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## Report

drawn up on behalf of the Committee on the  
Environment, Public Health and Consumer Protection

on the limiting of animal experiments and the  
protection of laboratory animals

- Part B - Explanatory statement

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## EXPLANATORY STATEMENT

1. Laws on animal welfare exist in many countries of the world, including all of the Community Member States and the member states of the Council of Europe with the exception of Malta, Liechtenstein, Cyprus, Spain, Portugal, Turkey and Greece.

The provisions of these laws vary widely, in accordance with the distinct cultural and legal traditions of the countries concerned.

Certain Community directives (which have already been transposed into national law or are in the process of transposition) and numerous laws of the Community Member States permit experiments on animals, either explicitly or by extension (see Annex I).

According to information from the Commission of the European Communities, no comparative examination has been conducted into the relevant legal provisions of the Member States.

The current legislation on animal welfare is about to be revised in some countries (e.g. Luxembourg, the United Kingdom, the Federal Republic of Germany and Switzerland) in the light of the developments in science, law and modern systems of animal husbandry and with particular reference to two subjects: intensive farming and animal experiments.

Attempts have also been made at international level to establish a legal framework for animal welfare and animal experiments. The Council of Europe submitted its controversial draft Convention on the protection of vertebrates (in 1982), the OECD has drawn up guidelines for toxicity testing and on 'good laboratory practice' (GLP), while the biotechnological research programme submitted by the Commission contains research proposals for the development of new 'in-vitro' techniques for toxicological tests.

### 2. Problems arising from the gaps in legislation

- (a) One area which is particularly problematic and as yet not sufficiently encompassed within the law is the 'grey market' in laboratory animals, i.e. the trade in stolen animals - especially dogs and cats. This market is not very important for industry, since the laboratory animals used there must satisfy certain requirements, if the findings of experiments are to be at all comparable. In addition, animals procured on the 'grey market' may be a source of disease.

However, it is clear that universities and research laboratories often use animals which have been obtained from dubious sources.

It might be possible to remedy this problem through binding legal provisions stipulating that only animals bred in special establishments may be used in experiments.

- (b) No-one knows precisely how many animals are used throughout the world or in individual countries for experiments (see Annex II). Such figures as are available tend to be based on estimates and, moreover, diverge radically, depending on the source of the estimates. To determine whether the number of animal experiments is being forced up by the constantly increasing body of legal requirements, or whether progress is being made in reducing that number, it will be essential to impose an obligation on all Member States to compile statistics on the experiments performed on animals.

Variations also exist in the conditions under which animal experiments may be carried out. The wording of the current legal texts requires interpretation. What, for instance, would one term a 'reasonable' or 'feasible' alternative method or 'indispensable' level?

- (c) The essential element of the two previous motions for resolutions is a call for a revision of general legal bases and specific legal requirements. These demands appear all the more justified in view of the fact that under certain rules, substances which have already been tested require re-examination where only minor changes are made - even to the name, in some cases - or where they are put on the market in a slightly modified formula.

The safety requirements in this area should be so laid down in law that tests which take the form of animal experiments need be carried out only where a new substance is to be used or where it appears necessary to test an entirely new combination of substances.

World trade poses a further problem in this connection. Legislation within the European Community, especially in the cases of medicines and cosmetics, is designed to ensure that a product licence issued in one Member State is automatically recognized by all the other Member States. However, this still gives rise to considerable practical difficulties, primarily in trade with third countries in and outside Europe and also in the Community itself.

Steps must be taken as a matter of urgency, to ensure that the licences are actually recognised.

3. What are animal experiments and why are they performed?

Animal experiments are principally carried out for the following reasons,

- (1) for the toxicological testing of the widest variety of substances, occurring naturally or produced synthetically, in other words testing these substances for any harmful or dangerous effects on humans, animals and the environment, and
- (2) for educational purposes and improving surgical techniques.

The most diverse activities are subsumed under the term 'animal experiment'. The term covers not only the observation of animals to study their behaviour but also vivisection, in other words operations on live animals, sometimes even without the administration of an anaesthetic. Toxicity tests are not vivisection. Nevertheless, suffering is inflicted on the animals used in toxicity tests when substances with toxic effects are administered to them. These toxic effects cannot be observed in an animal under anaesthetic:

- (1) because animals under anaesthetic do not always display symptoms,
- (2) because anaesthetics are also chemicals and it is not possible to determine which reactions should be ascribed to which substances,
  - to the substance being tested
  - to the anaesthetic, or
  - to a combination of the two.
- (3) many experiments extend over a period of years, an example being the tests carried out to determine whether or not a substance is carcinogenic. No animal can be kept alive under anaesthetic for that length of time.

(4) Are experiments on animals morally justified?

- a. Stormy and emotional public discussion has arisen all over the world on the questions of whether animal experiments can be justified at all, whether the findings and conclusions of animal experiments are in any way applicable to humans and whether there are not other possibilities (alternative methods) which would fulfil the same purpose, without the need for animals to suffer. The opponents and advocates of animal experiments are implacably opposed in this discussion. Moderate representatives of both sides recognize that animal experiments are unavoidable in certain cases, but their number must be reduced as far as possible and their conduct made subject to stringent conditions - regarding notification, authorization and on-the-spot supervision.

It would be useful to summarize the major problems and arguments of the two sides.

To begin with, however, one should not disregard the fact that the animal welfare organizations deserve great credit for having drawn attention, more and more forcefully, both to existing anomalies, such as absurd or abusively applied legal provisions which explicitly or implicitly prescribe animal experiments, and to the possibilities available for making greater use of other methods, such as 'in-vitro' techniques. It is incumbent on us to respond to legitimate demands and correct defects.

What cannot be accepted is that certain animal welfare organizations, at least in the Federal Republic of Germany and the United Kingdom, should resort to violence against persons and laboratories which carry out animal experiments.

If all experiments on animals ceased, it would mean that tests which had previously been recognized as necessary would have to be performed solely on humans.

- b. Is there a moral justification for animal experiments, especially those involving pain and suffering for the animals?

To answer this question, one must consider how animal experiments are conducted.

Apart from the development of veterinary medicines, all animal experiments should ultimately serve the interests of human health. Irrespective of that principle, even the churches are posing the question of whether experiments on animals should be permitted.

Approximately 95% of all experiments which may be classed as vivisection are performed on animals under anaesthetic, which are afterwards painlessly put to sleep, or at any rate killed by what pass for painless methods.

As far as toxicological testing is concerned, the proportion of animals on which pain is inflicted is significantly higher.

Man is bound by the moral principle of respect for life to protect animals too, which are his fellow creatures, and in particular must preserve them from pain and suffering. Of equal importance, however, is the imperative of sustaining human life and preserving one's fellow men from suffering, pain and hunger. To do this, man is in many instances dependent on animals.

Only by making a selection between what may be mutually exclusive values can this continuing conflict of priorities, which arises from man's place in creation, be resolved in a responsible fashion.

Even the churches are willing to accept animal experiments when viewed in this perspective. Coupled with this acceptance, however, are demands that the experiments may be conducted only under strictly controlled conditions, and that their numbers be drastically reduced.

## 5. Safety requirements of the public

The opponents of animal experiments claim that public health, freedom of research and consumer protection are mere pretexts for animal experiments: this argument is rejected by the advocates of increasingly stringent safety standards for existing and new products.

The safety requirements of modern society inevitably push up the number of animal experiments (see the law on chemicals Annex I). For instance, some people are demanding the re-examination of substances which have been in use for decades, even though no signs of any kind of danger have yet emerged, and no risk has ever been identified.

Many substances, not only synthetically produced substances (as are most chemicals), but also those which occur or are formed naturally, such as aflatoxins or snake venom, are extremely dangerous.

In frequent cases, the question of whether a substance is poisonous or harmful depends entirely on the dosage - a poison can be fatal in the smallest doses (millionths of a gramme) whereas cooking salt, if eaten by the spoonful, can be just as lethal.

The effects of various doses cannot be determined by purely theoretical calculation in a laboratory, nor can they be tested on humans. The only option open in many cases is to measure the effects in a gradual progression on creatures ranging from micro-organisms to primates.

Knowledge of how a substance acts, how harmful it can be under certain circumstances and what antidotes are available is fundamental for the development of medicaments, the treatment of accidents (e.g. cases of poisoning among children are very frequent) and the protection of human life in general.

6. Two questions arise from these considerations:

- can the requisite degree of safety actually be achieved through animal experiments, and
- do we really need this constant stream of new products, when we already have so many medicaments, cosmetics and other commodities - why is there this continual need for something different?

First of all, mention needs to be made of the freedom of research and teaching, a constitutionally protected right. This right is unquestionably of the highest importance for progress. However, animal experiments, even as a tool of research, should be justified only if they are restricted in type and number to the indispensable minimum and actually promise new insights.

(a) Medicaments

Humanity owes a significant part of its current medical knowledge to experiments on animals. 21 Nobel Prizes have so far been awarded for the development of medicines of particular importance to humanity. The knowledge which led to these discoveries all stems from the findings of animal experiments, e.g. the celebrated Pavlovian reflex, diphtheria vaccine, insulin, penicillin, sulfonamides and numerous vaccines which have saved many millions of human lives.

There are still no sufficiently effective remedies for many diseases - cancer, multiple sclerosis and large numbers of nervous diseases - not to mention newly discovered diseases such as AIDS or legionnaire's disease.

Many existing preparations have unpleasant and at times violent side-effects. Research is continuing in the field, to improve these medicaments and reduce the side effects.

This means that we need new and above all better medicaments.

In the case of medicaments which have been withdrawn from the market, the dangers have emerged only on wider application to humans and through the system of notification of the side effects caused by medicines. What cannot be determined experimentally prior to the licensing of medicaments must then be left to emerge from experience in the application to humans.

The thalidomide disaster is often mentioned in this context. When thalidomide was being developed, tests for damage to the foetus were not compulsory. It was precisely as a result of this experience that requirements were considerably tightened up. The most important argument used to counter this objection runs as follows: out of 8,000-10,000 agents examined, only one is ultimately used in a medicament. All the rest are eliminated for the widest variety of reasons before that, during the experimental phase, which may include experiments on animals. Without animal experiments, the cases of damage to the human body resulting from medicaments would increase immensely.

(b) Many people are able to accept animal experiments for medical purposes. For other purposes, such as the production of cosmetics, pesticides and chemicals, they are condemned. 90% of what is termed cosmetics covers articles used for cleanliness and hygiene; purely decorative beauty requisites, such as lipstick, make-up or hair colourants, account for only 10%. It is particularly important for products in everyday use, such as soap and shampoo, to be absolutely 'safe'.

Yet even beauty requisites in the narrow sense can have a significance extending beyond commercial considerations: they frequently make an important contribution to the emotional well-being of their users.

Only about 0.5% of all animal experiments are conducted in the cosmetics sector.

What is produced in our society depends ultimately on the wishes of consumers. This raises the problem of consumer information. However, the consumer for his part expects a certain guarantee from the State that he will not suffer harm from products present on the market.

In the opinion of the rapporteur, the demand for the indication 'Produced without the aid of animal experiments', or words to that effect, to appear on certain cosmetics would only mislead consumers.

In a number of Community Member States, the manufacturers of cosmetics are obliged to prove that their products are not health hazards before the products are allowed on to the market. Firms which carry out no animal experiments in the production of cosmetics use basic constituents and agents whose acceptability to health has been tested by the original manufacturers, in experiments on animals. In addition, test programmes are frequently subcontracted to scientific institutes.

(c) Animal experiments for instruction in special surgical techniques and for the training of doctors and scientists

It is clear that an appreciable proportion of the curriculum, even at university level, can be covered equally well in audiovisual teaching materials, demonstration experiments and practice on isolated organs, nerves and limbs.

However, many surgical techniques which are almost routine today can only be 'practised' and developed on living organisms (e.g. the development of artificial heart valves and organ transplants, to name but two prominent examples). Students of physiology are familiarized with the workings of various organs. This cannot be done through theoretical instruction alone but requires an element of practical work such as the examination of living organs or the observation of the organic processes of laboratory animals. The aim is to acquire skills which will be needed in the future when treating humans and animals. Just as a craft cannot be learned by mere watching, so practical exercises are necessary here. It is particularly true of medical training that experiments to determine specific reactions in animals and indeed humans cannot be avoided.

(d) Animal experiments for military purposes, including the treatment of injuries caused by chemical and other weapons

Little information has so far filtered through to the public on animal experiments for military purposes. What is certain is that experiments of this type are carried out in the development and testing of weapons and in attempts to find therapies for the injuries caused by weapons of all kinds.

The most topical and frightening example of such injuries is provided by the Iranian soldiers poisoned by gas, who are now being treated in hospitals in Europe and other Western countries.

Since it is probably impossible for anyone outside the military sphere to determine what purpose these experiments actually serve - the development of weapons or the treatment of injuries caused by weapons - a review of this practice by the defence officials responsible appears to be necessary.

## 7. Conclusiveness of animal experiments, applicability of the findings to humans

Some opponents of animal experiments flatly deny that they are in any way conclusive. They argue that animal experiments are valid only for the species on which they are performed, and that it is impossible to make any prognosis for humans.

Aside from the fact that the history of medical research furnishes numerous examples to the contrary, a more qualified approach needs to be adopted to the problem.

In certain sectors, e.g. cosmetic research, prevailing wisdom states that findings are to a very large extent applicable to humans, given that local sensitivity tests are the experiments most frequently carried out. In other cases, the species used has to be the one whose reaction corresponds most closely to a human reaction in the particular problem under consideration. This means that more highly evolved species often have to be used.

Examples of the applicability of animal experiments:

- Experiments to investigate the human renal function will be conducted on dogs, whose renal function is broadly similar to that of a human.
- Substances affecting the metabolism will be tested on pigs, which also live on a mixed diet and whose gastrointestinal system is very similar to the human system.
- The complications associated with addiction will be investigated in experiments on monkeys, whose reactions in such cases are similar to human reactions.

However, there are also instances in which animals and humans will display completely different reactions to a given substance, either because the differences in sensitivity and metabolism are extremely large or else, for instance, because the symptoms of an adverse reaction are not manifested in the particular species of animal and similar syndromes cannot be obtained. A great deal of experience is needed to evaluate the findings of an animal experiment and their significance for humans. Only experience with humans can confirm whether a given interpretation of an animal experiment is the correct one.

Substance in small quantities	Reaction (human)	Reaction (animal)
Prussic acid	Fatal	No reaction in toads and horses
Citric acid	No reaction	Fatal in cats and rabbits
Novalgine	Analgesic	Symptoms similar to rabies in cats
Atropine	Stimulant	Virtually no reaction in horses, monkeys, cats, rats and guinea pigs
Scopolamine	Stimulant	Reaction in dogs and cats only with the equivalent of 300 times the dose
Hemlock	Fatal	Good tolerance in mice, goats, sheep and horses
Methanol	Blindness	Harmless for most animals
Toadstools	Severe poisoning	No reactions in rabbits
Arsenic	Fatal	Sheep can tolerate immense quantities
LSD	Hallucinations	Improves spiders' ability to make webs; a dose of 300 mg is fatal in elephants

These examples show that the choice of the species to be used in a given experiment, the one which resembles humans most closely in the particular biological problem under consideration, will be influenced by the experience of the person carrying out the experiment. What they do not prove, however, is that it is invariably impossible to apply the findings of animal experiments to humans. The evaluation of the findings of an animal experiment and of their significance for humans also require a great deal of experience. Only experience with humans can prove beyond doubt that a given interpretation of an animal experiment is the correct one. It will be necessary for this purpose to develop a Community-wide system for the notification of side effects of pharmaceuticals and chemicals (or to use the technical terms for such a system, pharmaco-vigilance and toxico-vigilance).

8. The conclusiveness of individual experiments poses a different problem.

A test for acute toxicity is in many sectors required by law. Such a test is performed to determine all toxic effects, including the associated risk of death. This last is usually calculated in the LD 50% Test. 'LD' stands for lethal dose, i.e. the quantity of a substance sufficient to kill 50% of the sample group, in other words half of the animals used in the experiment. This gives a measure of the acute toxicity of the substance concerned.

This test is coming increasingly under criticism, not only from animal welfare organizations, but also from scientists.

These experiments are an indisputable cause of pain and suffering. It does not seem necessary from a scientific perspective to make this test the basis for certain laws.

Knowledge of the acute toxicity of a substance is important in many cases, yet it seems possible to calculate this acute toxicity, in other words the LD 50, by using smaller numbers of animals than is at present customary and required by national and international law.

It is standard practice today to use between 100 and 200 animals for determining acute toxicity. The OECD guidelines on toxicity and the directive being prepared by the Commission in implementation of Annex V of the 6th amending Directive (due to be adopted this year) reduce this number to 40. The limit test (limit dose) provided for in this draft requires only 10 animals. Estimates of LD 50 would be sufficient for toxicologists in most cases. The use of 6-10 animals per experiment would suffice to calculate this 'approximate lethal dose 50%'. It seems certain at all events that in certain specific cases the number of animal experiments could be reduced by up to 75% with this approximative test to determine death risks. In terms of animals used, this would mean a reduction of up to 130,000 per year in, say, the Federal Republic of Germany.

There is an urgent need to review those areas where death risks may be satisfactorily determined with the approximative lethal dose 50% test and those where the present Lethal Dose 50% test appears indispensable. However, no progress can be made in this area unless all the relevant laws are amended.

9. Are there other methods and processes to replace or supplement animal experiments?

(a) The opponents of animal experiments hope that it will in many cases be possible to replace them with 'in-vitro' tests and 'theoretical methods' - also known as 'alternative methods'. Recent scientific developments have certainly made it possible to replace a large number of animal experiments, with the result that tests may now be performed on, for instance, insensate matter, especially cell and tissue cultures, bacteria, amoebae, micro-fungi, chicken eggs etc. The prospects here have improved, since a way was found of preserving individual human and animal cell and tissue cultures under glass for longer periods of time.

For this reason, these experiments are called 'in-vitro' tests, as distinct from 'in-vivo' tests.

These in-vitro methods include, in addition to tests on insensate matter, examination of isolated organs, e.g. the heart, the kidneys, the liver, the intestines and the like. Although animals still have to die for this purpose too, because the organs must be removed from them beforehand, it can be done painlessly by anaesthetizing the animals before killing them.

Specific effects of a substance can be tested on such cell cultures or individual organs.

The following are classified as cell cultures: primary cultures, from fresh organs and tissue, continuous chains of cells, cells which are cultivated over a longer period of time (i.e. which have already divided on a number of occasions).

The difficulty here is that changes often occur in the characteristics of the cells. The cells are cultivated in a special liquid medium at a temperature of approximately 37°C.

After treating the cells with the substances which are to be tested, any toxic effects which may be observed can be assigned to one of three groups:

- short-term effects, mostly damage to the cell membrane
- medium-term effects, mostly damage to the metabolism or the organelles of the cell
- longer-term effects, mostly damage to the genotype.

Some examples of applied research using cell cultures:

- cardiants - isolated heart cells
- tobacco smoke and fibres - pleura
- neuropharmacological research - nerve cells
- effects damaging to the genotype
- vaccines.

The Ames test to determine the mutagenic effect of a substance is one example of a test which uses bacteria.

Nevertheless, the findings of experiments of this type need in many cases to be confirmed by additional experiments on animals. There are also many effects which cannot be simulated under glass. The effects of, for instance, a medicine with a hyper- or hypotensive action cannot be tested on an individual cell; this requires an animal with a measurable blood pressure. The same applies to the distribution and behaviour of certain substances in the body, the length of time they are lodged there and the reactions they provoke prior to their excretion. Similarly, the complex processes of the brain (relevant for many nervous diseases) cannot be investigated on individual cells.

#### (b) Theoretical methods

Apart from these in-vitro methods, 'theoretical models' can also supplement animal experiments or even remove the need for them.

##### 1. Computers

(a) The use of computers allows the best possible planning and evaluation of experiments. Computers make it possible to interrogate an electronic memory on the findings of previous experiments using the same substance, but in a different experimental context, and take account of them in an overall assessment. It is also possible in certain specific cases to use computers to calculate the effects of certain agents on various physiological functions, on the basis of known information on the interaction of these functions.

Experimental situations can to that extent be simulated with the aid of computers.

(b) Leaving aside these specific research applications, a Community data bank for animal experiments could help to prevent duplication and constant repetition of experiments and make it easier for scientists to establish which experiments had already been carried out. Nor should it be overlooked that in the biological sciences - for both economic and scientific reasons - work on the development of computer documentation systems began as long ago as the early 1960s. Research is being conducted on a large scale in scientific laboratories all over the world to solve bio-medical problems. Every scientist is anxious to have his research findings published.

To compile a Community data base, it would be necessary to examine and store over 15,000 scientific periodicals from all over the world, as well as treatises, dissertations, research and congress reports, trade magazines etc. There are already a number of pertinent information and documentation systems available at present (see Annex IV).

Apart from these existing systems, the German Bundesgesundheitsamt (Federal health office) is, in a current research project, examining the question of how far the central compilation of data on animal experiments, submitted in connection with the notification and licensing procedures, could effectively replace or limit animal experiments. Following the lead of this German research project, the Commission should determine how far a central Community data bank for animal experiments could help to reduce the numbers of such experiments.

## 2. Epidemiological investigations

There are two distinct forms:

- retrospective case studies: instead of collecting data for the purposes of the investigation, existing data are used;
- cohort studies, for which data are specially collected.

Statistical summaries are prepared from collections of individual studies, various factors are correlated with each other. Causes can thus be deduced indirectly. This method is becoming increasingly important, especially in cancer research.

### 3. Models

Certain specific functions can be examined or simulated on mechanical models (replicas) of organs such as the heart or lung.

(c) It can generally be concluded that the number of animal experiments could be reduced by an increased application of theoretical models and in-vitro methods. Scientific research must be directed more intensively into opening up these new avenues. This research needs financial incentives and support. Efforts must also be made to standardize these methods, as an essential preliminary to wider application. Finally, closer coordination must be established between in-vitro tests, animal experiments and clinical observation - including epidemiological observation - in order to improve the degree of health protection afforded to people who come into contact with toxic substances. The Commission should submit suitable proposals for Community action in this area.

(d) Conditions for the licensing of animal experiments

To prevent abuses in such animal experiments as may be deemed necessary, and to improve conditions for the animals kept in special breeding establishments for laboratory animals, the Community should lay down specific and uniform requirements for the conduct of animal experiments. First of all, compulsory notification and licensing procedures should be established to ensure that the only experiments carried out are those necessitated by the current level of scientific knowledge for the attainment of an objective which cannot be achieved by other methods and techniques. Compulsory notification and licensing of this type are also essential for the compilation of statistics on animal experiments. Compulsory notification should apply to all animal experiments required by law, and to all experiments on invertebrates.

All other experiments on animals should be made subject to strict licensing criteria. The problem which inevitably arises here is that scientists are in fact the only people able to judge whether or not a particular experiment on animals is actually necessary.

(e) Effective action must be taken to limit the suffering of laboratory animals, and this must include keeping even specially bred animals in conditions appropriate to their species. The administration of an anaesthetic and the veterinary treatment of laboratory animals after an experiment should be made compulsory in all cases. Experiments which are conducted without an anaesthetic and cause serious injury should be banned. Experiments which cause prolonged or repeated pain should be permitted only in exceptional cases to serve genuinely essential needs of humans or animals. Under no circumstances should animal experiments be permitted on grounds of saving labour, time or costs.

An ethical arbitration committee or an official with responsibility for animal welfare should conduct regular inspections at all establishments which carry out experiments on animals, to ensure that the rules and requirements for the conduct of such experiments are being observed.

10. Given the current state of science, it does not seem possible to dispense completely with animal experiments and hence impose a general ban on such experiments.

However, it seems equally certain that the number of animal experiments required by law, especially for testing the lethal properties of substances, could be reduced considerably, given the fund of scientific knowledge currently available. At the same time, strict rules on the conduct of animal experiments must be laid down by law.

In the opinion of the rapporteur, the European Community could make an important contribution in this area.

