

Animal experimentation – Legislation and Protection

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1 Introduction

1.1 Brief history of animal use

Since the beginning of human history man has tried to understand his environment by observation and also by experimenting with animals. It is generally said that first physiological investigations on animals started with observations of Alcmaeon of Croton (550-500 BC) and with Galen in Rome (130-201 AD) who performed physiological experiments on pigs, monkeys and dogs. The emergence of Christian era stopped any experimental approach in science and animal was then paid very little attention. Animal was considered without soul, sensitivity and consciousness and without interest for increase of knowledge. Consequently animal experimentation was considered no to lead to better knowledge of human body and medicine and investigations on animals were therefore banned for more than a millennium. Experimental medicine and biology recommenced in the 16th century with emphasis on anatomy (Vesalius, Da Vinci) and during the 17th century when also physiological functions were investigated (Harvey). Animals were considered as unconscious creatures and it was even assumed (Descartes) that animals could not suffer and that living mechanisms could be understood on purely mechanical principles. But it was accepted that animal experiments and their results could contribute to the development of medicine. Animal experimentation as such started in the 19th century with the works of Claude Bernard who emphasised the need of animal use to develop experimental medicine and physiology. He stated that animal experimentation was necessary for various scientific aims in fundamental research but also in applied medical research. Using that concept of animal experimentation eminent scientists discovered and tested their concepts in animals. Scientists like Pasteur and Koch, for instance, stated the evidence of causal relationship between microorganisms and infectious diseases. From the beginning of the 20th century development of biomedical disciplines and the development of pharmaceutical industry caused a rapid increase in animal use in experiments. Animal experimentation was then widely used for multiple scientific aims and not only the total number of animals used in experiments increased but also the number of animal species. Domestic animals were mainly used until the end of the 19th century. From the 20th century rodents are the most used animals but also other mammalians species or birds, reptiles, amphibians and fishes species are being used.

1.2 History of protection of animals used in scientific procedures

From the 19th century animal experimentation has been a subject of strong criticism. It is in UK that the first specific law on animal protection was published in 1822. First criticisms against animal experimentation began in 1850 in France and during the 1880's in United Kingdom. The first antivivisection organisation (The Victoria Street Society) was established in 1875 in London and the first law on the protection of experimental animals (the "Cruelty to Animal Act") was adopted by the UK parliament in 1876. Since then other countries have included into their legislation provisions to protect

animals used for experimental purposes but it took more than a century before laws specifically dealing with the protection of animals used for experimental purposes were adopted at international level.

2 Regulation on the protection of laboratory animals in Belgium

2.1 History: 1867 - 1975

In Belgium the first legislation on animal protection was enacted in 1867 with the provisions of different articles in the Penal Code. According to those articles however animals were only protected as property of man. Provisions were also only limited to farm animals and the Ministry of Agriculture was the competent authority for the control.

In 1929 the first law on animal protection as such (different than protection of property) was published. In that law article 7 considered vivisections and stated "experiments may only be carried out in university laboratories or similar (authorised) laboratories. Animals used in the experiments must be anaesthetised except if it is impracticable or if there are scientific reasons not to do it." That law was important but did not define vivisection and did not foresee any control or penalties and did not demand specific education for laboratory personnel.

In 1975 "Law of 2 July 1975 on the protection of animals" was published and article 6 of this law concerned vivisection and surgical operation. Vivisection was prohibited but the text of the article was structured on prohibitions and not on obligations. Surgical experiences for scientific research, medicine and veterinary medicine were allowed in university laboratories or similar (authorised) laboratories. The law did not consider non-surgical painful procedures.

At European level, it is only in 1986 that two fundamental documents in laboratory animal protection were published, one by the Council of Europe and the other one by the European Community.

2.2 Council of Europe

On 5 May 1949 the **Treaty of London**, establishing the **Council of Europe** was signed by ten states: Belgium, Denmark, France, Ireland, Italy, Luxembourg, the Netherlands, Norway, Sweden and the United Kingdom. The Council now counts 44 member countries (Albania, Andorra, Austria, Armenia, Azerbaijan, Belgium, Bosnia & Herzegovina, Bulgaria, Croatia, Cyprus, Czech Rep., Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Liechtenstein, Lithuania, Luxembourg, Malta, Moldova, Netherlands, Norway, Poland, Portugal, Romania, Russian Federation, San Marino, Slovakia, Slovenia, Spain, Sweden, Switzerland, 'the former Yugoslav Rep. of Macedonia', Turkey, Ukraine, United Kingdom).

In 1986 the member states agreed on the "**Convention for the Protection of Vertebrate Animals used for Experimental or other Scientific**

Purposes (ETS¹ 123)". The fundamental principle of the convention is the acceptance of the use of animals in experiments but also the reduction of that use by replacing experiments by alternative methods. The Council is not in a position to impose the rules of that Convention to the member states but once a state has signed and ratified the Convention it is bound by international law to implement the convention and its regulations. Animal rights, as well as human needs are priorities of the Convention. The general principles of the Convention are related to the purposes for which animal experimentation may be approved and to the rules for using animals in the procedures. The agreed purposes in the Convention are research on:

- (i) prevention of diseases,
- (ii) diagnosis and treatment of diseases,
- (iii) protection of environment,
- (iv) scientific research,
- (v) education and training,
- (vi) medico-legal investigations.

The member states agreed that:

- (i) procedures using animals should be used only if no other method exists,
- (ii) alternatives to animal experimentation should be encouraged,
- (iii) procedures using less painful methods, fewest and less sensitive animals should be prioritised,
- (iv) systems to control animal experimentation and to avoid replication of experiments should be in place.

As a member state of the Council of Europe **Belgium** signed and ratified the "ETS 123 convention" which means that Belgium is a "Party" to the convention (together with Cyprus, Denmark, Finland, France, Germany, Greece, Netherlands, Norway, Spain, Sweden, Switzerland and United Kingdom) and that the guidelines of the convention be respected by the national legislation. In 1991 therefore the provisions of the convention were enacted in the Belgian legislation through the "**Law of 18 October 1991 approving the European Convention on protection of vertebrate animals used for Experimental or other Scientific Purposes and its Annexes A and B done at Strasbourg on 18 March 1986**". Other countries like Ireland, Portugal, Slovenia and Turkey are only "signatories" to the convention, which means the convention is not ratified so far and is not entered into force yet. Only Parties to the Convention have right to vote.

On the other hand in **May 1997** the parties to the Convention recognised to improve laboratory animals welfare through (i) **enrichment of the environment**, (ii) **general and specific recommendations** with respect to ventilation and social handling and to individual species, and (iii) **research in the areas the biological requirements of the animals**.

In **June 1998**, Signatories to the Convention decided to adopt a protocol of amendment of the Convention ETS 123. That protocol (ETS 170) will enter into force after its ratification by all States Party to the Convention. The protocol of

¹ European Treaty Series

amendment aims to introduce a simplified procedure that will help up-date the terms of the convention, to take account of the development of scientific understanding and practice since the Convention was opened for signature in 1986. These terms concern the norms set by the convention for care and accommodation of laboratory animals, as well as the presentation of statistical data on animal experimentation. So far total number of signatures not followed by ratifications are 5 and total number of ratifications are 7.

2.3 European Union

In 1986 the **European Commission** published a "**Directive for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (86/609/EEC)**". Aim of that directive is to harmonise national regulations in order to avoid distortion and unfair competition within the Community. The provisions of the Directive are based upon the Convention ETS 123.

Belgium as a member of the European Community must follow the provisions of the Directive 86/609 in its national legislation.

2.4 Implementation of the European regulations in Belgium

In Belgium an important step in the protection of animals was the publication of the "**Law of 14 August 1986 related to protection and welfare of animals**". That law was modified in 1993 (Law of 26 March 1993) and in 1995 (Law of 4 May 1995). An important chapter (chapter 8: articles 20 to 30) relates to experiments on animals.

In 1994 the "**Royal Decree of 14 November 1993 related to the protection of experimental animals**" was enacted to implement on the field the provisions of the law of 14 august 1986 but also the provisions of the Directive 86/609 in the national legislation.

2.5 Law of 14 August 1986 related to protection and welfare of animals

2.5.1 Definitions

All the main official definitions on animals and experiment are included in the provisions of the law.

"Experimental animals" means any live non-human vertebrate, including free-living larval and/or reproducing larval forms, but excluding foetal or embryonic forms that is used or to be used in experiments.

"Experiment on animal" means any use of an animal for experimental or other scientific purposes which may cause it pain, suffering, distress or lasting harm, including any course of action intended, or liable, to result in the birth of an animal in any such condition, but excluding the least painful methods accepted

in modern practice (i.e. 'humane' methods) of killing or marking an animal. An experiment starts when an animal is first prepared for use and ends when no further observations are to be made for that experiment; the elimination of pain, suffering, distress or lasting harm by the successful use of anaesthesia or analgesia or other methods does not place the use of an animal outside the scope of this definition. Non-experimental, agricultural or clinical veterinary practices are excluded. Experiment is therefore limited to live animals and removal of organs from animals after they have been humanely killed is not considered as an experiment.

That definition includes therefore all experiments other than:

- (i) experimentation on invertebrates or embryonic forms of oviparous vertebrates,
- (ii) observation of animals in an environment causing no suffering or discomfort to animals.

“Laboratory” means any installation, building, group of buildings or other premises where animals are used for experiments.

2.5.2 General Provisions

Agreement

Main provisions of the Law consider the animal welfare. In the field of experimental animals that Law specifies that:

- (i) the responsible person of a laboratory where experimental animals are housed with the objective to carry out non-painful experiment must declare it the competent authority,
- (ii) the competent authority must approve any laboratory where experiments that may cause pain, suffering, distress or lasting harm are carried out,
- (iii) the competent authority must also approve any establishment for breeding and/or supplying laboratory animals.

Experiment

Provisions of the Law also state that:

- (i) experiment starts when animal is being prepared for the procedure and stops when no more observation is necessary;
- (ii) experiments must be strictly limited and carried out only when no alternative methods are available;
- (iii) selection of animals and methods for an experiment must always be very strict and prioritise:
 - procedures using the less number of animals and the less sensitive animal species,
 - less painful or damaging procedures,
 - use of anaesthetics in painful and suffering procedures,
 - use of analgesics in uncomfortable procedures,
 - procedures with strictly limited restriction of physiological needs.

Suffering

As far as suffering and pain are concerned no specific definition is given for the words pain, suffering, distress and damage but it is agreed that prick of a needle is considered as threshold of pain. Number of painless experiences is therefore very limited.

Animals

The Law provides the possibility to specify animal species that are used in research and scientific procedures, their origin, identification and housing (articles 20, 23).

Ethical consideration

The law includes the idea to avoid unnecessary use of experimental animals and to organise animal ethics committees.

Already in 1959 Russel and Burch in their publication "The principles of Humane Experimental Technique" proposed that every effort should be made to *Replace* animals to be used in experiments with non-sentient alternatives, to *Reduce* to a minimum their number or to *Refine* experiments to cause the minimum pain and stress

The concept of those 3R's principle is highlighted in article 24 of the law where indeed it is clearly defined that:

- (i) experiments on animals should be strictly limited;
- (ii) an experiment shall not be performed if another method of obtaining the result sought, not entailing the use of an animal is available;
- (iii) when an experiment has to be performed, the choice of species shall be carefully considered and in a choice between experiments, those which use the minimum number of animals, involve animals with the lowest degree of neurophysiological sensitivity, cause the least pain, suffering,

- distress or lasting harm and which are most likely to provide satisfactory results shall be selected;
- (iv) all experiments causing distress, pain and suffering to the experimental animals shall be carried out under general or local anaesthesia unless anaesthesia is incompatible with the object of the experiment. In such cases analgesics or other appropriate methods should be used in order to ensure as far as possible that pain, suffering, distress or harm are limited and that in any event the animal is not subject to severe pain, distress or suffering.

With respect to the implementation of those 3R's and to the ethical evaluation prior to the carrying out of experiments specific committees play an important role and the law states that:

- (i) a National Ethics Committee of experts in animal experimentation shall be organised (article 28)
- (ii) local ethics committees shall be arranged to evaluate research protocols on ethical and animal welfare aspects.

2.6 Royal Decree of 14 November 1993 related to the protection of experimental animals

The **Royal Decree of 14 November 1993 related to the protection of experimental animals** was promulgated to implement the law of 14 August 1986 and also to transpose the Directive 86/609/EC in the national regulations. To complete that transposing of provisions of the Directive and to harmonise the Belgian legislation with the evolution of the rules of the European Community that Royal decree was modified in 1998 (introduction of new standards of statistical tables, specification of education of laboratory personnel), 2000 (interdiction of duplication of experiments) and 2001 (ethic commissions in laboratory, derogation for using non specifically bred animals).

The Law of 1986 (Article 20) states that any Royal decree on protection of experimental animals must be debated in Council of Ministers and approved by Council of State before being signed by the King. Practically it means that the minister in charge of animal welfare must always submit any modification of the Royal decree of 14 November 1993 to approval of Council of Ministers and Council of State.

3 Organisation of the regulation on the protection of laboratory animals in Belgium

3.1 Scientists and laboratory personnel

All staff involved in animal experimentation and in care to laboratory animals needs to be trained and approved by the competent authority (Law, articles 23, 25, 26 and 29; Royal decree, article 5 § 5).

Staff is classified in several categories:

Director of laboratory: he is the responsible manager and must:

- (i) ensure that the laboratory is in accordance with all the conditions related to laboratory approval,
- (ii) provide all administrative and statistical information that is requested by the Federal Public Office in charge of animal welfare.

Master of experiment: he is responsible for experiments that he carries out on animals. He is also responsible for the post-operative care to these animals. If the animal is a horse, a cat, a dog, a pig, a ruminant or a primate he must call a veterinarian for the treatments. Master of experiment must hold university degree from faculty of medicine, veterinary medicine, biology, agronomy or other degree defined by the King. He must be specifically qualified to carry out experiments on animals.

Expert: he must take charge of protection of health and welfare of laboratory animals. If laboratory animals are horses, dogs, cats, pigs, ruminants or primates, the expert must be a veterinarian. For other laboratory animals if the expert is no veterinarian a veterinarian must supervise him.

Laboratory technicians and workers: (Royal decree, article 5) all laboratory personnel must be properly trained and qualified in animal experimentation. The director of the laboratory is entitled to testify that laboratory personnel are properly trained.

Authorisation to experiment is granted to personnel after the director has introduced an application for approval of the laboratory. All the necessary information on personnel and qualification must be provided prior any experiment is carried out in the laboratory. Laboratory staff is authorised to carry out experiments only in their own duty station. Any modification in the organisation and identification of staff must be communicated to the Federal Public Office in charge of animal welfare.

Education of laboratory personnel is compulsory and control of degree of education may be organised by the Authority. Universities grant university degrees. Belgian Council for Laboratory Animal Science provides education of laboratory personnel. In Belgium the Ministry of Agriculture usually endorsed degrees for technicians and workers. The Ministry may also endorse degrees for laboratory personnel that are granted in other European countries provided that the programme is officially approved in the country of origin.

3.2 Laboratories

Can be considered as a laboratory a total university or pharmaceutical institution as well as a faculty, a department, a division or a unit in the same institution. The request for approval can relate to all the institution or a part of that institution.

Declaration

In all laboratory where experimental animals are housed the Director of that laboratory must declare it to the Federal Public Office in charge of animal welfare (usually to the local veterinary inspection).

A special form needs to be filled (Royal decree, article 2) and sent to Veterinary Inspector. Following important information must be communicated with the application form:

- (i) plan of the laboratory buildings,
- (ii) description of the equipment,
- (iii) comprehensive list of personnel (director, scientists, technicians, workers, training) and education specifications,
- (iv) description of the experiments with a specific attention to their objective and to the description that those experiments do not cause pain, suffering, distress or lasting harm,
- (v) list of animals that are housed in the laboratory (number, species, origin).

Agreement

Prior to any start of experiments on animals that may cause pain, suffering, distress or lasting harm, the Director of a laboratory must apply for an approval to the Federal Public Office in charge of animal welfare (usually to the local veterinary inspection - Law, article 21; Royal decree, article 2). Different steps are followed for that request.

A special form needs to be filled (Royal decree, article 2) and sent to Veterinary Inspector. Following important information must be communicated with the application form:

- (i) plan of the laboratory buildings,
- (ii) description of the equipment,
- (iii) comprehensive list of personnel (director, scientists, technicians, workers, training) and education specifications,
- (iv) description of the experiments that cause pain, suffering, distress or lasting harm and their objective and if necessary, reasons why no anaesthetic are used,
- (v) list of animals used in the experiments (number, species, origin)
- (vi) notification of organisation of a local ethics commission (six members minimum, list of members and qualification, the local veterinary inspector is a member of the commission).

After the Veterinary Inspector receives the application he visits the laboratory facilities with the director of the laboratory in order to control conditions of animal housing and care.

The request and the report of the control visit are submitted to the National Ethics Committee who may give negative or positive comments on the request. Additional information may also be requested from the laboratory.

After approval by the Committee the request is submitted to the Minister who is in charge of animal welfare.

After approval by the Minister a specific number is attributed to the laboratory and the number is organised as follows:

- (i) LA for LABORATORY
- (ii) First figure = 1 for laboratory
- (iii) Second and Third figures for the code of province and region where the laboratory is operational: (Antwerp = 10, Flemish Brabant = 21, Walloon Brabant = 22, Brussels = 23, Western Flanders = 30, Eastern Flanders = 40, Hainaut = 50, Liege = 60, Eastern Belgium = 61, Limburg = 70, Luxemburg = 80, Namur = 90)
- (iv) Fourth to Seventh figure: unique serial number

(Ex. : LA 1 10 0015 means a laboratory in province of Antwerp with serial number 15 in the database)

The approval is granted indefinitely but it may be suspended or withdrawn any time in case of transgression of Law. Any modification in the laboratory organisation (address, personnel, experiments, animals...) must be declared to the Veterinary Inspector.

The director of the laboratory must keep a register where he records:

- (i) all entries and exits of animals (species, number, supplier, destination, date),
- (ii) all information on animal mortality,
- (iii) individual identification number of dogs, cats and primates,
- (iv) all information on animals used in experiments.

The register must be stored for three years and fits for use as a permanent inventory book. All animals or batches of animals used in a laboratory must be recorded in the register. A specific invoice issued by the establishment where the animals have been purchased must also be kept.

A database with all the necessary details on the laboratories in Belgium is handled at the Federal Public Office in charge of animal welfare and regular updating of the database is carried out.

Experiments

The National Ethics Committee analyses experiments when the laboratory applies for agreement and when local ethics commissions request an opinion about a specific procedure.

Usual experiments and scientific procedures are carried out for biological studies of a fundamental nature, research and development of products and devices for human medicine and dentistry and for veterinary medicine, production and quality control of products and devices for human medicine and dentistry and for veterinary medicine, toxicological and other safety evaluations (including safety evaluation of products and devices for human

medicine and dentistry and for veterinary medicine), diagnosis and studies of human and animal diseases, education and training in high school and laboratories when no other method is available.

Some tests are compulsory because of regulatory requirements in national legislation, EC legislation (European Pharmacopoeia), Member Country of Council of Europe legislation or other legislation (International Pharmacopoeia).

3.3 **Experimental animals**

Type and origin of laboratory animals

The origin of experimental animals is a very sensitive topic. The use in experimentation of stray, lost or abandoned dogs and cats is forbidden (Royal decree, article 8). Use of captured wild animals (Royal decree, article 11) or CITES protected animals (Royal decree, article 12) is allowed only in very exceptional cases and always submitted to a preliminary specific authorisation from the authority (Federal Public Office in charge of animal welfare after advice of National Ethics Committee).

Experimental animals other than farm domestic animals must come from a registered supplier or breeder (Royal decree, article 9 §§1,2). Furthermore all mice, rats, guinea pigs, hamsters, rabbits, monkeys, dogs, cats and quails must have been purpose bred for experimentation or other scientific purposes.

Derogation to article 9 §§1,2 of the Royal decree

Veterinary services of Federal Public Office in charge of animal welfare is entitled to grant derogation to the obligation of buying purpose bred animals.

Regulations to request for such derogation has recently been changed and a specific application form must be used and follow the hereunder-mentioned way:

- (i) the request must be first submitted by the director of the laboratory to the local ethics commissions of the laboratory,
- (ii) the local ethics commission must endorse the request,
- (iii) only one application per animal species is valid,
- (iv) the application form needs to detail origin of animals, exact number of animals to be used in the experiment, the description of the experiment,
- (v) the applicant must clearly justify why purpose bred animals cannot be used in the experiment and those statements must be strongly endorsed by the local ethics commission,
- (vi) the request must be approved by the National Ethics Committee,
- (vii) specific derogation is granted by the veterinary service and the supplier must registered.

Derogation may be granted only in very exceptional cases and the director of the laboratory is eventually responsible for control of origin of animals.

Supply and breeding of laboratory animals

All the establishments where laboratory animals are kept for supplying or breeding must be approved by the Federal Public Office in charge of animal welfare (Royal decree, article 4). All animals or batch of animals that are used for experimental or scientific purpose must come from an approved institution.

Prior to any start of activity the director of the establishment must request a licence from the Federal Public Office in charge of animal welfare (usually to the local veterinary inspection - Royal decree, article 4). As for the laboratories different steps are followed.

A special form is also used and is sent to the Veterinary Inspector. The following information must be communicated when the request is submitted:

- (i) plan of buildings,
- (ii) description of equipment,
- (iii) comprehensive list of staff (identification, number, training),
- (iv) provision of adequate veterinary support,
- (v) list of animals in the buildings (number, species),
- (vi) details on the housing and care of laboratory animals.

After he has received the application the Veterinary Inspector visits the premises with the director of the establishment in order to control all conditions of animal housing and care.

Application and report of the control visit are submitted to the National Ethics Committee. The Committee may issue any comment or advice about the application.

After approval by the Committee the request is submitted to the Minister in charge of animal welfare.

When the laboratory is approved by the Minister a specific number is attributed to the establishment and the number is organised as follows:

- (i) LA for Laboratory purpose bred animals,
- (ii) First figure = 2 for supplier and breeder, 3 for supplier only,
- (iii) Second and Third figures for the province and region where the institution is operational,
- (iv) Fourth to Seventh figure: unique serial number.

(ex: LA 2 10 0062 means a breeding centre in province of Antwerp with serial number 62 in the database; LA 3 50 0123 means a supplier in province of Hainaut with serial number 123 in the database)

The approval is also granted indefinitely but it may be withdrawn any time in case of transgression of Law. Any modification in the organisation (address, personnel, animals...) must be communicated to the Veterinary Inspector.

Housing and care of animals

Provisions for housing and care of experimental animals are given in annex III of the Royal decree. Those provisions are based on EC Directive 86/609 and

appendix A to European Convention ETS 123. All data that are given in annex III are guidelines so far. However since 1997 countries that are Parties to the European Convention have decided to amend the annex A of the Convention ETS 123 and meet regularly to discuss and revise norms of housing. Revision should conclude on new more constraining measures for housing of laboratory animals.

Identification

Legislation (Royal decree, article 13) defines that all cats, dogs and primates must be individually identified and at the latest at weaning period. The responsible of the institution is free to select method of identification but he needs to ensure that the identification is individual, permanent and painless. Identification of dogs is also regulated by Royal decree of 17 November 1994.

A register must also keep all information on:

- (i) all entries and exits of animals (species, number, supplier, destination, date),
- (ii) all mortality in animals,
- (iii) individual identification number of dogs, cats and primates,

The register must also be kept for three years and fits for use as a permanent inventory. All the animals or batches of animals must be recorded in the register. Records on the origin of animals are paramount.

Importation from third countries

Animals that are imported (Royal decree, article 10) for use in experimental or other scientific procedure must come from an approved breeder or supplier except if the animals are legally imported. This provision is translated from EC Directive and is unclear. Possibility to adopt more constraining provisions for import of laboratory animals is discussed at EEC level.

3.4 Control

The Royal decree provides means of control of laboratories and establishments. Those means are:

- (i) the registers (Royal decree article 14),
- (ii) the local ethics commissions (Royal decree article 3bis),
- (iii) the information that are provided by the responsible person in case of any modification in the laboratory or establishment (Royal decree articles 2 & 3),
- (iv) the obligation to issue statistical information on the use of animals in the experiments is provided both in Law (article 25) and Royal decree (article 15). The director of the laboratory must send statistical data to the local veterinary inspector each year and before 31st of January. Information on number of animals species used per type of experiment is compulsory. Figures must be provided on specific forms (Royal decree, annex IV). Licence holders have to record the statistical data in accordance with the requirements of the Council of Europe Convention: "Animals to be counted are those which will be put to use which may cause them pain, suffering, distress or lasting harm. The counting should take place when the animals are put to use in a procedure. Each animal

should be counted once only. Animals not subject to procedures as defined by the convention should not be counted for the purpose of collecting statistical information". Licence holders submit their statistics in confidence. The Federal Public Office in charge of animal welfare publishes general statistical information and information about individual establishments is not provided to the public. Statistical tables are now harmonised in the European Community and each country inform European Commission and European Council on their statistics.

Control is also achieved through missions of veterinary inspectors when they attend meetings of ethics commissions and when they visit buildings and equipment of laboratories and breeding/supplying institutions. Director of laboratories and institutions must accept all control by competent authority and in case of mismanagement or transgression to the Law penalties are foreseen (Law, chapter XI).

Because all modifications in a laboratory/institution (changing of personnel, animal species, type of experience, addresses...) must be declared to the veterinary inspectors the latter usually take the opportunity to visit the premises when important modification is mentioned.

4 Animal experimentation and ethics

4.1 National Ethics Committee

Ethical issue on scientific experiences in laboratories is supervised by a National Ethics Committee that is nominated by the Minister in charge of animal welfare (Law, article 28; Royal decree, article 15). The National Ethics Committee is chaired by a judge nominated by the Minister of Justice and gathers representatives of:

- (i) scientific and academic institutions,
- (ii) ministries (agriculture, public health, scientific policy),
- (iii) pharmaceutical industries,
- (iv) animal welfare societies.

Role of the National Ethic Committee is to advice the Minister and the veterinary service and to submit proposals about all problems related to enforcement of the legislation on use of animals in experimentation.

The National Ethics Committee meets regularly and various topics are debated (licences for laboratories and establishments, use of derogations, transgenic animals...).

The Committee is organised with three workgroups:

- (i) the group "Science and techniques" who is in charge of considering all scientific and technical aspects of animal experimentation,
- (ii) the group "Alternatives" who follows all the evolution of alternative methods to animal experimentation that follow the concept of the 3R's principle,
- (iii) the group "ethics" who studies the ethical aspect of animal experiments.

4.2 Local ethics commissions

Since November 2001 local ethics commissions in institutions where painful experiences are carried out on animals (Law, article 21; Royal decree article 3bis) are compulsory.

A local ethic commission must gather at least 6 members two of which being an external independent consultant and the veterinary inspector. One local ethics commission may supervise several different laboratories.

Role of the commissions is to:

- (i) evaluate experiments,
- (ii) advise scientists on ethical aspects of experiments,
- (iii) inform the control authorities on experiments in the laboratory(ies),
- (iv) define the ethical criteria of experiments,

5 Animal experimentation and alternative methods

Legal requirements to use alternative methods are found in the Convention ETS 123 (article 6, 1°; Directive 86/609, article 7, 2°; Law of 14 august 1986, article 24). The leading principle is the concept of the 3R's of Russel and Burch. Those 3R's are assured in the Law. Replacement principle is covered by point 2 of article 24 (*"experiments on animals are forbidden if any valid alternative method not using animals is available"*), Reduction is considered in points 1 and 3 of article 24 (*"experiments on animals must be strictly limited"* and *"procedures demanding less number of animals must be selected"*) and Refinement is followed in points 3 and 4 of article 24 (*"less painful methods and less sensitive animal species must be selected"* and *"anaesthetics must be used when painful procedures are carried out"*).

In the field of protection of consumers and of environment despite legal requirements to use any scientifically adequate available alternative method practical implementation usually still needs that the alternative method is officially validated. For instance OECD² guidelines now contain regulations that animal experiments are not allowed when a validated in vitro method is available. European directives also consider compulsory alternative methods in the European Union when the methods are properly validated.

So far in Belgium some methods are to be considered:

- (i) The tests on animals for skin corrosivity and phototoxicity are forbidden (Directive 2000/33/CE),
- (ii) The classical LD 50 toxicity test must be replaced by refined methods using less animals (directive 2001/59/CE),
- (iii) Various in vitro Monoclonal Antibodies production systems have been developed to meet the needs of a diverse range of users making the ascites method of Monoclonal Antibodies production redundant, the in vivo production of with ascites method should therefore be prohibited (ECVAM³ recommendation)

² OECD : Organisation for Economic and Commercial Development

³ ECVAM : European Centre for the Validation of Alternative Methods

6 Protection of laboratory animals in other countries than Belgium

Most highly developed countries have implemented specific provisions in their legislation to protect the animals that are used in scientific and research procedures. Some of those countries have also developed rules and regulations to minimise the risk of pain and distress when the animals are used in such procedures. Considering the effort in harmonising and co-ordinating the regulations and rules for protection of animals in experiments two groups of countries can be identified:

- countries without common rules such as the USA, Canada or Japan;
- countries with harmonised regulations such as:
 - New Zealand and Australia,
 - State members of the Council of Europe,
 - State members of the European Community.

The current status of several countries is briefly reviewed hereafter. Only countries with relevant and recent information have been considered.

6.1 Legislation in non-European countries

USA

The use of animals in research is controlled by the Health Research Expansion Act and by the Animal Welfare Act (AWA). The AWA was issued in 1966 and amended in 1976 and 1980. The amendments set standards to minimise pain or distress of animals and requires researchers to consider alternatives to painful procedures. Each research facility is required to establish an Institutional Animal Care and Use Committee to approve and monitor all research conducted at the institution. The statistical reporting of animal experimentation follows a specific recording of experiments that involve pain or distress with or without supplying pain relief drugs. Each research facility has to assess the potential pain or distress prior to any experiment (prospective assessment). The retrospective assessment of pain is optional. The Animal and Plant Health Inspection Service (APHIS) currently carry out a process to re-define pain or distress of animals.

Canada

The animal welfare is controlled by the Criminal Code at a federal level. In some provinces (Alberta, Ontario, Saskatchewan, Quebec) specific provincial bills deal with the animal experimentation. In 1968 the Council of Medical Research in Canada decided to establish Canadian Council of Animal Care (CCAC). The mission of the CCAC is to formulate guidelines in animal experimentation and also to carry out control missions in the research facilities. In each research facility an Animal Care Committee (ACC) is in charge of assessing the experiments on animals. The duty of those committees

is also to ensure the proper application of the guidelines issued by the CCAC. The guidelines are published by the CCAC to give clear direction to institutional animal care programmes. ACC members have responsibilities for the humane care and use of experimental animals. As far as pain or distress is concerned the guidelines establish that animals may not be subjected to unnecessary suffering. Specific guidelines even determine the endpoint of an experiment and specify that in experiments involving animals, any actual or potential pain, distress, or discomfort should be minimised or alleviated by choosing the earliest endpoint that is compatible with the scientific objectives of the research. Fixing of this endpoint by the investigator should involve consultation with the Animal Care Committee.

Japan

The law concerning the protection and control of experimental animals (law 105 of October 1973) declares that experimental research or other scientific purposes is to use methods that cause minimum pain possible to animals within the limits imposed by the said purposes (article 11). An Animal Protection Council debates important matters relating to animal protection and advises the prime minister's office where necessary. The prime minister may prescribe standards applicable to the methods used in the experiments.

New Zealand

A National Animal Ethics Advisory Committee (NAEAC) has been established in 1984 and covers the use of animals in research, teaching and testing. In addition to that National Committee an Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART) has been set up. The National Committee in New Zealand is not entitled to inspecting the laboratories but he can visit the research facilities.

Since 1998 all organisations manipulating live animals for the purpose of research, testing, teaching or the production of biological agents are required to respect a new code of ethical conduct recommended by the National Committee and approved by the relevant authorities. Within each organisation where live animals are manipulated for research or other above mentioned purposes an Animal Ethic Committee (AEC) must control the respect of that code. The AECs are independently reviewed by experts of the National Committee and any issue may be raised to this Committee.

In the research centres any experiment is submitted to the AEC. To approve the experiment the AEC takes into account amongst other aspects the experimental techniques and the use of anaesthetic. A specific justification is required for all procedures with potential to cause pain or distress and the steps taken to avoid or minimise pain or distress must be detailed. The Code of Ethical conduct also provides guidelines for pain or distress assessment and advises that animals should always be given the benefit of any doubt concerning pain relief. Some experiments not using any anaesthetic are considered to be unacceptable.

Australia

Regional authorities (Queens land, New South Wales, Victoria, Tasmania South Australia, Western Australia, Northern Territory...) have the responsibility for the control of animal experimentation as laid down by several animal welfare acts (Animal Protection Act, Animal Research Act, Prevention of Cruelty to Animals Act, Animal Welfare Act...). Codes of practice define that experiments on animals may only be performed if the procedures are designed in order to avoid or minimise pain or distress to animals. When this cannot be avoided anaesthetics must be used and when appropriate anaesthesia is not possible the endpoint of the experiment must be as early as possible. Each institution using animals for scientific purposes must establish an Animal Experimentation Ethics Committee (AEEC) the terms of reference of which are all ethical and animal welfare aspects. The Australian and New Zealand Council for the Care of Animals in Research and Teaching (ANZCCART) promotes in both countries standards of care for animals used in research and teaching and encourages discussion of related ethical issues.

6.2 Legislation in European countries

Member states of the European Council and the European Community other than Belgium and for which relevant data on the animal welfare are available are briefly reviewed hereafter.

Austria

In Austria the Animal Testing Act (1988) regulates animal testing and how to get permission for carrying out tests on live animals. Codes of practice provide the Animal Experimentation Ethic Committees with guidance for the animal experimentation. Any scientific procedure on live animals must be designed as to avoid or minimise pain or distress on the animals. When pain or distress is caused by the experiment anaesthetics must be used. If the procedure requires that no pain relief drug may be used clear endpoint limits to the experiments must be defined. When unpredicted signs of pain or distress occur during a procedure the pain must be alleviate without delay, if not the animal must be humanely killed.

Czech Republic

The Animal Protection Act states that the experiments on live animals have to be approved by the Central Commission for Animal Welfare (CCAW). The state authorities are supposed to control the respect of the provisions of that Act by means of professional commissions that are mandatory in the research institutions.

Finland

The Statute on Animal Experimentation (1985) requires that institutions involved in research and animal experimentation dispose on a Committee of

Animal Experimentation. Experiments causing severe distress or pain need a special approval of the Provincial State Office.

France

Several decrees (1988) regulate the use of live animals in the scientific procedures. Most experiments must be assessed and endorsed by scientific or ethical committees. A code of good laboratory practice has to be respected by the laboratories.

Germany

An Animal Welfare Act is available at the Federal level and the majority of the Länder published their own Animal Welfare Act. The Animal Welfare Act demands ethical justification of the experiments on animals in research and scientific purposes. Committees are set up to assist the authorities in deciding whether to authorise experiments on animals. The scientific and ethical aspects are discussed before granting any licence to research facilities to carry out experiments.

A system of research plan review based on the cost-benefit principle is into practice.

Greece

According to the National Legislation local veterinary directorates are responsible for the scientific evaluation of the experiments on animals. Those directorates consider the ethical aspects of the experiments and when necessary the opinion of other experts can be required before granting any licence to carry out an experiment.

Ireland

The Minister for Health and Children licences the use of live animals in medical and scientific experiments. It is the policy of the Department of Health and Children to keep the level of experimentation on live animals to the minimum and to ensure that no pain, suffering, distress or lasting harm are inflicted unnecessarily. The balance of medical and scientific opinion at present is that properly controlled animal experimentation contributes to advances which lead to the saving of human and animal life and the alleviation of suffering in humans and animals. Ireland like the other European countries supports the work of the European Commission who established a European Centre for the Validation of Alternative Methods (ECVAM) that encourages the development and validation of alternative techniques

Italy

The Veterinary Department of the Ministry of Health grants the licence to carry out animal experimentation. The authorisation is based on the scientific background of the project but the procedures involving pain or stress to

animals without anaesthesia need a specific approval. In many institutions Animal Care and Use Committees regularly review the acceptance of experimental programmes as far as ethical aspects are concerned.

Norway

The Ministry of Agriculture through the Norwegian Animal Welfare Act regulates animal experimentation in Norway. The Act states that experiments may not be performed without a special permission being granted by the National Animal Research Authority (NARA). The Ministry may refuse to allow such use of animals if there is doubt on its necessity.

For practical reasons, the day-to-day approval of the majority of animal experiments in approved laboratory units is delegated to a competent person appointed by the NARA at each facility for a period of 4 years. That person ensures that the research is carried out in such a way that the animal is not exposed to suffering more than that is strictly necessary for the purpose. Total or local anaesthesia on the animals can be used. Procedures deliberately withholding painkillers are handled by the NARA and although lacking legal foundation, a consensus has been established on a number of practices that are considered to be unethical.

Netherlands

The Dutch Animal Experimentation Act (1977) demands the research establishments to request a licence from the Ministry of Welfare, Public Health and Cultural Affairs prior to carry out any experiment. Research plans must be approved by local ethical review committees that have to consider the benefit emanating from an experiment and whether this justifies the distress caused to the animals used in the procedure. The pain assessment is prospective and a system of research plan review based on the cost-benefit principle is also into practice.

A statistical reporting system of all animal experimentation leaves the opportunity to count the number of experiments involving pain or distress to the animals with or without pain relief drugs.

Poland

Local Scientific Committees assess the experiments to be carried out on live animals. In some institutions ethical committees are appointed in order to consider the ethical aspects of the procedures on animals.

Portugal

The Act for the Protection of Animals requires a justification of all the scientific and research procedures carried out on animals. A National Advisory Committee advises the Veterinary Inspectorate but there are no ethical reviews of experiments on animals at national level.

Slovenia

The Law on Animal Health shows provisions dealing with experiments on animals. Licences to experiment on live animals are regulated through a directive. Animal Experiments Boards operate in the main institutions that are involved in animal experimentation. These boards include ethics committees that give the consent to approve research projects.

Sweden

The Swedish system of regulating animal research comes under a general law controlling animal welfare the Animal Welfare Act (1988). Animals may only be used for scientific research or education, the diagnosis of diseases, the production of drugs or chemical products or for other similar purposes where the activity is organised in such a way as not to subject the animals to greater suffering than is absolutely necessary. Permission must be granted from the Government or, where the Government so decides, the National Board of Agriculture, before animals can be used for scientific purposes. Under the Swedish Ministry of Agriculture there is a National Board for Laboratory Animals that can adopt rules to lay down conditions for or to prohibit the breeding, keeping, supply or use of animals for experiments. The National Board for Laboratory Animals is also responsible for setting up seven regional Ethical committees on animal experiments for the purpose of ethical approvals. When considering specific cases the Ethical committees shall weigh the importance of the experiment against the suffering inflicted on the animal. Before a vertebrate animal is used for scientific purposes the animal shall, if the use may involve physical or mental suffering, be anaesthetized. However, if it is necessary in view of the purpose of the surgical procedure, or if the anaesthetic would cause more suffering than the use in itself, the procedure may take place under partial anaesthesia or without an anaesthetic. Where possible, an analgesic or tranquilliser shall be used in such cases to alleviate the animal's suffering, in order to ensure that the animal is not subjected to severe pain, severe anxiety or any other severe suffering.

Switzerland

A Federal Veterinary Office is in charge of the animal experimentation. A cantonal authorisation must be granted prior to any experiment on live animals. Academic bodies in the different Institutions and Universities must also approve the experiments before requesting the authorisation from the cantonal authorities. The Law on the Protection of Animals (1978) clearly states that no unjustifiable painful or distressing experiments can be carried out on animals. Only strictly limited painful procedures are allowed on experimental animals. The Federal Veterinary Office regularly issues guidelines to inform the relevant regional and local authorities on the recent technical and ethical development in the field of animal experimentation. A code of conduct for all scientists and other people involved in practising the animal experimentation has been formulated by the Swiss Academy of Medical Sciences and the Swiss Academy of Sciences (Ethical Principles and Guidelines for Scientific Experiments on Animals). As far as pain and distress on animals

are concerned two specific guidelines have been published by the Federal Office and for the attention of the cantonal authorities and commissions responsible for the animal experimentation. The purpose of the specific guidelines is to refine the experiments through a prospective and also a retrospective assessment of pain.

United Kingdom

The Animals for Scientific Procedures Act (1986) does not require Ethical Committees in the different Institutions where animal experimentation is carried out. Correct management structures and communications are required to ensure the welfare of laboratory animals. A National Animals of Scientific Procedures Inspectorate reviews project licences applications before advising the Secretary of State to grant the licence.

A national advisory Animal Procedures Committee reviews the working of the legislation.

The Animals for Scientific Procedures Act (1986) provides guidance on the application for Project Licences. The application form requires details on description of the procedures and the assessment of potential severity of the experiments. The Act requires that a project licence cannot be granted unless the likely adverse effects (pain, suffering, distress or lasting harm) of the procedures have been weighed against the benefit likely to accrue as a result of the proposed programme of work.

Applicants for project licences must assess the likely severity resulting from the procedures in order that this may be balanced against the potential benefit.

In assessing the severity of a series of regulated procedures, account is taken of action carried out to mitigate adverse effects and to apply endpoints to the procedures. Licence holders must always familiarise themselves with the signs of pain, discomfort and distress in the species they are using. Suffering can be controlled by reliable analgesia and care and licence holders are required to minimise any pain, suffering or distress.

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