Terms of Reference

FELASA Working Group on
Harmful and non-harmful phenotypes

Background

The directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes states in § 3.1 that: "'procedure' means any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice.
This includes any course of action intended, or liable, to result in the birth or hatching of an animal or the creation and maintenance of a genetically modified animal line in any such condition […]".

In the light of article § 4.3 stating that "Member States shall ensure refinement of breeding, accommodation and care, and of methods used in procedures, eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals", it is crucial to reach consensus on what should be assessed as harmful with respect to the directive definition of threshold, as per article § 17.1 - that is "to experience pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle".
Currently, many publications, websites and national guidelines provide multiple definition and interpretations, leading to non-standard evaluation among Countries. Accurate review of existing bibliography and regulations will allow to build evidence-based guidelines to review and update the concepts of harmful and non-harmful phenotypes. This will help National Regulatory Entities, hence Animal Welfare Bodies and project applicants to rely on a common ground of severity assessment – paving the way for consistency on severity degree definition among EU geographical area.

To this purpose, an expert working group should gather professionals including veterinarians and welfare specialists who are familiar with the generation, breeding, maintenance and care of wild type and genetically altered animals used in research and education. They are expected to compile the most recent references to support recommendations for accurately defining harmful vs non-harmful phenotypes in the relevant species.

Tasks, proposed line of work

The working group shall:

- Review state of the art policies – including when possible national guidelines - publications and websites related to welfare assessment of genetically altered animals.
- Provide a summary of the most updated approaches to assess their welfare.
- Provide a set of clinical signs as indicators that are relevant to define harmful vs non-harmful phenotypes.
- Provide evidence-based explanation for each clinical sign/indicator to be assessed as harmful or non-harmful and why.
- Wild-type animals may show occasional harmful traits. When genetically altered animals are generated, the intrinsic burden of the background strain requires the same consideration and methodological approach applied to genetically modified subjects, per se and in the light of cumulative suffering. Each phenotypic abnormality determined in the genetically altered line should be compared to the occurrence in the wild-type line with corresponding genetic background (i.e., control or reference line). If the abnormality also occurs in the background line, then this should be taken into account, and statistical tests should be used to calculate if the level of abnormality seen in the genetically altered line is significantly different from the background line (i.e., to determine if a phenotype is modulated by the genetic modification). The working group will provide guidance on how to compare statistically the burden of wild-type and genetically altered lines.
- Liaise with other FELASA working groups relevant to the topic.
- The species to be considered are rodents (mouse and rat), rabbits and zebrafish. The working group will divide the tasks according to species and provide species-specific recommendations.

Composition of the working group

To facilitate activities, the working group should operate in two subgroups – one dedicated to rodents and rabbit, another one dedicated to zebrafish. This will allow accurate focussing on the species-specific cluster of relevant bibliography and subsequent work without jeopardizing time and resources. Full alignment on general review and methodological approaches between the two subgroups must be safeguarded. The subgroups will have individual working schedule and meetings, and common (whole working group) meetings to secure consistency.

The working group will comprise up to 10 persons.
Members should include:

- the convenor (transversal to subgroups)
- up to 4 experts for rodents and rabbits
- up to 4 experts for zebrafish
- 1 statistician (transversal to subgroups)

Veterinarians, welfare specialists or any other professional with a well-documented track record on generation, breeding, maintenance and care (particularly phenotyping and welfare assessment) of wild-type and genetically altered animals used in research and education should be considered for this working group. A statistician must be included among the group – transversally covering both sub-groups – to support consistent approach when defining statistical relevance of samples (test, animal number, and confidence interval) to confirm or exclude the harmfulness of a phenotype.

Budget

A total of 10000 Euro for telephone conferences and 1-2 face to face meetings.
Up to 10000 Euro to be made available for Open Access publications (one general paper and/or one paper per subgroup based on work results and timelines of report completion).

Deadline

Two years after start.