

AREC Classification of Severity Categories in Animal Research

1. **Category A. Non-recovery:**

Procedures, which are performed entirely under general anaesthesia from which the animal shall not recover consciousness.

2. **Category B - Mild:**

Procedures on animals as a result of which the animals are likely to experience short term mild pain, suffering or distress.

Procedures with no significant impairment of the wellbeing or general condition of the animals.

Examples:

Pharmacokinetic study where a single dose is administered and a limited number of blood samples are taken (totalling < 10% of circulating volume) and the substance is not expected to cause any detectable adverse effect;

Non-invasive imaging of animals (eg MRI) with appropriate sedation or anaesthesia;

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 behaviour;

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 tumours, or spontaneous tumours, that cause no detectable clinical adverse effects (e.g. small, subcutaneous, non-invasive 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 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.

3. Category C – 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.

Examples:

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 anaesthesia and appropriate analgesia, associated with postsurgical pain, suffering or impairment of general condition. Examples include: thoracotomy, craniotomy, laparotomy, orchidectomy, lymphadenectomy, thyroidectomy, orthopaedic surgery with effective stabilisation 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 tumours, or spontaneous tumours, that are expected to cause moderate pain or distress or moderate interference with normal behaviour;

Irradiation or chemotherapy with a sublethal dose, or with an otherwise lethal dose but with reconstitution of the immune system. Adverse effects would be expected to be mild or moderate and would be short-lived (<5 days);

Breeding of genetically altered animals which are expected to result in a phenotype with moderate effects;

Creation of genetically altered animals through surgical procedures;

Use of metabolic cages involving moderate restriction of movement over a prolonged period (up to 5 days);

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.

4. Category D – 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:

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 a device where failure may cause severe pain, distress or death of the animal (e.g. cardiac assist devices);

Vaccine potency testing characterised by persistent impairment of the animal's condition, progressive disease leading to death, associated with long-lasting 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 tumours, or with spontaneous tumours, that are expected to cause progressive lethal disease associated with long-lasting moderate pain, distress or suffering. For example tumours causing cachexia, invasive bone tumours, tumours resulting in metastatic spread, and tumours that are allowed to ulcerate;

Surgical and other interventions in animals under general anaesthesia 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;

Immobilisation stress to induce gastric ulcers or cardiac failure in rats;

Forced swim or exercise tests with exhaustion as the end point.

5. Category O - Studies or experiments on most invertebrates, or on non-entire living material

Examples:

These include: tissues obtained at autopsy, necropsy or from the slaughterhouse; eggs < 50% development, protozoa and related single celled organisms; studies or experiments involving containment, incision or other invasive action on metazoa.

Cephalopods and some other higher invertebrates have nervous systems as well developed as some vertebrates and therefore Categories of Invasiveness B, C and D may apply.

NOTES:

The severity of a procedure is determined by the degree of pain, suffering, distress or lasting harm expected to be experienced by the animal during the course of the procedure. The procedure consists of a combination of one or more technical acts carried out on an animal which may cause that animal pain, suffering, distress or lasting harm. The assignment of the severity category takes into account any intervention or manipulation of an animal within a defined procedure. The severity category shall be assigned based on the most severe effects likely to be experienced by an individual animal after applying all appropriate refinement techniques.

Modified from the: Expert working group on severity classification of scientific procedures performed on animals

Accessed at: http://ec.europa.eu/environment/chemicals/lab_animals/pdf/report_ewg.pdf

ONLY UNDER EXCEPTIONAL CIRCUMSTANCES WILL CATEGORY D EXPERIMENTS BE APPROVED.