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Animal Welfare

Technical information animal experimentation

Proficient and animal welfare-compliant anaesthesia and analgesia of laboratory animals 3.03

Mouse, rat, hamster, guinea pig, rabbit, zebrafish, clawed frog

1 Objective

This document is addressed to the authorities responsible for animal experiments, their advisory committees and all persons concerned with, carrying out or having responsibility for animal experiments.

Competent anaesthesia and analgesia has to accompany each laboratory animal effectively through all situations entailing fear, stress or pain. Careful planning, selection and conduct of anaesthetic and analgesic protocols contribute substantially to minimising the constraint on laboratory animals. Continuous improvement of anaesthetic and analgesic methods makes an effective contribution to protecting laboratory animals and helps to ensure that 3R principles are implemented in a targeted and consistent manner in everyday routine.

This document explains where information on careful, competent anaesthesia and analgesia for laboratory animals is available, and which anaesthetic methods are admissible, conditionally admissible and inadmissible.

Not all anaesthetic methods listed in this document meet the definition of anaesthesia (section 4.1). For the sake of simplicity, however, this document uses only the term “anaesthesia”.

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2 Legal bases

2.1 No person may improperly subject an animal to pain, suffering, harm or fear, or otherwise violate its dignity (Art. 4 para. 2 of the Tierschutzgesetz (Animal Welfare Act, AWA), SR 455).

2.2 Pain, suffering or harm may be inflicted on an animal only if this is unavoidable for the purpose of the experiment (Art. 20 para. 1 AWA).

2.3 Interventions causing pain may only be performed under general or local anaesthesia by a competent person (Art. 16 AWA).

2.4 If experimental procedures or other measures cause an animal more than minimal pain, then they shall only be performed under local or general anaesthesia, followed by adequate pain control measures, provided this is permitted by the objective of the experiment (Art. 135 para. 5 of the Tierschutzverordnung (Animal Welfare Ordinance, AWO)).

2.5 Throughout the experiment, the condition of the animals shall be checked regularly and often enough to ensure that pain, suffering, harm, fear and disturbances of general well-being can be detected and appropriately assessed in good time. If such findings are observed, the animals shall be cared for and treated according to the state of the art; as soon as the objective of the experiment permits or the criteria for withdrawal are met, the animals shall be removed from the experiment and, if necessary, euthanised (Art. 135 para. 4 AWO).

2.6 An animal experiment may be approved if the method is appropriate for achieving the objective of the experiment, and the indispensible need is not exceeded, taking into account the state of the art (Art. 137 AWO).

3 Principles and responsibilities

3.1 Anaesthesia and analgesia are an integral part of the animal experiment.

3.2 Only best-practice anaesthetic methods compliant with animal welfare have to be used (admissible anaesthetic methods, Section 5). The approval of conditionally admissible anaesthetic methods (Section 6) requires a reasoned justification. No exceptions are granted for inadmissible anaesthetic methods (Section 7).

3.3 To select the best method of analgesia, see the relevant recommendations (Section 8).

3.4 Non-use of anaesthesia and/or analgesia or selection of methods that do not minimise constraint on the animals may result in the experiment being assigned a higher severity degree. This is taken into account in the weighing of interests.

3.5 Specific knowledge of anaesthesia and analgesia is required. Various forms of training and information are available for an introduction to the topic and for continuing education. Knowledge must be continuously expanded and kept up to date. A selection of training and information opportunities and relevant publications is given in Section 9.

Detailed knowledge of the following is required:
- the individual stages of anaesthesia and the species-specific and anaesthetic-specific clinical signs in the animal
- species-specific pain behaviour and expression, strain-specific differences have to be taken into account
- the physiological, biochemical and metabolic characteristics of the species or strain of animal used
- the spectrum of action and pharmacokinetic properties of the anaesthetics and analgesics used (uptake, distribution, conversion and excretion time and organ)
- the different sensitivities to the anaesthetics and analgesics used (intensity and duration of action), depending on the species or strain of animal. This factor has to be taken into account in the dosage.
- the possible interactions between anaesthetics and analgesics as well as the objective of the experiment

3.6 Anaesthesiology is also a demanding field in veterinary medicine, and one in which an additional qualification can be gained. The experts in anaesthesia and analgesia (ECVAA[1], ACVAA[2]) are excellent contacts, as are the experts in laboratory animal medicine (ECLAM[3], ACLAM[4]). Ideally, they should be consulted as early as the experiment planning stage. This approach is especially recommended for animal experiments in severity degrees 2 and 3, for repeated anaesthesia, and for experiments requiring complex peri-, intra- and post-anaesthesia care of laboratory animals.

3.7 Study directors are responsible for the best selection, planning and implementation of anaesthesia and analgesia, and for the qualifications of persons carrying out anaesthesia and analgesia and caring for the animals before and after anaesthesia.

3.8 Even animal welfare-compliant anaesthesia and analgesia may cause constraint on the animals if poorly performed. Anaesthetic and analgesic methods have to therefore be practised in the presence of an experienced person.

3.9 The authorities check the quality of anaesthesia and analgesia during the licensing procedure and their conduct during inspections. They also ensure that only animal welfare-compliant best-practice methods are used, and that they are carried out by competent persons who have undergone theoretical and practical training.

[1] ECVAA – European College of Veterinary Anaesthesia and Analgesia
[2] ACVAA – American College of Veterinary Anesthesia and Analgesia
[3] ECLAM – European College of Laboratory Animal Medicine
[4] ACLAM – American College of Laboratory Animal Medicine

4 Anaesthesia

4.1 Animal welfare-compliant general anaesthesia means a reversible, controllable state in which the perception of painful and other stimuli by the central nervous system is completely eliminated. It induces unconsciousness and insensibility, usually accompanied by relaxation of the muscles. The term “anaesthesia” is used in this document in place of “general anaesthesia”.

4.2 Some substances used for immobilisation do not meet the definition of anaesthesia given in Section 4.1. In particular, there is a lack of reliable evidence regarding the state of consciousness and elimination of pain sensation during immobilisation.

4.3 Preventive (pre-emptive) analgesia plays a crucial role in any painful intervention on animals under anaesthesia. Prompt administration of analgesics before anaesthesia or a surgical procedure prevents central sensitisation and reduces postoperative pain. Animals can thus be treated more effectively and with fewer analgesics after the procedure. The quality and especially the depth of anaesthesia must be continuously monitored and documented during the procedure.

4.4 For each laboratory animal and for each indication, the anaesthetic method and preventive analgesia must be selected in accordance with the best-practice principle in such a way as to minimise constraint on the animals.

4.5 An insufficient depth of anaesthesia must never be masked by restraining animals or by administering substances which paralyse the muscles. The use of muscle relaxants is admissible only in well-founded exceptional cases, after consultation with experts, by using suitable monitoring equipment, and must be carried out by specially trained persons.

4.6 Recent findings have shown that repeated isoflurane anaesthesia places more constraint on mice than was previously assumed. Repeated uses of isoflurane anaesthesia has therefore to be carefully monitored. Where possible, other anaesthetic methods have to be used.

4.7 The following points have to be considered before and during anaesthesia:

Laboratory rodents and rabbits do not have their food withdrawn before anaesthesia. If this is necessary for the purposes of the experiment, the duration of fasting has to be kept as short as possible.

Due to the relatively large body surface area of small laboratory animals, there is a risk of hypothermia during anaesthesia and the recovery phase. The smaller the animals, the more important it is to keep them warm during and after anaesthesia, until they are awake. Their body core temperature has to be monitored during anaesthesia.

If anaesthesia lasts for longer than five minutes, the cornea of the eyes must be protected against drying out (eye ointment).

4.8 In each case of anaesthesia incident the entire anaesthesia method, anaesthesia protocol and the experimental elements performed during anaesthesia must be reviewed. If necessary, experts should be consulted. In the case of repeated anaesthesia incidents, the authorities must be contacted. To make changes to anaesthetic protocols, a supplementary application has to be submitted.

5 Admissible anaesthesia methods

Anaesthetic methods are admissible if there is reliable evidence from an animal welfare perspective regarding their suitability and efficacy in the animal species and age categories concerned. To select the best anaesthetic method for the planned procedure, consult the specialist literature (Section 9) or experts.

Mouse	According to specialist literature or experts' recommendations, taking into account Sections 6 and 7 of this document
Rat	
Hamster	
Guinea pig	
Rabbit	
Zebrafish	
Clawed frog	

6 Conditionally admissible anaesthesia methods

Animals can be immobilised with the substances listed in this chapter. However, there is no reliable evidence that the animals become unconscious and sensitivity to pain is eliminated. A well-founded justification must be provided for the use of conditionally admissible anaesthesia methods. Any additional constraint on animals caused by these methods has to be taken into account when assigning the experiment a severity degree and in the weighing of interests.

Mouse, rat	α-chloralose, terminally only
	Urethane, terminally only
Zebrafish	Etomidate
	Metomidate
	Tribromoethanol
	Phenoxyethanol
	Tricaine methanesulfonate (MS222)
Clawed frog	Tricaine methanesulfonate (MS222)

7 Inadmissible anaesthetics, substances and methods

Anaesthetics, substances and methods are considered non-animal welfare-compliant on various grounds and therefore inadmissible. Reasons include adverse effects or side effects for the animals, such as a stressful induction or recovery phase, severe irritation at the application site, insufficient evidence of efficacy, carcinogenicity, or the availability of newer methods that are less straining for the animals concerned.

Mouse, rat, hamster, guinea pig, rabbit

CO_2	Not an anaesthetic in the true sense
Ether	Causes severe irritation of mucous membranes
Hypothermia, including in newborns	It remains unclear whether hypothermia only causes immobilisation or torpor, or unconsciousness and elimination of pain (anaesthesia). It can also not be ruled out that pain may occur during warming of the animals, reperfusion of tissue and the return of peripheral nervous system and muscle function.
Inhalation anaesthetics without vaporiser	The effect of inhalation anaesthetics must be controllable.
Retrobulbar injection of anaesthetics and analgesics	There is no scientific evidence that this injection method minimises constraint on the animals. In addition, other injection options are available.
Tribromoethanol	Causes adhesions and necrosis in the abdominal cavity (serositis, peritonitis) after intraperitoneal administration (usual injection route)

Zebrafish, clawed frog

Hypothermia	It remains unclear whether hypothermia only causes immobilisation or torpor, or unconsciousness and elimination of pain (anaesthesia). It can also not be ruled out that pain may occur during warming of the animals, reperfusion of tissue and the return of peripheral nervous system and muscle function.
Clove oil	There is no reliable evidence from an animal welfare perspective on the effect of this substance.

8 Analgesia

8.1 Pain recognition is a prerequisite for any therapeutic measure. The NC3Rs[5] website offers an introduction to analgesia and pain recognition https://www.nc3rs.org.uk/analgesia and to the use of grimace scales for pain recognition in mice, rats and rabbits https://www.nc3rs.org.uk/grimacescales.

8.2 Many animal species express different pain qualities (e.g. acute, chronic, neurogenic, abdominal pain, bone pain) and pain intensities in different ways. In prey animals, even severe pain can be difficult to recognise. To assess whether or not an animal is in pain, it is therefore vital to be familiar with the ways in which animals express pain and to know which quality or qualities of pain may occur during the experiment. Recognising pain and pain intensity is also a prerequisite for assessing the effectiveness of analgesics.

8.3 Competent performance of the experiment and post-anaesthetic care (protection and care of wounds, avoidance of stress, gentle handling of the animal) prevent unnecessary pain and avoidable interactions with the result of the experiment. The frequency of monitoring and the resulting measures must be geared to the well-being of the animals.

8.4 Animals in situations entailing pain must be given analgesics. Any non-use of analgesics must be substantiated in the licence application. This generally means that the experiment will be assigned a higher severity degree.

8.5 For each laboratory animal and for each indication, analgesia must be selected in accordance with the best-practice principle in such a way as to minimise constraint on the animals. Before any potentially painful procedure, it has to be checked whether updated analgesia recommendations are available. These have to be applied, if necessary after consultation with experts. Also clawed frogs must be given analgesics.

Mouse	According to specialist literature or experts' recommendations
Rat	
Hamster	
Guinea pig	
Rabbit	
Zebrafish	
Clawed frog	

[5] NC3Rs – National Centre for the Replacement, Reduction and Refinement of Animals in Research

9 Training, information, publications

FLAIRE Learning eModule - Anaesthesia https://flairelearning.com/course-cat/anaesthesia

FLAIRE Learning eModule - Laboratory animal anaesthesia for minor procedures (EU Module 20) https://flairelearning.com/course/anaesthesia-for-minor-procedures

FLAIRE Learning eModule - Recognition and prevention of pain, suffering and distress in laboratory animals https://flairelearning.com/course/recognition-and-prevention-of-pain-suffering-and-distress

Flecknell PA - 2015 - Laboratory animal anaesthesia. 4th edition, Elsevier, ISBN 9780128005781

Grimm KA et al - 2015 - Veterinary anesthesia and analgesia: The Fifth Edition of Lumb and Jones. Wiley, ISBN 978-1-118-52623-1

GV-Solas 2016 - Anaesthesia FAQs http://www.gv-solas.de/fileadmin/user_upload/pdf_stellungnahme/Statement_on_anaesthesia_methodologies_2016.pdf

GV-Solas 2015 - Pain management for laboratory animals http://www.gv-solas.de/fileadmin/user_upload/pdf_publikation/Anaest._Analgesie/Schmerztherapie_Mai2015_e.pdf

NC3Rs - Analgesia https://www.nc3rs.org.uk/analgesia

NC3Rs - Grimace scales for mice, rats and rabbits https://www.nc3rs.org.uk/grimacescales

Readman et al - 2017 - Species specific anaesthetics for fish anaesthesia and euthanasia. Scientific Reports 7, 7102 https://www.nature.com/articles/s41598-017-06917-2

University of Michigan - 2016 - Guidelines on Amphibian Anesthesia Analgesia and Surgery https://az.research.umich.edu/animalcare/guidelines/guidelines-amphibian-anesthesia-analgesia-and-surgery

10 Legislation

Tierschutzgesetz (Animal Welfare Act, AWA) of 16 December 2005 (SR 455) As at 1 May 2017

Art. 4 AWA	Principles
Art. 16 AWA	
Art. 17 AWA	Limitation to the indispensable minimum
Art. 20 AWA	Conduct of experiments
Art. 21 AWA	
Art. 26 AWA	Maltreatment of animals
Art. 40 AWA	Supervision by the Federal Government

Tierschutzverordnung (Animal Welfare Ordinance, AWO) of 23 April 2008 (SR 455.1) As at 20 March 2018

Art. 60 AWO	Feed and grooming
Art. 113 AWO	Permitted deviations from the provisions of this ordinance
Art. 135 AWO	Performance of experiment
Art. 137 AWO	Criteria for assessing the essential measure of animal experiments that entail constraint on the animal
Art. 139 AWO	Approval procedure
Art. 178 AWO	Stunning/anaesthesia requirement

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