BS20: Animal use policies

Animal Experiments – the Principle of Proportionality as Key Principle of Ethical Evaluation

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Summary
Since 1986 animal experiments in Germany may only be approved by the authorities if they are indispensable for a permissible purpose and the inflicted suffering is not classified as disproportionate to the benefits thereof. In order to verify these conditions, an ethical evaluation procedure has been developed, which – based on the Principle of Proportionality – fulfils not only bioethical but also legal requirements. The ethical evaluation procedure is performed first by the scientist applying for the authorisation, second by the animal experimentation committee of each competent authority, and third by the competent authority itself. Based on the outcome of the ethical evaluation procedure every year several applications are rejected in Germany.

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1 Introduction

Since 1986, animal experiments in Germany may only be approved by the authorities if they are indispensable for a permissible purpose (*unerlässlich*) and the inflicted suffering is not classified as disproportionate to the benefits thereof (*ethisch vertretbar*, Article 8, paragraph 3 German Animal Protection Act, TierSchG). In order to verify these conditions, each competent authority is required to convene one or more committees consisting of scientists experienced in the assessment of animal experiments and of selected members of proposed lists of animal welfare organisations (Article 15 TierSchG). These Animal Experimentation Committees have been gaining experience in the ethical review of applications for animal experiments since 1986. Because rejected applications of animal experiments are often resolved judicially, an ethical evaluation procedure has been developed, which – based on the Principle of Proportionality – fulfils not only bioethical but also legal requirements.

2 The Principle of Proportionality

The Proportionality Principle is an ethical tool mostly used to regulate ethical dilemmas by law. In ethical dilemmas, every feasible option leads to an outcome which must be judged as ethically problematic or even immoral. Ethical dilemmas have therefore only ethically problematic solutions. In such situations, the Proportionality Principle helps to find the least problematic way out. The Principle of Proportionality is a political maxim accepted worldwide and used for the solution of a great variety of social problems (including animal welfare), and it is a fundamental principle of EU law in the allocation of legislative competencies within the Union. In animal protection legislation the Proportionality Principle works worldwide as the key principle.

Although often reduced to one or two steps, the Proportionality Principle consists, for logical reasons, of not less than four steps. When using it to find the least problematic solution in an ethical dilemma one must test every alternative action (including omission, i.e. doing nothing) by four test steps. The Proportionality Principle is designed in such a way that only one alternative is able to fulfil the requirements of all four test steps: this will be the ethically least problematic and therefore the an ethically justifiable option. The four test steps are:

1. Check whether the stated purpose of the intended action (or omission) is *permissible*!
2. Check whether the action (or omission) is in fact fit to promote the stated purpose! In addition, the action (or omission) should, compared to alternatives, be the most likely to achieve the benefits of the stated purpose.

3. Check all adverse effects of the action (or omission) on humans, animals and the environment to see if each is *indispensable* (i.e. necessary, essential) to achieve the stated purpose! This includes checking for and considering all possibilities of compensating adverse effects.
4. Check whether the action (or omission) is proportionate compared with the hoped-for benefits of the action (or omission) in regard to every adverse effect! To be proportionate, the action (or omission) must fulfil the following conditions:
   a. The action (or omission) must lead to a less adverse result than the omission (or any action).
   b. Every action (or omission) must be in itself permissible, i.e. may not harm absolute (deontological) moral rights which have been proposed, to be protected against weighing, e.g. human rights; in animal ethics at least the right not to undergo severe suffering, i.e. suffering that would be judged "unbearable" by a human proband (test person).
   c. The action (or omission) must, in spite of its moral shortcomings, be judged adequate, proper and fair in its context by the majority of citizens of the corresponding territory who have developed a sound moral attitude.

In Germany, animal experiments have been restricted by the Proportionality Principle for several decades. Today, its four test steps are incorporated into the Animal Welfare Act (Article 7 and the following). While any person wishing to conduct experiments on vertebrates must obtain authorisation of the planned experiment from the competent authority, authorisation is to be granted only if and when scientific evidence is produced by the scientist a) that the experiment is *indispensable* for and *fit* to promote a *permissible* purpose (Article 7 paragraphs 2, 4 and 5 define "*permissible* purposes") and b) that the pain, suffering or harm that can be expected is "ethically justifiable" (*proportionate*) compared with the hoped-for benefits of the experiment. Thus, a precondition of the authorisation is the fulfilment of the requirements of all four test steps. The test is performed first by the scientist applying for the authorisation (these results are set out in the application), second by the animal experimentation committee of each competent authority (their results are to assist the authority in deciding whether to authorise the experiment), and third by the competent authority itself (those results ultimately decide whether the authorisation is granted or not).

Step 1: Check whether the stated purpose of the intended procedure is permissible!

The following are regarded as "permissible purpose" (in Germany):

1. the prevention, diagnosis or treatment of diseases, suffering, bodily defects or other abnormalities or the detection or exertion of influence of physiological conditions or functions in human beings or animals;
2. the detection of environmental hazards;
3. the testing of substances or products to ensure that they are safe in terms of human or animal health or that they are effective against animal pests;
4. basic research.

Experiments on animals to develop or test weapons, ammunition and related equipment are prohibited, as are, subject to an exemption clause, experiments on animals to develop tobacco products, detergents and cosmetics.

A problematic shortcoming with regard to the first test step is, however, that in practice only experiments subject to authorisation must be checked. Since in Germany no "authorisation from", but only a "notification to" the authority is required for planned experiments expressly required by a statute, an ordinance or the *Pharmacopoeia*, or another binding provision, these experiments continue to be performed for many years even if their ethical justification is more than dubious (e.g. the mouse bioassay as gold standard for detecting biotoxins in shellfish for human consumption, or the LD_{50} test for every batch of Botox produced even when applied for cosmetic reasons). Animal testing of luxury goods like shellfish or those Botox batches that are used for cosmetic purposes cannot comply with the Principle of Proportionality and is, therefore, "ethically unjustifiable". For testing shellfish there an alternative method already exists, and an alternative is under development for Botox testing. Consequently the use of Botox for cosmetic reasons should be provisionally banned (since it would also be unjustifiable to use untested batches).

Step 2: Check whether the intended procedure is in fact fit to promote the stated purpose!

Only protocols that are *fit* to promote the stated purpose may be authorised. Therefore it is necessary to check, among other things:

1. whether the number of animals to be used is the *minimum* necessary to ensure a meaningful interpretation of the findings and the statistical validity of the findings;
2. whether *species*, *sex* and *age* of the experimental animals are fit to promote the stated purpose;
3. whether there are doubts that the results might not be transferable to the species of the stated purpose;
4. whether protocols and endpoints are the most *likely* to produce satisfactory scientific results.

Step 3: Check deterioration of the quality of life at all stages of the animal's life to see if each is indispensable to achieve the stated purpose! – The Three Rs principle.

Only experiments with animals that have a good life quality during their whole life span except for those cutbacks that are each indispensable to achieve the stated purpose can fulfil the requirement of this test step. This includes checking for and considering not only all the possibilities to avoid adverse effects, but also those to compensate them. Thus, within the third test step one has to check compliance with the the Three Rs principle (Replacement, Reduction and Refinement).

1. *Replacement*: means the attempt to replace animals by non-living or at least non-sentient alternatives. – Therefore, a check must be made to see:

- whether the purpose of the specified programme of work

could be achieved satisfactorily, in whole or in part, by any other reasonable and practicable method that does not require the conduct of procedures on animals (in particular, whether in advance performed *in vitro* screening would influence the ethical test results of the protocols);
- whether there are chances to replace animals by non-sentient (e.g. early stages of development) or nonliving alternatives, or by a protocol in which the animals are gently made unconscious prior to the experiment and are then killed before they regain consciousness.

2. *Reduction*: means the attempt to reduce the number of animals to the minimum necessary without compromising the quality of scientific results. The UK Home Office rightly advises: "It is recognised, however, that the number of animals that need to be used can sometimes be reduced if *additional suffering* is allowed to be caused to fewer animals. The method licensed will be the one judged to cause *the least suffering* or distress." (Guidance on the Operation of the Animals (Scientific Procedures) Act 1986, Chapter 5, No. 5.15) – Therefore, a check must be made to see:
- whether the number of animals is reduced to the minimum (e.g. check group size, indispensability of each group, in particular, of identical but not contemporaneous groups, sequence of protocols, and used means of statistical analysis), subject to the exemption that a higher number of animals allows for less suffering or distress of individual animals.

3. *Refinement*: means the employment of methods to ensure that any possible pain, suffering, distress and harm is reduced to the minimum, as well as to improve the care, treatment and living conditions of the animals to enhance their well-being. – Therefore, a check must be made to see:
- whether protocols and endpoints, compared with feasible alternatives, cause the least pain, suffering, distress or harm (only *unavoidable* pain, suffering, distress or harm may be authorised; in Germany pain, suffering, distress or harm may not be inflicted "to save work, time or costs" (Article 9 (2) No.3); to be considered are, in particular, inspection schedules, opportunities for general or local anaesthesia, analgesics and today's *most* humane way of killing);
- whether there are sufficient measures proposed to prevent or minimise the extent, duration and incidence of the adverse effects (measures should include reasonably designed control measures, because it is indispensable for the laboratory animal to be monitored closely, and as an individual animal);
- whether there are chances to refine techniques, management or housing in a way that the harm caused to the animals is minimised (to be considered are "*environmental enrichment*" and sheltered positions for the animals to retreat to);
- whether protocols incorporate best practice and will be applied competently (only by skilled personnel);
- whether all sick or injured animals get treatments that alleviate pain or suffering (in Germany the applicant must produce scientific evidence of incompatibility with the objective of the experiment for each untreated but suffering animal);
- whether all reasonable steps are taken to ensure that the physical, health and behavioural needs of the animals are met in accordance with both good practice and scientific knowledge (the Commission Recommendations 2007/526/EC on guidelines for the accommodation and care of animals used for experimental and other scientific purposes define minimum standards);
- whether choice of species and stage of development is made in order to use animals that have the lowest degree of neurophysiological sensitivity (i.e. have the least capacity to experience pain, suffering or distress).

Step 4: Check whether the deterioration of the quality of life is proportionate compared with the hoped-for benefits of the experiment!

Scientists are often not familiar with the requirement of the fourth step of the Proportionality Principle to let the majority of the (morally developed) citizens (of the corresponding territory) decide whether a scientific procedure on animals is "proportionate" (adequate, proper and fair) in its context. Since in Germany the whole Animal Welfare Act refers to the Proportionality Principle, even its central idea of justifiability, the "good reason" (*vernünftiger Grund*), is bound to what the majority of the (morally developed) German citizens believe to be a "good reason".

Step 4a: Check for protocols that are *absolutely prohibited*, for they are likely to conflict with absolute (deontological) moral rights, such as, in particular, the animal's moral right not to undergo severe suffering (i.e. suffering that would be judged "unbearable" by a human proband). Absolute (deontological) moral rights (e.g. human rights, the bans on slavery, torture etc.) have been proposed to be protected *against weighing*. Exemptions are not intended; it is, therefore, not possible to argue e.g. on the basis of the eminent importance of the experiment. While "severe suffering" is expressly prohibited by UK law (experiments must include the specification of "*humane endpoints*", i.e. animals are to be humanely killed before the procedure has finished, and some of the expected gain in knowledge is waived), in Germany procedures will not be authorised if pain, suffering, distress or harm are considered "ethically unjustifiable" by the authorities. The local authorities decide without federal guidelines (but often after consultation with each other or with external experts), what (parts of) protocols must be considered as "ethically unjustifiable". Experiments on non-human hominids (great apes) are regarded as "ethically unjustifiable" too. According to the results of a questionnaire of the EU Commission for the general public on the revision of Directive 86/609/EC, 80% of the (European) participants consider all primate experiments "not acceptable". In Germany, every year several applications are rejected because the authorities have good reasons to assume that the public judge some protocols to be "ethically unjustifiable" (e.g. just recently the case of the neurophysiological procedures on primates in the city of Bremen, which has, as in many cases, been linked to considerable and balanced news coverage by the media).

Ethical Principles and Guidelines for Experiments on Animals (Switzerland)

"Certain experimental set-ups can be expected to cause such severe suffering for animals that the weighing up of ethical concerns will always fall in favour of the animals. If it is not possible to find less harmful and more ethically acceptable test arrangements by changing the research hypothesis, it will be necessary to refrain from carrying out the experiment and to forgo the expected gain in knowledge."

Swiss Academy of Medical Sciences (SAMS) & Swiss Academy of Sciences (SCNAT): Ethical Principles and Guidelines for Experiments on Animals, 3rd edition 2005, Paragraph 3.5: http://www.samw.ch/en/Ethics/Guidelines/Currently-valid-guidelines.html

Step 4b: *Cost/Benefit Assessment*: Check whether the hoped-for benefits really outweigh the likely harm to the animals (performing the procedure must globally, in the medium term, result in less pain, suffering, distress or harm than its omission). In ethics the pain, suffering, distress or harm of the experimental animals ("cost") can only be balanced against the contribution to future reduction of pain, suffering, distress and harm, which counts as a "benefit" (identical units are required on both sides of the equation).

In order to weigh the potential benefit against the likely adverse effects, one must find the "value" and the "severity level" of each procedure. The value of a procedure is defined by the contribution of the specific outcomes of the programme of work to future reduction of pain, suffering, distress and harm, rather than by the importance of the general area of activity. The severity level of a procedure, on the other hand, is mostly defined as the upper limit of the expected adverse effects that may be encountered by an animal, taking into account the measures for avoiding and controlling adverse effects. The severity level of a procedure represents the worst potential outcome for any animal, even if it may only be experienced by a small number of the animals to be used. If several procedures are combined, the stress level for the animal will most likely increase, and the *cumulative effect* must be taken into account (e.g. water deprivation + fixation); therefore, in some cases, the severity level of combined protocols must be set higher than the level of the protocols alone. Furthermore, the cumulative effect of the repetition of identical protocols within a procedure can, in some cases, justify setting the severity level higher than the level of a single protocol. What are useful are official lists with examples for severity levels (e.g. the Swiss "Classification of Animal Experiments according to Grades of Severity prior to the Experiment": http://www.bvet.admin.ch/themen/tierschutz/00777/00778/index.html?lang=de, or the German "Guidelines to help evaluate the stress factor for laboratory animals during authorised animal experiments", released by the Berlin Work Group of Animal Welfare Officers: http://www.charite.de/tierschutz/download/Orientierungshilfe-englisch.pdf). Anyhow, much experience is needed to draw the line between "moderate" and "severe" suffering. And it is particularly difficult to assign severity categories when adverse effects are uncertain or unpredictable, for example in the production of genetically modified animals or in toxicity testing.

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