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GV-SOLAS
Gesellschaft für Versuchstierkunde
Society for Laboratory Animal Science

Statement

from the GV-SOLAS Committee for Anaesthesia in collaboration with Working Group 4 in the TVT

Recommendations on anaesthesia methodologies for animal experimentation in rodents and rabbits

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Contents

This recommendation is intended for licence applicants, animal welfare officers, and authorities. Its purpose is to support work practices that maintain animal welfare standards. Anaesthesia methods are constantly evolving. It is everyone's responsibility to be informed about current standards and most recent developments in anaesthesia for laboratory animals.

1. Introduction

The recommendations below were elaborated and summarized in 2015-2016 based on knowledge and experience of the authors. The recommendations were reviewed, authorized and published by the managing board of the GV-SOLAS in 2016.

The **recommendations are focused on anaesthesia** in laboratory rodents and rabbits; they do not cover methodologies used for killing animals.

Extensive **information regarding methods and agents** can be found on public web sites, in scientific literature, textbooks and manuals. Since literature and other background information are extremely comprehensive and manifold the steadily increasing list of specific literature has not been added to this summary.

Occupational safety and legislation (e.g., animal protection ordinances, narcotics regulations, pharmaceuticals laws, medicine act, veterinary drug regulations), as well as local guidelines should be consulted regarding agents and equipment used for anaesthesia in laboratory animals.

Personnel involved in animal anaesthesia should have acquired and maintained the adequate level of theoretical knowledge through education and practical experience in anaesthesiology enabling them to fulfill their function in managing anaesthesia in the context of animal experimentation. This includes particularly to be well-informed about effects (e.g., analgesic and/or hypnotic effects; signs indicating stage/depth of anaesthesia) and side-effects of the agents administered.

2. Recommendations on the necessity to include an analgesic component in anaesthesia

Non-painful interventions in acute procedures (non-recovery) and chronic procedures

No analgesic component necessary.

Painful interventions in acute procedures (non-recovery)

An analgesic component is not mandatory if unconsciousness is assured during the entire procedure until death of the animal, but any analgesic component administered locally, regionally and/or systemically is recommended in order to assure adequate depth of anaesthesia and to improve anaesthetic safety.

Painful interventions in chronic procedures

In chronic experiments (i.e. recovery after anaesthesia) an analgesic component is mandatory in order to block intraoperative nociceptive responses and to avoid/minimize postoperative pain. The analgesic component should be effective before the nociceptive stimulus is applied (pre-emptive analgesia, preventive analgesia).

3. Recommendations relating to the route of administration

Retrobulbar application of anaesthetics for animal experimentation in rabbits and rodents is in general not accepted*.

Intramuscular injection of anaesthetics in animals <100 g body weight is in general not recommended*.

Uncontrollable vaporization of inhalation anaesthetics with cotton wick in a jar (chamber, bag) or a nose cone (face mask, tube) is in general not recommended*.

Administering inhalational anaesthetics with **non-precision vaporizers** (e.g., Komesaroff anaesthesia device) is not recommended*.

Anaesthetised animals require a higher inspiratory concentration of oxygen (at least 30%) to prevent hypoxia than non-anaesthetized individuals. Therefore, oxygen or oxygen enriched air (oxygen flow ≥ 1/8 of the total fresh gas flow or at least 1 part by volume oxygen and 7 parts by volume air) should be used as **carrier gas** for volatile anaesthetics such as isoflurane or sevoflurane. Same is true with general anaesthesia using injectable anaesthetics, therefore supplemental oxygen is recommended.

*The terms “not recommended” and “not accepted” are not based on legislation or regulatory law. For further information and comments (e.g., interpretation of terms), please see next chapter, page 5.

4. Species-specific recommendations and restrictions regarding selected agents and techniques for anaesthesia

Some of the methods and agents occasionally used for anaesthesia in small animals are subject to controversy. The reasons to question and concerns about specific anaesthesia regimens are manifold. It could not only be a lack of sufficient information on efficacy and adverse effects in rarely used regimens, but also rising occupational health and safety issues could be used to argue against formerly widely used regimens. In cases where traditional anaesthetics still are routinely in use, *state-of-the-art* and *best practice* aspects may lead to a re-evaluation/reconsideration for a change to *up-to-date* regimens if possible.

In addition, some agents are not commercially available to date in a pharmaceutical grade and thus may not satisfy quality requirements for medications in human/veterinary medicine (medicinal products). Particularly if anaesthetics are formulated *in-house* (e.g., from mixing chemicals) conditions and precautions (e.g., regarding solubility, temperature, pH, microbiological contamination, stability etc) must be followed. Therefore, anaesthetics produced in-house should be prepared, handled and applied with caution by qualified personnel.

Beside the above-mentioned aspects, animal welfare and actual knowledge and skills in animal anaesthesia are most important arguments when anaesthesia regimens are judged for their use in animal experimentation. On the other end, the need for specific regimens with experimental goals, where agents and methods commonly accepted and routinely applied to

date are not feasible or excluded (e.g., from interference with the aim/read-out of the experiment) is seriously considered.

Based on an evaluation including all arguments and aspects mentioned above, recommendations for the use of several questioned or criticized agents and methods have been finalized and are summarized in the table below. Anaesthesia methods (left column) and their recommendations for small rodents (middle column) and guinea pig, rabbit (right hand side column) are commented as follows.

Accepted* means, that the procedure can be used as a routine.

Not recommended* means, that this procedure should not be used as a routine. The regimen contains disadvantages or adverse effects that could be related to the animal species (e.g., species-specific sensitivity etc), to the route of application (e.g., inducing aversion, local inflammation, necrosis, pain etc) or several other aspects as outlined above (e.g., occupational health and safety, limited information on effects etc).

For some agents, extensive background information is provided in other publications of GV-SOLAS. In some agents and methods, only the few well-known key aspects are given in the table, however, estimation of an anaesthesia regimen is in general not limited to these obvious facts.

Altogether, before using a “not recommended” regimen, all pros-and-cons including pitfalls should be considered and balanced against the research purpose and experimental goal. In some cases, conditions for the use of a regimen are specified in the table below.

Not accepted* means, that this procedure should be avoided whenever possible. Such regimen contains substantial drawbacks and/or risks that outweigh almost any research purpose. For some agents, detailed background information is provided in other publications of GV-SOLAS. In some other agents and methods, only the few well-known key facts are given in the table, however, judging an anaesthesia regimen is in general not limited to them.

Therefore, when using “not accepted” regimens, all drawbacks and risks, particularly regarding animal welfare and personnel protection must be clarified and evaluated.

Such exceptional anaesthesia regimens must be managed very carefully, and drawbacks and risks should be minimized or excluded. In some cases, exceptional conditions are defined in the table below.

*The terms “accepted”, “not recommended” and “not accepted” are not based on legislation or regulatory law.

	Mouse, Hamster, Rat, Gerbil	**Guinea Pig, Rabbit**
Induction of inhalation anaesthesia with Isoflurane or Sevoflurane without preliminary sedation or other medication	Accepted (e.g., induction using Isoflurane (≤5%) or Sevoflurane (≤8%) in a chamber does not mandatorily require an additional agent to relief the aversive stimulus of gas exposure on mucous membranes)	Not recommended
CO_2 (e.g., as sole agent used for anaesthesia only)	Not accepted Could be accepted as an exception only if scientifically and/or methodologically justified	Not accepted
Hypothermia (e.g., crushed ice or ice water avoiding direct contact with the pup's skin)	Not accepted. Could be accepted as an exception only in neonatal animals ≤4 days of age if scientifically and/or methodologically justified.	Not accepted
Tribromethanol (Avertin®)	Not accepted Could be accepted as an exception only for ongoing experiments in which a change of anaesthesia methods would demonstrably affect the results. (See detailed statement of GV-SOLAS 2007)	Not accepted
Barbiturate	Not accepted if administered IM or SC. [animal welfare: pain and tissue damage when injected IM or SC]	
Propofol	Not accepted if administered IP, IM, SC (See detailed statement of GV-SOLAS 2011)	
Chloralhydrate	Not recommended. Not accepted if administered IM, SC, IP. (See detailed expert information of GV-SOLAS 2016)	
Chloralose (e.g., mixtures with undefined/low amounts of alpha-Chloralose)	Not accepted. (See detailed expert information of GV-SOLAS 2016)	
Alpha-Chloralose α-Chloralose	Not recommended. Not accepted for recovery studies. (See detailed expert information of GV-SOLAS 2016)	
Urethane	Not recommended. Not accepted for recovery studies. (See detailed expert information of GV-SOLAS 2016)	

	Mouse, Hamster, Rat, Gerbil	**Guinea Pig, Rabbit**
Di-ethyl-Ether	Not accepted. [occupational health and safety: explosive, animal welfare: distress during induction and recovery phase]	
Methoxyflurane (Metofane ®)	Not accepted. [occupational health and safety: toxicity in personnel]	
N_2O as mono-anaesthetic	Not accepted. [low efficacy in most animal species]	
Ketamine as mono-anaesthetic	Not accepted. [animal welfare: as sole agent Ketamine does not lead to an acceptable anaesthetic state, i.e. not all necessary effects of anaesthesia are provided by ketamine]	

The above list does not claim to contain all methods and agents that might be under controversial discussion elsewhere. The recommendations can be regarded as valid until a revised version of this publication is released.

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