

Biotechnology, animal health and animal welfare within the framework of European Union legislation

F. De Simone ⁽¹⁾ & J. Serratosa ⁽²⁾

(1) Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna, Dipartimento di Ricerca, Via A. Bianchi 7, 25100 Brescia, Italy

(2) Scientific Coordinator of the Panel on Animal Health and Welfare of the European Food Safety Authority, Rue de Genève 10, 1140 Evere, Brussels, Belgium

Summary

Experimental and farm animals are used in biomedical research and in biotechnology studies that are designed to improve agricultural productivity. European legislation governing such research, which is modelled on existing National Laws regarding animal health and welfare, is agreed after several preliminary sessions in which contributions and opinions from large sections of European society are sought. Special attention is paid to opinions expressed by ethical and animal rights associations, which emphasise that animals should be considered as 'sentient beings' and not mere 'goods' or 'property'. A statement to this effect is included in the Treaty establishing a Constitution for Europe, which was signed in Rome in 2004 by the 25 European Union member states.

Keywords

Animal health – Animal protection – Animal welfare – Biotechnology – European Union – Legislation.

Introduction

European legislation is the result of a detailed process involving large numbers of qualified representatives from European countries. The body in charge of proposing and drafting European legislation is the European Commission, which is also the body responsible for changing or adapting legislation in the light of any new scientific findings. The Commission is assisted by a civil service which consists of 36 Directorate-Generals (DGs) and services. There are at least three DGs that are directly involved with animal health and welfare: the Health and Consumer Protection DG, the Environment DG and the Enterprise and Industry DG. The Health and Consumer Protection DG is principally concerned with animals that produce food; the Environment DG addresses the welfare of laboratory animals; and the Enterprise and Industry DG concentrates on issues related to veterinary medicines.

There are many procedures in the development of a legal framework for animal health and welfare, but all of them

involve the same three basic tools: Regulations, Directives and Decisions. The body of European Union (EU) law relating to health and consumer protection (most of which is related to food, animal health and animal welfare) comprises many hundreds of Directives and Regulations, together with Commission Decisions that must be respected and implemented. The implementation of Directives is subject to transposition in national law, whereas Regulations and Decisions apply directly without transposition into national law (Regulations are binding upon all Member States and Decisions are binding only upon those to whom they are addressed). Regulations and Directives on animal health and welfare follow the co-decision procedure involving Commission, Council and Parliament. The time frame for approving such legislation is between two and five years.

Decisions are one of the executive tasks of the Commission; they are the result of the comitology

procedure whereby proposals are discussed by the relevant standing Committees, with representatives of the 25 member states, and approved if at least a minimum number of votes are obtained.

Commission Decisions are principally concerned with the application of existing Regulations and Directives, and since 1988 the procedure for developing Decisions has become easier and faster. The principal concern now is to improve and harmonise, at international level, the conditions under which animals are used in different fields (in particular, agriculture and scientific research). Taking into account new scientific evidence and practical experience acquired, existing legal instruments will be adapted and new ones will be created to facilitate the implementation of the five European Conventions for the protection of animals, namely:

- the European Convention for the protection of animals during international transport (1968) (2)
- the European Convention for the protection of animals kept for farming purposes (1976) (3)
- the European Convention for the protection of animals for slaughter (1979) (4)
- the European Convention for the protection of vertebrate animals used for experimental and other scientific purposes (1986) (5)
- the European Convention for the protection of pet animals (1987) (8).

This paper deals principally with the areas of animal welfare and the protection of experimental animals as outlined in the Convention for the protection of animals kept for farming purposes and the Convention for the protection of vertebrate animals used for experimental and other scientific purposes.

Biotechnology and the protection of experimental animals in the European Union

Council Directive 86/609/EEC

The work of the Council of Europe on animal protection was started during the 1960s when it recognised that respect for animals counted among the ideals and principles which were the common heritage of its member states.

The basis of legislation on experimental animals is Council Directive 86/609/EEC of 24 November 1986 (7), which

deals with the housing, use, handling and slaughter of experimental animals in laboratories and with the activities of the breeding establishments that supply experimental animal species.

Directive 86/609 follows the three Rs concept developed by Russell and Burch in 1956, which states that those working with experimental animals should aim to **replace** or **reduce** the use of animals in specific laboratory procedures, or **refine** procedures so that animals experience less pain or suffering (34). The three Rs are central to reducing the number, or improving the living conditions, of experimental animals, and to replacing the use of experimental animals with other biotechnological methods. Two Articles of the Directive in particular are related to this concept:

- Article 7.2 states that ‘an experiment shall not be performed if another scientifically satisfactory method of obtaining the result sought, not entailing the use of an animal, is reasonably and practicably available’ (7)
- Article 23.1 states that ‘the Commission and Member States should encourage research into the development and validation of alternative techniques which could provide the same level of information as that obtained in experiments using animals but which involve fewer animals or which entail less painful procedures, and shall take such other steps as they consider appropriate to encourage research in this field’.

Clearly, these two articles are consistent with the three Rs concept and, in particular, with the most desirable of the three Rs, which is the replacement of the use of animals by other methods. In spite of this, one of many criticisms of Directive 86/609 is that it ‘does not explicitly mention the concept of the 3 Rs – Reduction, Refinement and Replacement’ (23). To be useful, the concept should be continuously and actively pursued.

However, it is not easy to replace the use of experimental animals with other tests (e.g. to substitute *in vivo* with *in vitro* assays) or to require that such substitution tests be used.

The rapid development of new biotechnologies has made it particularly important to find alternatives to the use of experimental animals and has also necessitated a revision of some of the relevant legislation. For example, it became increasingly apparent that Directive 86/609 needed to be revised, and many local, national and international groups of European citizens lobbied the Commission to undertake a revision. Three European groups were particularly keen to see the Directive revised: the European Centre for the Validation of Alternative Methods (ECVAM), the European Biomedical Research Association and the Eurogroup for Animal Welfare.

To revise the Directive, the Commission convened a Technical Expert Working Group, which completed the revision in November 2003. The conclusions were reported in four chapters: 'scope', 'authorisation', 'ethical review' and 'cost-benefit analysis and severity classification'.

European Centre for the Validation of Alternative Methods

For a new test to replace an *in vivo* test, the new test must be validated, i.e. submitted to a process by which the reliability and relevance of a procedure are established for a specific purpose. It was principally for this reason that ECVAM was established in 1992. The Centre campaigns for the active support of the development, validation and acceptance of methods that conform to the three Rs concept, as well as coordinating the validation of alternative test methods at EU level and promoting dialogue between the various stakeholders involved in substitution methods.

In 1995, the ECVAM published recommendations concerning the practical and logistical aspects of validating alternative test methods (1), based on the five principal stages in the evolution of new substitution tests, i.e. test development, prevalidation, validation, independent assessment and progression towards regulatory acceptance. Furthermore, ECVAM has been an active supporter of the new EU policies on animal testing for the cosmetic (21) and chemical industries (the newly proposed REACH system: Registration, Evaluation and Authorisation of Chemicals).

The ECVAM Scientific Information Service has a comprehensive database of information on various aspects of alternative assays. The reports and recommendations of ECVAM workshops and Taskforce meetings are published in *ATLA (Alternatives to Laboratory Animals)* and are available at <http://ecvam.jrc.it/index.htm>.

Animal transgenesis and cloning

Animal transgenesis and cloning are by far the most promising biotechnologies involving animals and, at the same time, the most worrying.

Transgenesis

Transgenic animals are 'genetically modified organisms', which are defined in article 2.2 of Directive 2001/18/EC as 'an organism, with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination' (19). This Directive deals with the deliberate release of such organisms into the environment; other than the definition, it contains no specific reference to animal transgenesis.

Protection of transgenic animals falls under Directive 86/609 which addresses the protection of all animals used for experimental and other scientific purposes. For example, article 2d defines 'experiment' as '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'. Furthermore article 24 states that the Directive 'shall not restrict the right of the member states to apply or adopt stricter measures for the protection of animals used in experiments or for the control and restriction of the use of animals for experiments'. However, although Directive 86/609 does provide some protection for experimental animals that have been genetically modified, this situation is criticised because 'experiments on transgenic animals, cloning and xenotransplantation, require specific attention' (26).

Common feeling and ethics suggest that the wellbeing of a transgenic animal should be at least as good as that of its unchanged homologous counterpart. However, wellbeing is not always easy to determine. If legislation based on specific knowledge is lacking or there is uncertainty about the scientific basis for decision making, there should be recourse to the 'precautionary principle'.

Some EU member states have already passed specific laws and guidelines on the use of genetically modified animals, for example Finland (29), the Netherlands (30) and the United Kingdom (28).

At present, the potential of transgenesis appears limitless; furthermore, the breeding of transgenic animals would allow the benefits of this technology to be utilised on a large scale. It can be used in both medical research and agriculture, as follows:

- to study patterns of human disease, to produce experimental animals tailored for the study of genes or to generate organs for xenotransplantation
- to synthesise chemical substances needed in medicine, for example through blood or milk
- to obtain animals with better food conversion, resistance to diseases, etc.

Cloning

Cloning is another rapidly growing technology, which has been used in the last two decades to obtain 'copy animals' through nuclear transfer and embryo splitting. Recently it has become possible to clone animals from adult somatic cells, as in the famous lamb Dolly, which was the first in a series of clones of many animal species.

In the opinion of the Group of Advisers to the European Commission on the Ethical Implications of Biotechnology (GAIEB), cloning may well be able to contribute to human

wellbeing, and in a recent report on the ethical aspects of animal cloning techniques (27) they cite the following potential uses of the technology:

- in medical research (to generate models for human diseases; to produce proteins such as milk proteins to be used for therapeutic aims; and as a source of organs for xenotransplantation)
- in agriculture (to select or produce animals with desirable qualities, such as longevity and resistance to disease).

The cloning of farm animals may have medical, agricultural and economic benefits, but according to GAIEB Opinion No. 7 on the genetic modification of animals, it is acceptable only when the aims and methods are ethically justified and when it is carried out under ethical conditions (26). These ethical conditions involve:

- a duty to avoid or minimise animal suffering; unjustified or disproportionate suffering is unacceptable
- a duty to reduce, replace and, when possible, refine research experiments that use animals (the three Rs concept)
- demonstrating the lack of better alternatives
- a human responsibility for animals, nature and the environment, including biodiversity
- paying particular attention to the need to preserve genetic diversity.

Legal protection for biotechnological inventions

Obtaining animals or animal products by transgenesis or cloning is a very long and expensive procedure. It is understandable, therefore, that companies using these technologies have sought legal protection for their biotechnological inventions. However, the patentability of biological materials is a matter of considerable public concern, particularly where the patent concerns animals or the human body.

Directive 98/44/EC (17) addresses the legal protection of biotechnological inventions and includes the following provisions:

- Article 3 states that inventions shall be patentable if they are new, involve an inventive step and are likely to have industrial applications
- Article 4 states that animal varieties and biological processes for the production of animals are not patentable, but that inventions that concern animals are patentable if the invention is not confined to a particular animal variety

– Article 6 (2, d) states that processes for modifying the genetic identity of animals which are likely to cause them suffering without any substantial medical benefit to man or animal (and animals resulting from such processes) are considered unpatentable

– Article 7 states that the Commission's European Group on Ethics in Science and New Technologies evaluates all ethical aspects of biotechnology.

It is interesting that article 6 (2, d) does permit some flexibility, i.e. processes for modifying the genetic identity of an animal are unpatentable if they are likely to cause suffering 'without any substantial medical benefit to man or animal'. This means that such processes are patentable if they will be of ultimate benefit to man, e.g. process to produce animals that will be used in medical experiments and drug testing (e.g. the 'oncomouse', a type of laboratory mouse which has been genetically modified to carry a gene that significantly increases its susceptibility to cancer).

A high sense of morality in the treatment of animals is a particular feature of EU legislation.

Biotechnology reagents for the diagnosis of animal diseases

Improving animal health requires better control of animal diseases and biotechnology has been helpful in this respect as it has led to the development of quality reagents such as monoclonal antibodies and recombinant antigens. When assembled into *in vitro* diagnostic kits, these reagents allow for the laboratory diagnosis of most of the metabolic, parasitic and infectious diseases that affect livestock and companion animals.

Methods and standards for the diagnosis of infectious diseases listed by the OIE (World Organisation for Animal Health), and therefore notifiable to national Veterinary Services, are described in the OIE *Manual of diagnostic tests and vaccines for terrestrial animals* (33). (New criteria for listed diseases were adopted by the OIE International Committee in May 2004. There are now no longer two different lists, A and B, but one single list. For inclusion on the list, diseases are first evaluated in terms of their potential for international spread, then in terms of their zoonotic potential and/or their capacity to cause significant mortality and/or morbidity within naïve populations.)

The only *in vitro* diagnostic kits that fall under EU legislation (Regulation 1053/2003 [22]) are those for the rapid diagnosis of bovine spongiform encephalopathy. The use of *in vitro* diagnostic kits for diseases that are not governed by EU regulations but which appear on the former OIE list A (i.e. diseases of serious socio-economic or public health consequence which have the potential for

very serious and rapid spread) (33), is subject to legal restrictions in the member states because any incidence of a disease on the former OIE list A must be reported to the relevant veterinary authorities. This should effectively prevent the use of diagnostic kits for list A diseases outside the official network of national or community reference laboratories and without the use of standards specified by the OIE.

A number of *in vitro* diagnostic kits are available from commercial companies for the diagnosis and control of many non-listed diseases. Some member states do not have any regulations relating to these kits, but most countries have adopted one or more of the following:

- official registration of the *in vitro* kit and official testing of different batches
- classification of the *in vitro* kit as a medicinal veterinary product
- mandatory registration of *in vitro* kits
- automatic acceptance of an *in vitro* kit if it has been registered in another EU country
- seeking the opinion of experts in veterinary research institutes.

The European Union and animal welfare

The Treaty of Amsterdam, which came into force on 1 May 1999, established new ground rules for the actions of the EU on animal welfare in a special 'Protocol on the Protection and Welfare of Animals' (16). The protocol recognises that animals are sentient beings and obliges European institutions to pay full regard to the welfare requirements of animals when formulating and implementing EU legislation. The protocol also defines the limits of EU competence to legislate.

The mission of the European Food Safety Authority (EFSA) in relation to the protection of animals and to animal health and welfare is to provide scientific advice and technical support in the formulation of the legislation and policies of the EU.

The areas of EFSA's scientific activities that are related to animal health include:

a) the provision of scientific opinions and advice in response to questions formally addressed to EFSA by the European Commission (currently the principal consumer), the European Parliament, the member states or EFSA itself (i.e. through 'self-tasking')

b) the monitoring of specific risk factors and diseases, and the provision of scientific opinions on tests and other tools to control these

c) the application and promotion of new and harmonised scientific approaches to and methodologies for hazard and risk assessment.

One of the objectives of EFSA's 2004 work programme was to seek to build scientific networks involving EU institutions, national authorities, scientific institutions and international organisations, in order to do the following:

- facilitate the exchange of information and expertise
- evaluate possible collaboration in areas of mutual interest
- continuously improve its own scientific knowledge and expertise.

European Union legislation regarding animal welfare

Although it might be argued that animal welfare issues do not strictly fall within the food safety control system, the two are, of course, inextricably linked, and animal welfare issues will have a direct impact on food safety in areas such as on-farm animal welfare, animal welfare during transport and animal welfare at slaughter. Furthermore, animal welfare issues could be a barrier to trade within the EU (in cases of non-compliance) but not to trade between member states and countries outside the EU.

The first directives governing animals kept on the farm were adopted in 1986 and concerned the protection of laying hens (6, 9). In 1998, Council Directive 98/58/EC (18) gave general rules for the protection of animals of all species, including fish, reptiles and amphibians, that are kept for the production of food, wool, skin or fur or for other farming purposes. These rules are based on the European Convention for the protection of animals kept for farming purposes (3). The rules reflect the so-called 'five freedoms' adopted by the Farm Animal Welfare Council (25), namely:

- freedom from hunger and thirst – by ready access to fresh water and a diet to maintain full health and vigour
- freedom from discomfort – by providing an appropriate environment including shelter and a comfortable resting area
- freedom from pain, injury or disease – by prevention or rapid diagnosis and treatment
- freedom to express normal behaviour – by providing sufficient space, proper facilities and company of the animal's own kind

– freedom from fear and distress – by ensuring conditions and treatment which avoid mental suffering.

European Union legislation lays down minimum standards for the welfare conditions of farm animals, as it does for experimental animals. National governments may adopt more stringent rules provided that they are compatible with the provisions of the Treaty of Amsterdam.

International approach: World Trade Organization, World Organisation for Animal Health, Food and Agriculture Organization and Council of Europe

The OIE has been the principal international animal health organisation for 80 years, and in 1995, at the inception of the World Trade Organization (WTO), it was designated the world reference organisation for animal health in the WTO Sanitary and Phytosanitary (SPS) Agreement (35). More recently, OIE Member Countries expressed their wish that the Organisation provide international leadership in the area of animal welfare, and in its 2001-2005 strategic plan the OIE identified this issue as a priority. Member Countries have sought to increase their understanding of animal welfare in order to propose innovative recommendation in response to public concerns in this area.

Animal welfare is not currently covered by the WTO agreement on SPS measures (35). Nevertheless, OIE Member Countries wish to have guidelines and recommendations on the subject drawn up by the OIE to assist them in their trade negotiations with other countries. The Director General of the OIE convened an ad hoc group on animal welfare to address these issues and the International Committee unanimously adopted its recommendations at its 70th General Session in May 2002 (31). A permanent working group on animal welfare was then established, which held its first meeting in October 2002. On 23 February 2003 the First OIE International Conference on Animal Welfare took place, where the leadership of the OIE on animal welfare issues was internationally recognised.

It was decided that the OIE would initially give priority to animal welfare issues relating to animals used in agriculture and aquaculture. Within these target groups, the OIE will begin by examining the conditions of transport, slaughter and killing for disease control, and will then move on to examine housing and management.

In addition, the OIE will assume the following specific roles in the area of animal welfare:

– to develop standards and guidelines leading to good animal welfare practices

– to identify where research into animal welfare is needed and to encourage collaboration among research centres

– with the support of leading international experts, to provide expertise on specific animal welfare issues to OIE stakeholder groups, other international organisations, animal production sectors, industry and consumer groups (32).

Among the five European animal protection conventions (2, 3, 4, 5, 8), the 1976 Convention for the Protection of animals kept for farming purposes (3) is a 'framework convention' that sets out principles for the keeping, care and housing of animals, particularly in intensive breeding systems. A Standing Committee for Animal Protection (T-AP), composed of representatives of the Parties to the Convention, is responsible for making more detailed recommendations to the Parties concerning particular animal species and implementing the principles set out in the Convention. The T-AP follows developments in scientific research and new methods of animal husbandry. The recommendations of the T-AP differ from the final recommendations of the Council of Europe (voted by the Committee of Ministers as representatives of the member states) in that they become binding on the Parties six months after their adoption. The T-AP works closely with non-governmental organisations representing the different groups concerned: veterinarians, farmers, animal protection associations, animal behaviour specialists and zoo technicians; these non-governmental organisations participate as observers in meetings of the T-AP.

Twelve recommendations have been adopted by the T-AP since 1976. The recommendations refer to pigs, cattle, sheep, goats, domestic fowl, ratites, ducks, domestic geese, Muscovy ducks and hybrids of Muscovy and domestic ducks, fur animals, and turkeys.

In 1992, a Protocol of Amendment to the Convention for the protection of animals kept for farming purposes was opened for signature (13). This Protocol provides for the scope of the Convention to be extended to the breeding of animals produced as a result of genetic modification or novel genetic combinations. The Protocol is not yet in force, and currently animals may be fed with food that contains genetically modified organisms.

The Council of Europe is currently drafting two new recommendations concerning rabbits and farmed fish, respectively. In addition, the Council has adopted a new recommendation concerning pigs which will come into force on 2 June 2005, replacing the recommendation adopted in 1986.

Owing to the current framework of EU legislation and the impact of the WTO and the SPS Agreement (35), some

recommendations could face problems because of the reluctance of some countries to accept specific concrete recommendations (densities, space allowances, etc.) in the absence of a complete scientific review and scientific justification.

Conclusion

Article III-121 of the Treaty establishing a Constitution for Europe (24), signed in Rome on 29 October 2004, says:

‘In formulating and implementing the Union’s agriculture, fisheries, transport, internal market, research and technological development and space policies, the Union and the Member States shall, since animals are sentient beings, pay full regard to the requirements of animal welfare, while respecting the legislative or administrative provisions and customs of Member States relating in particular to religious rites, cultural traditions and regional heritage’.

This article is the culmination of the efforts of competent and qualified European groups to obtain dignity for animals as ‘sentient beings’ rather than mere ‘goods’ or ‘property’.

However, the Sixth European Framework Programme on life sciences (20) selected life sciences, genomics and

biotechnology for health as priority themes, in line with a major political and strategic choice of the Union and in response to the expectations of society, at global as well as European level. Developing biotechnology and genomic studies will have a dramatic impact on experimental animal species. As a result, these conflicting aims adequate regulatory legislation.

European legislation for the protection of experimental animals and the welfare of breeding animals is produced only after careful and specialised evaluation of scientific, veterinary and ethical aspects of animal protection. Therefore, a high sense of morality is a particular feature of this part of EU legislation.

Acknowledgements

We thank Professor Mariachiara Tallacchini (Università Cattolica, Piacenza, Italy) and Dr Ana Mateo Rosell (European Patent Office, Berlin, Germany).



Appendix

Other European legislation relating to the protection of farm animals

Further information can be found on the Animal Health and Welfare pages of the website of the European Union at http://europa.eu.int/comm/food/animal/index_en.htm.

General

Treaty of Amsterdam amending the Treaty on European Union, the Treaties establishing the European Communities and certain related acts – Protocol annexed to the Treaty of the European Community – Protocol on protection and welfare of animals (16).

Calves

Council Directive 91/629/EEC of 19 November 1991 laying down minimum standards for the protection of calves (11).

Pigs

Council Directive 91/630/EEC of 19 November 1991 laying down minimum standards for the protection of pigs (12).

Protection at the time of slaughter and killing

Council Directive 93/119/EC of 22 December 1993 on the protection of animals at the time of slaughter or killing (14).

Protection during transport

Council Directive 91/628/EEC of 19 November 1991 on the protection of animals during transport and amending Directives 90/425/EEC and 91/496/EEC (10).

Wildlife Trade Legislation

Council Regulation No. 338/97 of 9 December 1996 on the protection of species of wild fauna and flora by regulating trade therein (15).

Biotechnologie, santé animale et bien-être animal dans le cadre de la législation de l'Union européenne

F. De Simone & J. Serratos

Résumé

Des animaux d'expérimentation et des animaux d'élevage sont utilisés dans la recherche biomédicale et dans les études de biotechnologie destinées à améliorer la productivité agricole. La législation européenne, qui s'inspire des lois nationales existantes concernant la santé et le bien-être des animaux, est adoptée après plusieurs sessions préliminaires au cours desquelles sont recueillis le concours et l'avis de grands groupes de la société européenne. On prête une attention particulière aux opinions exprimées par les associations d'éthique et de protection des droits des animaux, qui soulignent que les animaux doivent être considérés comme des « êtres sensibles » et non comme de simples « biens » ou « marchandises ». Une déclaration à cet effet est incluse dans le Traité établissant une Constitution pour l'Europe, signé à Rome en 2004 par les 25 États Membres de l'Union européenne.

Mots-clés

Bien-être animal – Biotechnologie – Législation – Protection des animaux – Santé animale – Union européenne.



Biotecnología, sanidad y bienestar animal en la legislación de la Unión Europea

F. De Simone & J. Serratosa

Resumen

La biomédica y la biotecnología emplean animales de laboratorio y de granja para sus investigaciones dirigidas a mejorar la productividad pecuaria. La legislación Europea, que se basa en las legislaciones nacionales en vigor relativas a la sanidad y el bienestar animal, se aprueba tras varias reuniones preliminares en las que se recaban las contribuciones y opiniones de amplios sectores de la sociedad europea. En ellas se presta una especial atención a los pareceres de las asociaciones dedicadas a la defensa de la ética y los derechos de los animales y que sostienen que estos últimos deben tratarse como "seres sensibles", y no como simples "mercaderías" o "bienes". El Tratado por el que se establece la Constitución Europea, suscrito en Roma por los 25 Estados Miembros de la UE, incluye una disposición a esos efectos.

Palabras clave

Bienestar animal – Biotecnología – Legislación – Protección de los animales – Sanidad animal – Unión Europea.



References

1. Balls M., Blaauboer B.J., Fentem J.H., Bruner L., Combes R.D., Ekwall B., Fielder R.J., Guillouzo A., Lewis R.W., Lovell D.P., Reinhardt C.A., Repetto G., Sladowski D., Spielmann H. & Zucco F. (1995). – Practical aspects of the validation of toxicity test procedures. The report and recommendations of ECVAM workshop 5. *ATLA*, **23**, 129-147.
2. European Communities (EC) (1968). – European Convention for the Protection of Animals during International Transport. Paris, 13.XII.1968. European Treaty Series No. 65. Website: www.conventions.coe.int/Treaty/en/Treaties/Html/065.htm (accessed on 11 April 2005).
3. European Communities (EC) (1976). – European Convention for the Protection of Animals kept for Farming Purposes. Strasbourg, 10.III.1976. European Treaty Series No. 87. Website: www.conventions.coe.int/Treaty/EN/Treaties/Html/087.htm (accessed 11 April 2005).
4. European Communities (EC) (1979). – European Convention for the Protection of Animals for Slaughter. Strasbourg, 10.V.1979. European Treaty Series No. 102. Website: www.conventions.coe.int/Treaty/EN/Treaties/Html/102.htm (accessed on 11 April 2005).
5. European Communities (EC) (1986). – European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes. Strasbourg, 18.III.1986. European Treaty Series No. 123. Website: www.conventions.coe.int/treaty/en/treaties/html/123.htm (accessed on 11 April 2005).
6. European Communities (EC) (1986). – Council Directive 86/113/EEC of 25 March 1986 laying down minimum standards for the protection of laying hens kept in battery cages. *Off. J. Eur. Communities*, **L 095**, 10/04/1986, 45-48.
7. European Communities (EC) (1986). – Council Directive 86/609/EEC of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes. *Off. J. Eur. Communities*, **L 358**, 18/12/1986, 1-28.
8. European Communities (EC) (1987). – European Convention for the Protection of Pet Animals. Strasbourg, 13.XI.1987. European Treaty Series No. 125. Website: www.conventions.coe.int/Treaty/EN/Treaties/Html/125.htm (accessed on 11 April 2005).

9. European Communities (EC) (1988). – Council Directive 88/166/EEC of 7 March 1988 complying with the judgment of the Court of Justice in Case 131/86 (annulment of Council Directive 86/113/EEC of 25 March 1986 laying down minimum standards for the protection of laying hens kept in battery cages). *Off. J. Eur. Communities*, **L 074**, 19/03/1988, 83-87.
10. European Communities (EC) (1991). – Council Directive 91/628/EEC of 19 November 1991 on the protection of animals during transport and amending Directives 90/425/EEC and 91/496/EEC. *Off. J. Eur. Communities*, **L 340**, 11/12/1991, 17-27.
11. European Communities (EC) (1991). – Council Directive 91/629/EEC of 19 November 1991 laying down minimum standards for the protection of calves. *Off. J. Eur. Communities*, **L 340**, 11/12/1991, 28-32.
12. European Communities (EC) (1991). – Council Directive 91/630/EEC of 19 November 1991 laying down minimum standards for the protection of pigs. *Off. J. Eur. Communities*, **L 340**, 11/12/1991, 33-38.
13. European Union (EU) (1992). – Protocol of Amendment to the European Convention for the Protection of Animals kept for Farming Purposes. Strasbourg, 6.II.1992. European Treaty Series No. 145. Website: www.conventions.coe.int/Treaty/EN/Treaties/Html/145.htm (accessed on 11 April 2005).
14. European Union (EU) (1993). – Council Directive 93/119/EC of 22 December 1993 on the protection of animals at the time of slaughter or killing. *Off. J. Eur. Communities*, **L 340**, 31/12/1993, 21-34.
15. European Union (EU) (1997). – Council Regulation (EC) No. 338/97 of 9 December 1996 on the protection of species of wild fauna and flora by regulating trade therein. *Off. J. Eur. Communities*, **L 061**, 03/03/1997, 1-69.
16. European Union (EU) (1997). – Treaty of Amsterdam amending the Treaty on European Union, the Treaties establishing the European Communities and certain related acts – Protocol annexed to the Treaty of the European Community – Protocol on protection and welfare of animals. *Off. J. Eur. Communities*, **C 340**, 10/11/1997, 110.
17. European Union (EU) (1998). – Directive 98/44/EC of the European Parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions. *Off. J. Eur. Communities*, **L 213**, 30/07/1998, 13-21.
18. European Union (EU) (1998). – Council Directive 98/58/EC of 20 July 1998 concerning the protection of animals kept for farming purposes. *Off. J. Eur. Communities*, **L 221**, 08/08/1998, 23-27.
19. European Union (EU) (2001). – Directive 2001/18/EC of the European Parliament and of the Council of 12 March 2001 on the deliberate release into the environment of genetically modified organisms and repealing Council Directive 90/220/EEC - Commission Declaration. *Off. J. Eur. Communities*, **L 106**, 17/04/2001, 1-39.
20. European Union (EU) (2002). – Decision No 1513/2002/EC of the European Parliament and of the Council of 27 June 2002 concerning the sixth framework programme of the European Community for research, technological development and demonstration activities, contributing to the creation of the European Research Area and to innovation (2002 to 2006). *Off. J. Eur. Communities*, **L 232**, 29/08/2002, 1-33.
21. European Union (EU) (2003). – Directive 2003/15/EC of the European Parliament and of the Council of 27 February 2003 amending Council Directive 76/768/EEC on the approximation of the laws of the Member States relating to cosmetic products (Text with EEA relevance). *Off. J. Eur. Communities*, **L 066**, 11/03/2003, 26-35.
22. European Union (EU) (2003). – Commission Regulation (EC) No 1053/2003 of 19 June 2003 amending Regulation (EC) No 999/2001 of the European Parliament and of the Council as regards rapid tests (Text with EEA relevance). *Off. J. Eur. Union*, **L 152**, 20/06/2003, 8-9.
23. European Union (EU) (2004). – Revision of Directive 86/609/EEC on the protection of Animals used for Experimental and other Scientific purposes. Website: www.europa.eu.int/comm/environment/chemicals/lab_animals/revision_en.htm (accessed on 11 April 2005).
24. European Union (EU) (2004). – Treaty establishing a Constitution for Europe. Part III: The Policies and Functioning of the Union. Title I: Provisions of General Application, Article III-121. *Off. J. Eur. Union*, **C 310**, 16/12/2004, 55-56.
25. Farm Animal Welfare Council. – The 5 freedoms. Website www.fawc.org.uk/freedoms.htm (accessed on 11 April 2005).
26. Group of Advisers to the European Commission on the Ethical Implications of Biotechnology (GAIEB) (1996). – Ethical aspects of genetic modification of animals. Opinion No. 7, 21 May 1996. Website: www.europa.eu.int/comm/european_group_ethics/gaieb/en/opinion7.pdf (accessed on 11 April 2005).
27. Group of Advisers to the European Commission on the Ethical Implications of Biotechnology (GAIEB) (1997). – Ethical aspects of cloning techniques. Opinion No. 9, 28 May 1997.
28. Home Office of the British Government (1992). – Supplementary guidance to applicants for project licences: projects to generate and/or maintain genetically modified animals. Website: www.homeoffice.gov.uk/docs/sub_transgenic.html (accessed on 11 April 2005).
29. Ministry of Social Affairs and Health Finland, Board of Gene Technology (1995). – Gene Technology Act (377/1995).
30. Ministry of Welfare, Public Health and Cultural Affairs, the Netherlands (1997). – Revised Experiments on Animals Act, 5 February 1997.
31. OIE (World Organisation for Animal Health) (2002). – Resolution XIV: animal welfare mandate of the OIE. In Resolutions adopted by the International Committee of the OIE during its 70th General Session, 26 May-31 May. OIE, Paris, 31-33.

32. OIE (World Organisation for Animal Health) (2002). – The OIE's initiatives in animal welfare. Website: www.oie.int/eng/bien_etre/en_introduction.htm (accessed on 11 April 2005).
 33. OIE (World Organisation for Animal Health) (2004). – Manual of diagnostic tests and vaccines for terrestrial animals, 5th Ed. OIE, Paris, 1178 pp.
 34. Russell W.M.S. & Burch R.L. (1959). – The Principles of Humane Experimental Technique. Methuen, London, 238 pp.
 35. World Trade Organization (WTO) (1995). – The results of the Uruguay Round of multilateral trade negotiations: the legal texts. WTO, Geneva, 69-84.
- 

