

# ETHICAL STANDARDS AND GUIDELINES FOR ANIMAL EXPERIMENTS IN TOXINOLOGICAL RESEARCH

## 1. Introduction

Animal experiments are one way in which men make use of animals, but, unlike mass breeding, killing of livestock or fur-bearing animals and pest control, animal experiments have become in recent years a focus of public comment and criticism. Concern is primarily expressed in relation to experiments in which animals suffer pain and fear.

Because of such ethical considerations, for reasons also of finance and of the legal obligations imposed by various government agencies, much thought has been given to ways in which experiments on whole animals can be replaced by alternative experimental techniques that give the information sought without causing suffering to live animals. The three main ways to achieve this goal are as follows:

1. REPLACEMENT by methods that do not involve whole animals but depend on observations on cells, organs or explants from animals (which, of course must die in order to provide the tissues in the first place).
2. REDUCTION in the number of animals used to obtain desired information.
3. REFINEMENT of the experimental techniques in order to minimise the pain and suffering and the duration of the experiment in whole animals.

Biomedical research cannot, in the foreseeable future, be carried out without experiments on living animals since the function of whole organisms and their reactions to foreign substances cannot usually be deduced from studies on isolated organs or tissues from animals. They require studies *in vivo*.

Members of the International Society on Toxinology (ISI) agree, nevertheless, that experiments on conscious animals likely to be in pain must be reduced to a minimum, independently of whether animal protection legislation exists in the country in which the experiments are performed. Experiments on fully anaesthetised animals that are not permitted to recover from the anaesthesia are not so restricted. On the occasion of the 6th European Symposium on Animal, Plant and Microbial Toxins (Basle, Switzerland, 27.-31. 8. 84), a committee was appointed in order to establish ethical standards and guidelines for animal experiments in toxinological research.

The following code of practice has been formulated and has been accepted by the members of the IST.

## 2. Aim and Scope

The International Society on Toxinology deals with the study of toxins of animal, plant and microbial origin. At the present time it is impossible to carry out studies in this research field without investigating effects of such toxins in living animals. However, members of the IST agree that animal experiments should be carried out *only when necessary and on as small numbers of animals as possible*.

These guidelines constitute the ETHICAL STANDARDS for all future papers submitted for publication in the journal TOXICON.

### **3. Ethical principles**

- 3.1. Out of respect for all life, each scientist must include in his experimental design consideration of the necessity to protect the animals under his care.
- 3.2. Since some experiments on whole animals are essential in order to study the mode of action of toxins *in vivo* the scientist must be allowed to use a necessary number of animals for research purposes but must never be found to abuse the right to do such experiments.
- 3.3. The scientist must consider at the outset whether the aims of a particular experiment justify the use of whole animals.
- 3.4. Respect for life requires that the number of animals used be kept to the necessary minimum.

### **4. Ethical Requirements on the Allowance of Animal Experiments**

- 4.1. Animal experiments designed to lead to the saving of life or to improving the health of man or other animals are ethically justifiable.
- 4.2. Animal experiments are also justifiable on ethical grounds if there is a high probability that they will lead to a contribution to knowledge.
- 4.3. Experiments that cause substantial pain to an animal are justified only if the information gained is likely to be of direct relevance and value to the wellbeing of man or other animals. *No animal must be allowed to suffer prolonged or extreme pain.* The experimenter is responsible for terminating such experiments humanely.
- 4.4. Animal experiments should not be carried out if sufficiently accurate and feasible alternatives are available.
- 4.5. Without well-founded reasons members of the Society are advised not to repeat animal experiments already performed in a competent manner.

### **5. Ethical Requirements on the Performance of Animal Experiments**

- 5.1. It is an ethical necessity to obtain a maximum amount of new scientific information using a minimum of animal experiments.
- 5.2. The scientist should provide experimental animals with the best available maintenance conditions before, during and after the experiment.
- 5.3. Whenever possible, pain-causing tests must be carried out under local or general anaesthesia. General anaesthesia shall be obligatory in experiments involving the use of curareform neuromuscular blocking agents.
- 5.4. Pain-causing experiments must be carried out in such a way that the intensity and duration of the pain are minimal, consistent with achieving the objective of the experiment. If an animal at any time during an experiment is found to be suffering severe pain which is likely to endure, such animal shall forthwith be painlessly killed.
- 5.5. Test animals should ideally be obtained from special authorized breeding units. Wild animals can be used for animal experiments only in special cases and for definite reasons.
- 5.6. Animals that are likely to suffer as a consequence of experiments having been performed on them should be humanely killed at the end of the experiment or at any time that the animal shows unacceptable suffering.

### **6. Special Requirements for LD50 Determinations and Other Acute Toxicity Tests**

- 6.1. LD50 determinations are essential for standardization of antivenoms and venoms of natural origin.
- 6.2. The results of LD50 experiments may vary greatly according to the type of the toxin or venom to be tested, to the species, origin, sex, weight and health state of the test animal and to

the application mode. Therefore, the absolute numbers obtained from LD50 determinations are only of limited scientific value.

- 6.3. About 30 animals may be needed to establish an acceptably accurate value of the LD50 but with the use of as few as 12 animals, a value that is within a factor of 2 of the value obtained with 30 animals may be established. Information of this degree of accuracy is adequate for most purposes. Determination of LD50 values purely for the purposes of publication of the characterization of toxic materials cannot be justified on ethical grounds. A much broader definition of degree of toxicity should be sought, the measurement of which does not entail the sacrifice of large numbers of animals.
- 6.4. All LD50 determinations and similar acute toxicity tests should include observations on animal behaviour, survival times and, whenever possible, pathological examinations of the experimental animals.
- 6.5. Instruction of advanced students in toxicity testing should include ethical considerations and should be restricted to those students intending to specialise subsequently in this area of research.

## **7. Publication of Papers in the Journal *TOXICON***

- 7.1. These general ethical guidelines are the ethical standards required for every paper submitted for publication in *TOXICON*.
- 7.2. Every paper dealing with animal experiments must include in the "material and methods" section descriptions of species, strain, total number of animals, sex and weight range of the experimental animals used, as well as route of application and solvents used for dissolving the venoms or toxins under investigation. If anaesthetics have been used, their dose and application route must also be described.
- 7.3. Papers which do not meet these ethical standards will be rejected by the editors.

## **8. Conclusion**

It is the responsibility of experimenters to see that they and their assistants obey the laws concerning animal experimentation of the country in which the experiments are performed since breaking the law will provoke the demand for more stringent legislation.

### ***The Society furthermore expects that:***

- 8.1. Each member feels morally responsible for the justification, planning and performance of experiments in his laboratory, including the tasks allocated to more junior personnel.
- 8.2. Each member follows these guidelines in his field of activity.
- 8.3. Each member supports all possible measures for limiting the number of animal experiments, provided that human or other animal life is not thereby put at risk and that advances in scientific knowledge are not thereby jeopardized.
- 8.4. Each member supports the development of new experimental methods that could reduce or eliminate pain suffered by experimental animals.

## **9. Committee Members**

These ethical standards and guidelines were elaborated by the following members of the International Society on Toxinology:

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