# 'One Europe': The challenge of consistency in severity classification

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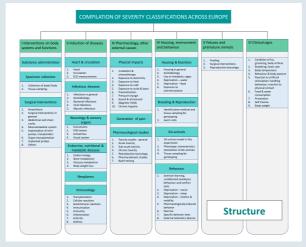
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## https://norecopa.no/severity

## Background

Severity classification is an important factor in the project authorisation of animal experiments and mandatory according to Directive 2010/63/EU. The assignment to a respective severity category needs careful evaluation of the impact on the animals' well-being. To facilitate a common understanding, and avoid decisions on a subjective basis, several guidelines are available on how experimental interventions could be classified. The guidelines are in use by scientists, Project Evaluation Committees and Animal Welfare Bodies (AWO). It is important to note that experiment-specific conditions, such as cumulative severity, setting early end-points or other refinements must be taken into account on a case-by-case basis, and may modify the recommended severity classification.

### COMPILATION OF SEVERITY CLASSIFICATIONS ACROSS EUROPE

**I Interventions on body systems and functions**

Substance administration

Specimen collection
1. Collection of body fluids
2. Tissue sampling

Surgical interventions
1. Anaesthesia
2. Surgical interventions in general
3. Abdominal and chest cavity
4. Musculoskeletal system
5. Implantation of mini-pumps, transponders
6. Organ transplantation
7. Implanted probes
8. Others

**II Induction of diseases**

Heart & circulation
1. Heart
2. Circulation
3. ECG measurements

Infectious diseases
1. Infections in general
2. Gnotobiology
3. Bacterial infections
4. Viral infections
5. Mycotic infections

Neurology & sensory organs
1. Convulsions
2. CNS lesions
3. Ischaemia
4. Visual system

Endocrine, nutritional & metabolic diseases
1. Endocrinology
2. Bone metabolism
3. Glucose metabolism
4. Body weight loss

Neoplasms

Immunology
1. Transplantation
2. Cellular reactions
3. Autoimmune reactions
4. Immunisation
5. Immunity
6. Inflammation
7. Arthritis
8. Asthma

**III Pharmacology, other external causes**

Physical impacts
1. Irradiation & chemotherapy
2. Exposure to electricity
3. Exposure to heat
4. Exposure to cold
5. Exposure to acids & basis
6. Traumatization
7. Pressure change
8. Sound & ultrasound
9. Magnetic fields
10. Chronic hypoxia

Generation of pain

Pharmacological studies
1. Toxicity studies - general
2. Acute toxicity
3. Sub-acute toxicity
4. Chronic toxicity
5. Reproduction toxicology
6. Pharmacokinetic studies
7. Batch testing

**IV Housing, environment and behaviour**

Housing & Nutrition
1. Housing in general
2. Gnotobiology
3. Use of metabolic cages
4. Deprivation – water
5. Deprivation – food
6. Exposure to overstimulation

Breeding & Reproduction
1. Identification method and tissue sampling for genotyping
2. Germ cells

GA animals
1. GA animal model in the experiment
2. Generation of GA animals
3. Tissue sampling for genotyping

Behaviour
1. Aversive learning, conditioned avoidance behaviour and conflict tests
2. Deprivation – social
3. Deprivation – sleep
4. Deprivation – motion & mobility
5. Pharmacologically induced behavior
6. Exercise
7. Specific behavior tests
8. External telemetry devices

**V Fetuses and premature animals**
1. Feeding
2. Surgical interventions
3. Reproductive toxicology

**VI Clinical signs**
1. Condition of fur, grooming, body orifices
2. Breathing, heart rate
3. Body temperature
4. Behaviour & body posture
5. Reaction to artificial stimulation; handling behaviour; reaction to physical contact
6. Food & water consumption
7. Prostration
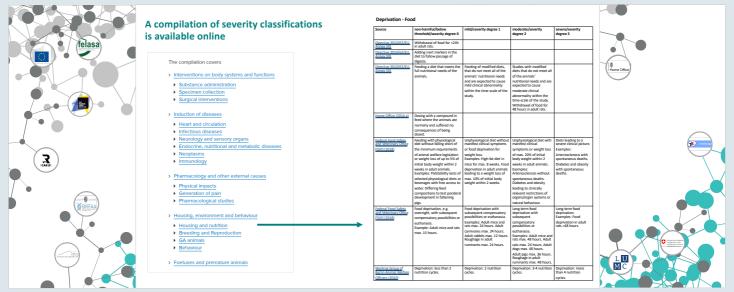8. Self trauma
9. Body weight

**Structure**

## Compilation as the first step

As an aid to the efforts being made to harmonise severity classification, we have collected existing guidelines and compiled their contents in tables, making it easier to compare them.
Severity classifications have been included from:
• EU Directive 2010/63
• The UK Home Office
• The Swiss Federal Food Safety and Veterinary Office
• The Working Group of Berlin Animal Welfare Officers
The compilation gives an overview of systems currently in use in Europe for severity classification of techniques and procedures, and for genetically altered laboratory animals.

## A compilation of severity classifications is available online

The compilation covers

> Interventions on body systems and functions
  ▸ Substance administration
  ▸ Specimen collection
  ▸ Surgical interventions

> Induction of diseases
  ▸ Heart and circulation
  ▸ Infectious diseases
  ▸ Neurology and sensory organs
  ▸ Endocrine, nutritional and metabolic diseases
  ▸ Neoplasms
  ▸ Immunology

> Pharmacology and other external causes
  ▸ Physical impacts
  ▸ Generation of pain
  ▸ Pharmacological studies

> Housing, environment and behaviour
  ▸ Housing and nutrition
  ▸ Breeding and Reproduction
  ▸ GA animals
  ▸ Behaviour

> Foetuses and premature animals

### Deprivation - Food

| Source | non-harmful/below threshold/severity degree 0 | mild/severity degree 1 | moderate/severity degree 2 | severe/severity degree 3 |
|---|---|---|---|---|
| Directive 2010/63/EU, Annex VIII | Withdrawal of food for <24h in adult rats. | | | |
| Directive 2010/63/EU, Annex VIII | Adding inert markers in the diet to follow passage of digesta. | | | |
| Directive 2010/63/EU, Annex VIII | Feeding a diet that meets the full nutritional needs of the animals. | Feeding of modified diets, that do not meet all of the animals' nutritional needs and are expected to cause mild clinical abnormality within the time-scale of the study. | Studies with modified diets that do not meet all of the animals' nutritional needs and are expected to cause moderate clinical abnormality within the time-scale of the study. Withdrawal of food for 48 hours in adult rats. | |
| Home Office (2014 a) | Dosing with a compound in feed where the animals ate normally and suffered no consequences of being dosed. | | | |
| Federal Food Safety and Veterinary Office FSVO (2018) | Feeding with physiological diet without falling short of the minimum requirements of animal welfare legislation or weight loss of up to 5% of initial body weight within 2 weeks in adult animals. Examples: Palatability tests of selected physiological diets or beverages with free access to water. Differing feed compositions to test ponderal development in fattening pigs. | Unphysiological diet without manifest clinical symptoms or food deprivation for weight loss. Examples: High-fat diet in mice for max. 8 weeks. Food deprivation in adult animals leading to a weight loss of max. 10% of initial body weight within 2 weeks. | Unphysiological diet with manifest clinical symptoms or weight loss of max. 20% of initial body weight within 2 weeks in adult animals. Examples: Arteriosclerosis without spontaneous deaths. Diabetes and obesity leading to clinically relevant restrictions of organs/organ systems or natural behaviour. | Diets leading to a severe clinical picture. Examples: Arteriosclerosis with spontaneous deaths. Diabetes and obesity with spontaneous deaths. |
| Federal Food Safety and Veterinary Office FSVO (2018) | Food deprivation, e.g. overnight, with subsequent compensatory possibilities or euthanasia. Example: Adult mice and rats max. 15 hours. | Food deprivation with subsequent compensatory possibilities or euthanasia. Examples: Adult mice and rats max. 24 hours. Adult carnivores max. 24 hours. Adult rabbits max. 12 hours. Roughage in adult ruminants max. 24 hours. | Long-term food deprivation with subsequent compensatory possibilities or euthanasia. Examples: Adult mice and rats max. 48 hours. Adult cats max. 24 hours. Adult dogs max. 48 hours. Adult pigs max. 36 hours. Roughage in adult ruminants max. 48 hours. | Long-term food deprivation. Examples: Food deprivation in adult rats >48 hours. |
| Working Group of Berlin Animal Welfare Officers (2010) | Deprivation: less than 2 nutrition cycles. | Deprivation: 2 nutrition cycles. | Deprivation: 3-4 nutrition cycles. | Deprivation: more than 4 nutrition cycles. |

## The way forward

The next step is to review the severity classifications, add more guidance notes and include more examples of severity classification like those compiled by FELASA working groups[1]. A systematic review of available literature is planned to supplement the compilation. Our aim is to offer a comprehensive tool to aid harmonisation of severity classification. If you would like to contribute literature on severity classification, or comment on the compilation, please send an email to anne.zintzsch@vetmed.uni-giessen-de.

[1] Classification and reporting of severity experienced by animals used in scientific procedures: FELASA/ECLAM/ESLAV Working Group report
David Smith, David Anderson, Anne-Dominique Degryse, Carla Bol, Ana Criado, Alessia Ferrara, Nuno Henrique Franco, Istvan Gyertyan, Jose M Orellana, Grete Ostergaard, Orsolya Varga, Hanna-Marja Voipio
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