

## Classification of severity of procedures

Member states shall ensure that all procedures are classified as "non-recovery", "mild", "moderate" or severe (EU directive 2010-63)

4 severity categories non-recovery, mild, moderate and severe are proposed

**Non-recovery:** Procedures, which are performed entirely under general anesthesia from which the animal shall not recover consciousness.

**Mild:** Procedures on animals as a result of which the animals are likely to experience short term mild pain, suffering or distress. Procedures that cause no significant impairment of the wellbeing or general condition of the animals.

**Moderate:** Procedures on animals as a result of which the animals are likely to experience short term moderate pain, suffering or distress, or long-lasting mild pain, suffering or distress. Procedures, which are likely to cause moderate impairment of the wellbeing or general condition of the animals.

**Severe:** Procedures on animals as a result of which the animals are likely to experience severe pain, suffering or distress, or long-lasting moderate pain, suffering or distress. Procedures, which are likely to cause severe impairment of the wellbeing or general condition of the animals.

### Examples

#### Mild

- Pharmacokinetic study (single dose is administered and a limited number of blood samples are taken (totally < 10% of circulating volume) The substance is not expected to cause detectable adverse effect
- Non-invasive imaging of animals (e.g. MRI) with appropriate sedation or anesthesia
- Superficial procedures, e.g. ear and tail biopsies, non surgical subcutaneous implantation of mini-pumps and transponders
- Application of external telemetry devices that cause only minor impairment to the animals or minor interference with normal activity and behavior
- Administration of substances by subcutaneous, intramuscular, intraperitoneal routes, gavage and intravenously via superficial blood vessels, where the substance has no more than mild impact on the animal, and the volumes are within appropriate limits for the size and species of the animal
- Induction of tumors, or spontaneous tumors, that cause no detectable clinical adverse effects (e.g. small, subcutaneous, noninvasive nodules)
- Breeding of genetically altered animals which is expected to result in a phenotype with mild effects
- 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
- Short term (<24h) restraint in metabolic cages
- Studies (<24h) involving short-term deprivation of social partners, short-term solitary caging of adult rats or mice of sociable strains
- Models, which expose animals to noxious stimuli which are briefly associated with mild pain, suffering or distress, and which the animals can successfully avoid.

#### Moderate

- Frequent application of test substances which produce moderate clinical effects, and withdrawal of blood samples (>10% of circulating volume) in a conscious animal within a few days without volume replacement
- Acute dose-range finding studies, chronic toxicity / carcinogenicity tests, with non-lethal endpoints
- Surgery under general anesthesia and appropriate analgesia, associated with post-surgical pain, suffering or impairment of general condition. Examples include: thoracotomy, craniotomy, laparotomy, orchidectomy, lymphadenectomy, thyroidectomy, orthopaedic surgery with effective stabilization and wound management, organ transplantation with effective management of rejection, surgical implantation of catheters, or biomedical devices (e.g. telemetry transmitters, minipumps, etc.)
- Models of induction of tumors, or Irradiation or chemotherapy with a sub lethal dose, or with an otherwise lethal dose but with reconstitution of the immune system. Adverse effects expected to be mild or moderate and short-lived (<5 days)
- Breeding of genetically altered animals expected to result in a phenotype with moderate effects
- Creation of genetically altered animals through surgical procedures spontaneous tumors, that are expected to cause moderate pain or distress or moderate interference with normal behavior
- 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
- Evoking escape and avoidance reactions where the animal is unable to escape or avoid the stimulus, and are expected to result in moderate distress.
- Use of metabolic cages involving moderate restriction of movement over up to 5 days

#### Severe

- Toxicity testing where death is the end-point, or fatalities are to be expected and severe pathophysiological states are induced. For example, single dose acute toxicity testing (see OECD testing guidelines)
- Testing of device where failure may cause severe pain, distress or death of the animal (e.g. cardiac assist devices)
- Vaccine potency testing characterized by persistent impairment of the animal's condition, progressive disease leading to death, associated with longlasting moderate pain, distress or suffering
- Irradiation or chemotherapy with a lethal dose without reconstitution of the immune system, or reconstitution with production of graft versus host disease
- Models with induction of tumors, or with spontaneous tumors, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering. For example tumors causing cachexia, invasive bone tumors, tumors resulting in metastatic spread, and tumors that are allowed to ulcerate
- Surgical and other interventions in animals under general anesthesia which are expected to result in severe or persistent moderate postoperative pain, suffering or distress or severe and persistent impairment of the general condition of the animals.
- Production of unstable fractures, thoracotomy without adequate analgesia, or trauma to produce multiple organ failure
- Organ transplantation where organ rejection is likely to lead to severe distress or impairment of the general condition of the animals (e.g. xenotransplantation)
- Breeding animals with genetic disorders that are expected to experience severe and persistent impairment of general condition, for example Huntington's disease, Muscular dystrophy, chronic relapsing neuritis models
- Use of metabolic cages involving severe restriction of movement over a prolonged period
- Inescapable electric shock (e.g. to produce learned helplessness)
- Complete isolation for prolonged periods of social species e.g. dogs and non-human primates
- Immobilization stress to induce gastric ulcers or cardiac failure in rats
- Forced swim or exercise tests with exhaustion as the end point.