentation was delivered by Liliana Oliveira from the i3S Institute for Research and Innovation in Health, who presented **refinements in a mouse model of sepsis**. Some sepsis studies are inherently severe, resulting in sudden and unpredictable deterioration of animals. She explained how her team aimed to refine humane endpoints,

noting that traditional criteria frequently rely on late-stage indicators, often during moribund stages, when animals are close to spontaneous death. By assessing body temperature, they identified hypothermia as an objective and clinically relevant indicator of disease progression and non-recovery. Their results showed a progressive decline in temperature before reaching clinical endpoints and a clear divergence in body temperature between non-survivors on the one hand and survivors prior to euthanasia on the other hand, representing an opportunity for early intervention. Finally, they proved that monitoring temperature subcutaneously via implanted PIT tags was an effective strategy for identifying non-recovery stages compared to standard indicators, such as weight loss.

In the final presentation of the session, Eddie Clutton from the University of Edinburgh discussed **refinement strategies for an ovine model of infectious lung cancer**. Ovine



pulmonary adenomatosis is a fatal, naturally occurring lung cancer in sheep caused by the Jaagsiekte sheep retrovirus. He explained that naturally occurring models rely on farm screening and subsequent transport of animals, often resulting in undetected clinical signs becoming apparent only after arrival. Many of these animals are not used because they develop severe clinical signs and have to be humanely killed, or because they only develop small diffuse nodular lesions. Furthermore, these animals may

suffer due to separation from their group and transportation. By transitioning to a refined experimental model, his team minimised such suffering through social housing and habituation to handling and the research environment. Notably, he demonstrated that integrating imaging with 3D reconstruction techniques enables continuous monitoring of disease progression and reliable prediction of tumour growth, offering the opportunity for timely intervention and the implementation of early humane endpoints.

Spotlight research

Pain assessment and management are fundamental priorities across all research disciplines. For this reason, the topic was included as a separate session to address these challenges.

The session opened with an interactive survey using Slido to examine practices regarding pain assessment and management among participants. Twenty-seven attendees participated in the survey, with some data exceeding 100% because participants were able to select more than one answer. Results indicated that mice were the most commonly used species (80%) (Figure 2). Furthermore, 68% of establishments reported that their highest level of severity was severe, followed by moderate (28%) and mild (12%).

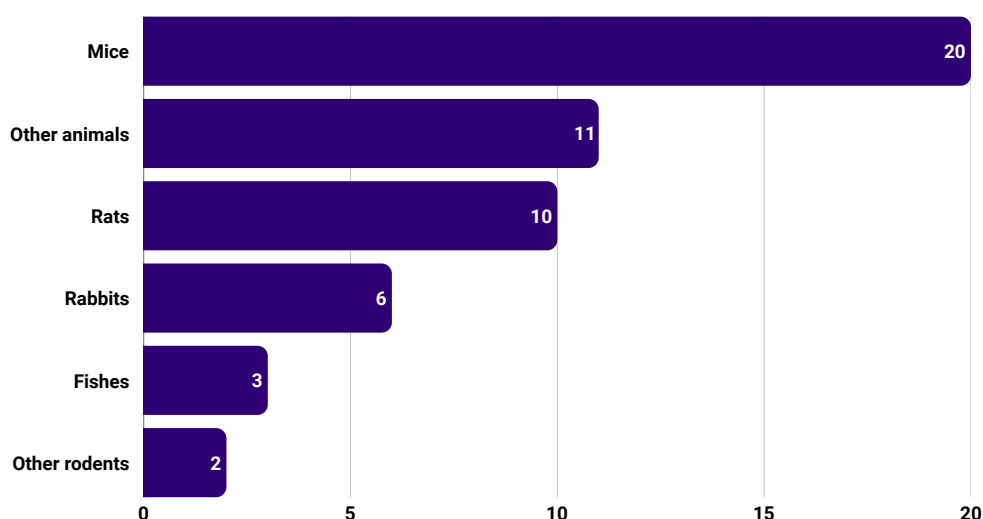
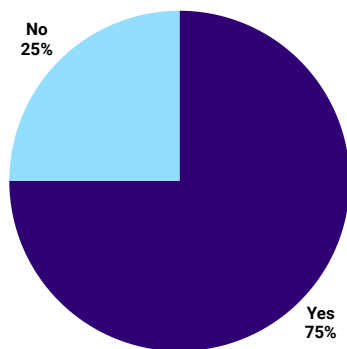


Figure 2. Species used among participants

While painful procedures were conducted in 81% of establishments, analgesia was provided to animals in only 75% of them. The most commonly used analgesics were local anaesthetics, opioids and NSAIDs (Figure 3). In addition, pain was assessed in 92% of establishments, mainly through behavioural observations, use of clinical score sheets, and response of animals to handling (Figure 4).

Do you provide analgesia to animals?



Commonly used analgesics

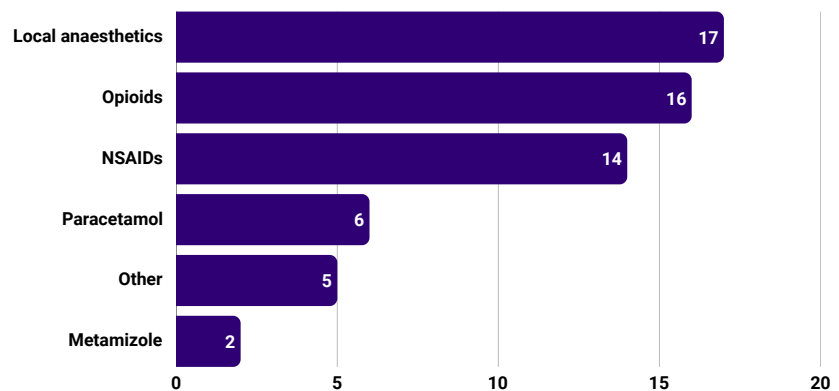
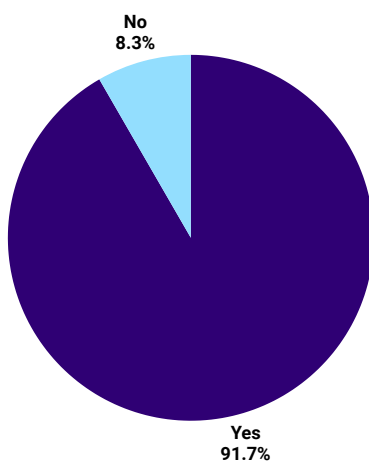


Figure 3. Analgesia practices among participants

Do you assess pain in the animals?



Pain assessment method

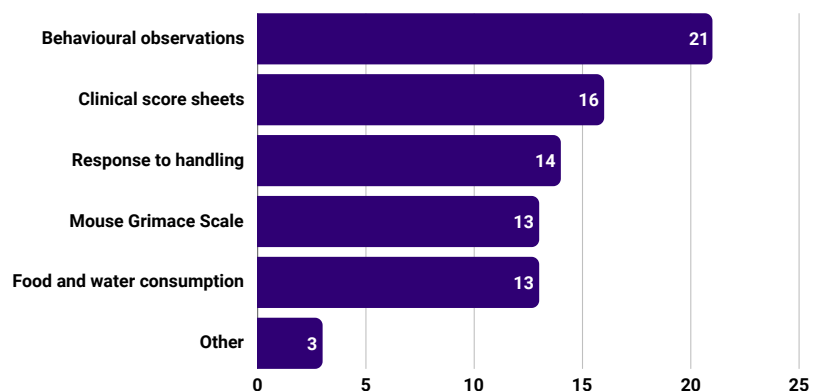


Figure 4. Pain assessment practices among participants

Next, Ignacio A. Gomez de Segura from the Complutense University of Madrid shared findings from the **2022 FELASA Working Group survey regarding attitudes and practices towards pain assessment and management** across various establishments. The survey gathered data from individuals using surgical and non-surgical protocols with varying severity levels. While the use of analgesia is common in most surgical procedures, its administration is less consistent in non-surgical models (e.g. models of stroke, arthritis, diabetes, cancer, etc.) despite analgesics, such as buprenorphine, meloxicam and

carprofen, being widely available to use in these models. The results also revealed that animal technicians are significantly more likely to administer pain relief in non-surgical models compared to researchers.

Notably, 8% of those surveyed reported never using analgesics for surgical models. Some of the reasons for not providing analgesia included concerns regarding interference with scientific outcomes, the belief that pain itself constitutes a humane endpoint, a perceived absence of signs of pain after surgery/procedures, or the assumption that administering analgesia causes excessive stress. While multi-modal approaches are frequently adopted, a limited range of analgesics is used, and there is significant inconsistency in dosing and schedules, likely stemming from a lack of evidence-based guidance for the specific model used and variations in pain assessment. Furthermore, while pain assessment is widely done, it often remains passive (i.e. analgesic protocols are not adjusted based on the findings of the assessment). Establishments primarily rely on clinical scoring sheets, the Mouse Grimace Scale, behavioral monitoring, response to handling and food/water consumption. Crucially, 61% of participants reported they do not adjust analgesic protocols based on these assessments, a gap that highlights the need to further evaluate if the methods used are effective or adequate.

The findings of this survey provided useful insights on pain assessment and management. However, these results are also a call for action to periodically review these practices. The avoidance and alleviation of pain is both a regulatory and ethical requirement and often relies on the use of analgesic agents. There are also sound scientific reasons for alleviating pain, because data quality will be affected if animals are struggling to cope with unrelieved pain, or are not feeding and drinking properly because they are reluctant to move¹. Hence, special attention should be paid to current procedural and analgesic protocols, and to review and refine them as needed to ensure that animals do not unnecessarily suffer. All animals undergoing surgery should receive adequate peri-operative analgesia. Similarly, non-surgical models should also receive pain relief, when needed, and the choice of analgesic, dosage and frequency should match the likely severity of this pain.

1. Flecknell, P. A. *Laboratory Animal Anaesthesia* (4th Ed.). (Academic Press / Elsevier, 2015).

Compassion fatigue

The session opened with a presentation from Chloe Stevens from the RSPCA, who discussed the concepts of **emotional labour and compassion fatigue**. She explored why individuals involved in the care and use of animals in science (and others, e.g. animal shelters) are susceptible to these challenges and emphasised the vital role of Animal Welfare Bodies in fostering a robust Culture of Care to help identify and mitigate emotional labour. Furthermore, she shared the available support for people experiencing this, including resources from the 3Rs Collaborative and Norecopa. She concluded by sharing several strategies for building resilience, such as practicing self-regulation, finding and setting intentions, changing individual perceptions, connecting with others, and staying active.

In the next presentation, Garikoitz Azkona from the University of the Basque Country discussed how **professional quality of life (PProQoL)** is defined by both compassion satisfaction and compassion fatigue. His team adapted the [standard PProQoL questionnaire](#) to specifically evaluate the experiences of researchers and animal facility staff. Their findings revealed that while animal care staff demonstrated higher levels of PProQoL and compassion satisfaction than researchers, both groups experienced comparable levels of compassion fatigue. Notably, PhD students reported the poorest PProQoL. The study further identified that mental wellbeing is improved by factors such as low levels of animal stress/pain, having control over humane killing methods, and having adequate social support. Furthermore, human–animal interactions were linked to secondary traumatic stress (i.e. higher bonds were linked to higher traumatic stress). The highest levels of this kind of stress were reported by those working with farm animals. He concluded by discussing the impact of income, loneliness and social support on wellbeing, noting that fewer than 20% of facility staff sought therapy support. These individuals reported having lower mental wellbeing and compassion satisfaction scores, as well as high secondary traumatic stress and burnout scores.

In the following presentation, Isabel Blanco from the Spanish National Cancer Research Centre discussed **the role of Animal Welfare Bodies in reducing the risk of compassion fatigue and providing support**. She opened by explaining how the decisions made by these bodies directly affect staff, noting that the presence of compassion fatigue has significant implications for animal welfare, as it can lead to absenteeism and poor

performance, with consequences for the person who is suffering, their colleagues, and the animals in their care. She shared several recommendations to enable Animal Welfare Bodies to support staff, including promoting a Culture of Care, recognising the risk (e.g. through anonymous surveys), providing specific training (e.g. stress management techniques), encouraging open communication, creating safe spaces for dialogue, and strengthening support networks. She concluded by highlighting that reviewing humane endpoints, analgesic protocols, and provision of environmental enrichment are fundamental to reduce severe suffering. Doing this, alongside ensuring clear communication of project objectives and results, is vital for reducing compassion fatigue and retaining caring, skilled and empathetic staff.

In the last presentation of the session, Helena Paradell from Zoetis shared **strategies to design a comprehensive compassion fatigue support programme**. She started by emphasising that the best starting point is recognising that compassion fatigue exists and that staff may be impacted at different times throughout their careers; hence, talking about compassion fatigue openly is a priority that requires a culture change at all levels.

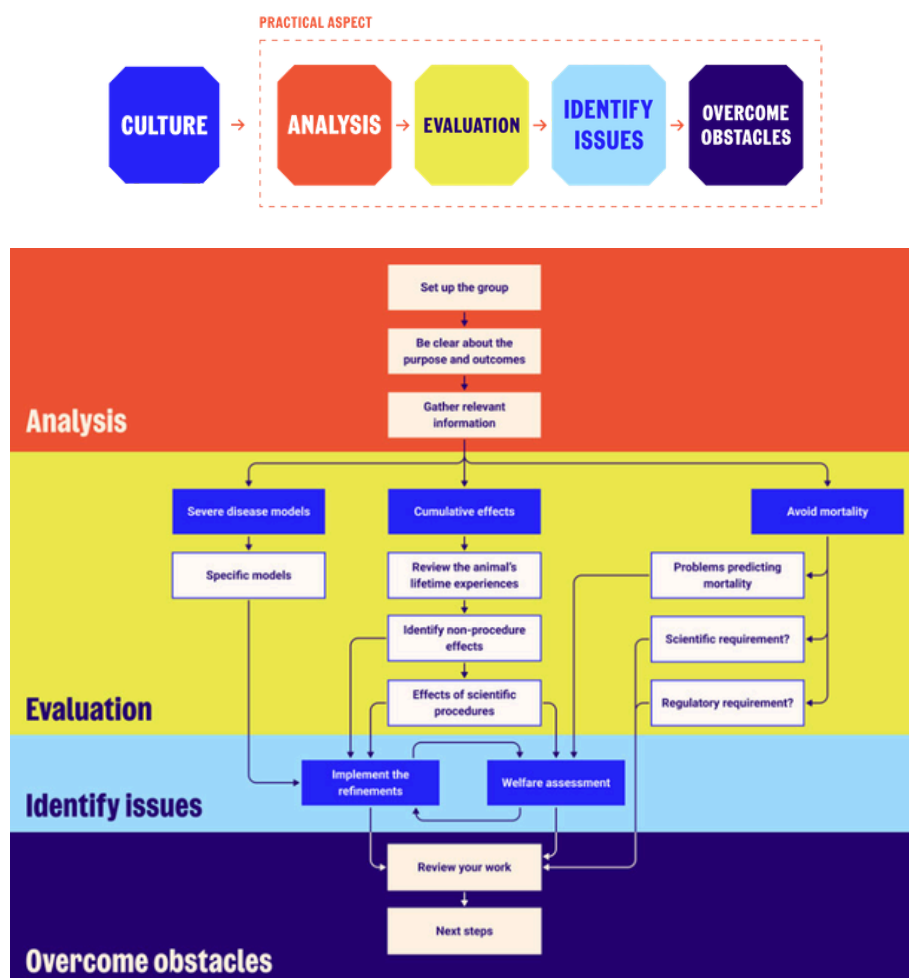
She suggested making efforts to normalise conversations, providing peer support and access to professional resources to help to protect wellbeing. In addition, she highlighted that addressing compassion fatigue should be included in the institution's health and safety programme, and that this programme should be visible, inclusive and built to last. She concluded by sharing how Zoetis' programme was created. After initial assessments to determine what staff



needed, they created a committee specifically designated to this purpose. Some of the changes derived from this programme include improving communication pre- and post-meetings, improving evaluation of clinical signs and endpoints, starting an adoption programme, initiating a dedicated support phone line for people struggling, and creating a memorial garden for people to meet and reflect.

Roadmap to reducing severe suffering

The final session of the event consisted of a workshop focused on the RSPCA's [Roadmap to reducing severe suffering](#). The Roadmap is a practical resource which was primarily designed to help identify and implement refinements to procedures that cause severe suffering in animals, although it can be applied to any level of severity. It involves a step-by-step exercise that addresses three key areas commonly associated with severe suffering: severe disease models, cumulative effects, and mortality. It provides detailed guidance on understanding animals' lifetime experiences and refining practices in all areas to reduce suffering and improve animal welfare. During the session, participants worked in groups to apply the Roadmap's steps to a case study, exploring how its recommendations can lead to significant overall refinements. The RSPCA offers in-person or online training sessions on using the Roadmap within institutions. For further details or to arrange a session, contact the RSPCA's Animals in Science team at animalsinscience@rspca.org.uk.



Action points

- Use the RSPCA [Roadmap](#) to review and refine the animals' life experiences including procedures, housing, husbandry and care.
- Always consider the cumulative effects when assessing prospective severity and throughout the study, and identify opportunities to implement refinements and reduce the level of suffering.
- Conduct pilot studies and review the literature to develop scoring systems tailored to the specific species, model and procedure/protocol, ensuring input from a variety of roles is included. Comprehensive scoring systems facilitate record-keeping and monitoring of animals, whilst providing data to improve study design and robust data collection.
- Design a welfare assessment protocol that is tailored to the specific species and procedures and includes robust indicators of pain, suffering, and distress, as well as clear criteria to inform timely intervention, including humane endpoints. In addition, ensure that pain management strategies are in place and appropriate analgesic protocols are provided when needed. Frequently reviewing welfare assessment records is essential for determining the efficacy of current protocols and identifying refinement opportunities.
- Use advanced monitoring technologies, such as home-cage monitoring, to identify model-specific clinical indicators and facilitate timely intervention to alleviate suffering.
- Ensure that environmental enrichment is tailored to the species and study, taking into account its quality and practicality, as well as the safety of the animals.
- Implement animal training programmes and habituation protocols that use positive reinforcement techniques to reduce animal stress and anxiety during handling and in procedures.
- Ensure humane endpoints are regularly reviewed and refined. While existing general guidelines are useful, it is best practice to tailor indicators to the specific species, disease, and model used.
- Promote a good Culture of Care within your institution and establish a comprehensive programme to address compassion fatigue. For those not serving on an Animal Welfare Body, engage with this committee to understand the specific initiatives being implemented to mitigate these challenges.

Note

The RSPCA is opposed to experiments that cause pain, suffering, distress and lasting harm to animals, and the Society's principal goal is replacement with non-animal methods. While animal use continues, we strive to help ensure the fullest possible implementation of the 3Rs, and robust ethical review that effectively challenges whether, and how, animals are used. The Focus on Severe Suffering initiative should be regarded in this context, and the RSPCA would like to acknowledge the strong support of the scientific community for the project. This has enabled an 88% reduction in experimental procedures causing severe suffering in the UK since 2014.

Visit the RSPCA '[Focus on Severe Suffering](#)' website for the latest information and resources on this topic, including the Roadmap and the summary and action points from previous meetings.

The RSPCA would like to thank ROEBA, SECAL and COLVEMA for helping us to make this meeting possible, and all the speakers and attendees for their valuable contributions. The insights gathered from the poll results and discussions will be integrated into our work on reducing severe suffering. This summary report has been produced by the RSPCA Animals in Science Department.



[RSPCA Animals in Science website](#)



[Animals in Science on LinkedIn](#)



[Focus on Severe Suffering website](#)



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