

International Agreements Governing Animal Use

Convention on International Trade in Endangered Species

In 1973, the Convention on International Trade in Endangered Species of Fauna and Flora (CITES) was signed by 61 nations. It has since been ratified by a total of 81 separate nations and has been enforced in the United States since 1977 (10,11).

In addition to protecting animals from extinction, the Convention specifies in seven different places that the Management Authority must be "satisfied that any living specimen will be so transported and cared for as to minimize the risk of injury, damage to health or cruel treatment." CITES is administered on an international basis by the International Union for the Conservation of Nature and Natural Resources headquartered in Gland, Switzerland. Endangered plants and animals are listed in three Appendixes to the Convention, according to level of endangerment. For purposes of monitoring, all primates have been included in Appendix 11 ("Threatened") except chimpanzees, which are classified as "Endangered." Under CITES provisions, the effect of the Appendix 11 classification has been to require export permits for all listed primates.

The U.S. agency responsible for administration of CITES provisions is the Research Division of the Fish and Wildlife Service, Department of the Interior, which has additional responsibilities regarding international trade in endangered or threatened species under Section 7 of the Endangered Species Act of 1973. (For a brief discussion of how this act affects experimentation in the United States, see ch. 13.) Current CITES Appendixes listings, by species of wildlife and family of plants, can be found in part 23 of title 50 of the Code of **Federal Regulations**; lists of endangered and threatened wildlife species and plant families affected by the Endangered Species Act are found in part 17.

The Convention's importance to research is twofold. First, it has limited trade in nonhuman primates and a few other species favored at one time or another in experiments (1). Second, continued review of the Convention by signatories has served as a forum for discussion of protection of laboratory animals. CITES signatories meet periodically in conferences, convened under CITES provisions, to discuss the required classification of species according to the terms of the Convention. Under regulations promulgated by the Fish

and Wildlife Service (50 CFR 23.31-,39), members of the public must be given notice of the U.S. negotiating position at CITES conferences and an opportunity to provide information and comments on the proposed agenda, including at least one public meeting. Humane groups have used these meetings to raise the issue of humane treatment of laboratory-animal species in relation to the Convention's articles (12). Recently, for example, CITES delegates were petitioned to ratify proposed interpretations of the Convention to reach that very question. The petition was ruled outside the terms of the Convention (9).

Bans on Exporting Primates

From time to time, nations with indigenous populations of nonhuman primates that have been in demand for various types of traditional research have considered or implemented prohibitions on their export, either to protect dwindling populations or because of high mortality rates suffered in transit. India ordered such a ban in 1955, for the latter reason. Because rhesus monkeys were in demand for testing polio vaccines at the time, India agreed to reopen trade with the United States on condition that the Surgeon General sign a certificate of need for each order of monkeys, with assurances that they be used humanely and only for medical research and vaccine production. The ban was reimposed by the Indian Government when it was revealed that military experiments, specifically prohibited under the agreement, were being done with some of the monkeys. Other countries have considered similar bans or have imposed ceilings on exports. Bans were enacted in Malaysia and Bolivia in 1984, and a U.S. dealer was ousted from Bangladesh in 1979 for selling Rhesus monkeys for military research (5). Some commentators have been critical of U.S. estimates of need for nonhuman primates in research, finding them overstated, and have faulted the research community for attempts to circumvent export bans (13).

Draft Convention of the Council of Europe

The Council of Europe, headquartered in Strasbourg, France, and with 21 member countries, was organized in 1949 to work for greater European unity,

to improve the conditions of life and develop humane values in Europe, and to uphold the principles of parliamentary democracy (6).

Historically, the Council has been concerned about the treatment of animals. It has drafted Conventions on the protection of animals in international transport (1968), on those kept for farming purposes (1976), on slaughter (1979), and on conservation of European wildlife and natural habitats (1979). In 1971, the Council adopted Recommendation 621, which contained three relevant proposals:

- Establish a documentation and information center on alternatives to animal use in testing and experimentation.
- Establish tissue banks for research.
- Establishment of an Ad Hoc Committee of Experts to study the problems rising out of the abuse of live animals for experimental industrial purposes. The Committee was given the task of drafting international legislation setting out the conditions under which, and the scientific grounds on which, experiments on live animals may be authorized (15).

The Ad Hoc Committee of Experts for the Protection of Animals began its work on the Draft Convention in 1978. In 1983, the committee presented a Draft Convention, guidelines for care and treatment, and a guidance note on data collection to the Council of Ministers plenary sessions and seven working party meetings under three successive chairmen. The committee was composed of experts from member countries. Observers from the United States and Europe, including representatives from several nongovernmental organizations (World Society for the Protection of Animals, Federation of Veterinarians of the European Economic Community, European Federation of Pharmaceutical Industries' Associations, and the International Council for Laboratory Animal Science) were admitted to the committee's meetings (2,14).

The form of the Draft Convention follows an earlier one on the treatment of farm animals. Its preamble, restating the general objective of European unity in the context of protection of experimental animals, balances the need of “man in his quest for knowledge, health and safety . . . to use animals where there is a reasonable expectation that the result will be to extend knowledge or be to the overall benefit of man or animal, just as he uses them for food, clothing and as beasts of burden” against the “moral obligation to respect all animals and to exercise due consideration for their capacity for suffering and memory.” As stated in the preamble, the general objective of the Convention is “(to limit wherever practicable the use of animals for experimental and other scientific purposes,

in particular by seeking alternative methods to replace the use of animals” (2).

Prospects for final ratification of the Draft Convention remain unclear. Twice in 1983 the Council's assembly failed to achieve the required two-thirds vote on the committee's report to urge the Committee of Ministers to adopt it as soon as possible. Reported accounts stated that some delegates did not believe the Convention goes far enough in controlling animal experimentation. The assembly, however, rejected amendments that would have outlawed the use of experimental animals (8).

The Convention itself is divided into 10 parts, which are summarized below.

General Principles

Article 1 applies the Convention “to any animal being used or intended for use in any experimental or other scientific procedure where that procedure may cause pain, suffering, distress, or lasting harm. It does not apply to any nonexperimental agricultural or clinical veterinary practice.” “Animal” means, “**unless otherwise qualified . . . any live non-human vertebrate, including free-living larval and/or reproducing larval forms, but excluding other foetal or embryonic forms.**” “(Procedure” is defined to include:

. . . any experimental or other scientific use of an animal which may cause it pain, suffering, distress or lasting harm, including any course of action intended to, 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; a procedure starts when the animal is first prepared for use and ends when no further observations are to be made for that procedure; the elimination of pain, suffering, distress or lasting harm by the successful use of anesthesia or analgesia or other methods does not place the use of an animal outside the scope of this definition.

Article 2 provides that a defined procedure can be performed on an animal for only one or more of the following purposes, subject to other restrictions contained in the Convention:

- the avoidance or prevention of disease, ill health or other abnormality, or their effects, in humans, vertebrate or invertebrate animals, or plants, including the production and the quality, efficacy, and safety testing of drugs, substances, or products;
- the diagnosis or treatment of disease, ill health or other abnormality, or their effects, in humans, vertebrate or invertebrate animals, or plants;
- the assessment, detection, regulation or modification of physiological conditions in humans, vertebrate and invertebrate animals, or plants;

- the prolongation or saving of life of humans, vertebrate or invertebrate animals or plants;
- the protection of the environment;
- the production and quality control of foodstuffs;
- the breeding of vertebrate or invertebrate animals; . scientific research;
- education and training; or
- forensic inquiries.

Article 3 requires all member nations “to take all necessary steps to give effect to [its] provisions . . . and to ensure an effective system of control and supervision” within 5 years of the Convention’s approval for ratification.

Article 4 stipulates that ratification by a member country does not bar it from adopting stricter measures to control experimental animal *use*.

General Care and Accommodation

Article 5 requires any animal to be used in a procedure to be provided with “accommodation, an environment, at least a minimum freedom of movement, food, water, and care all appropriate to its health and well-being. Any restriction on the extent to which an animal can satisfy its physiological and ethnological needs shall be limited as far as practicable.” Environmental conditions must be checked daily and as needed to prevent avoidable suffering.

Conduct of Procedure

Article 6 requires that procedures not be performed where “another scientifically satisfactory method, not entailing the use of an animal, is reasonably and practicably available,” and asks member nations to “encourage, if possible, scientific research into the development of methods which could provide the same information as that obtained in procedures.”

Article 7 requires careful consideration of choice of species in procedures and that choices be explained, where required, to the responsible authority. Procedures should use the minimum number of animals, cause the least pain, suffering, distress, or lasting harm consistent with providing satisfactory results.

Article 8 requires all procedures to be performed under general or local anesthetic or by other methods designed to eliminate to the extent practicable pain, suffering, distress, or lasting harm unless the methods are judged to be more distressing than the procedure or are incompatible with the aim of the procedure.

Article 9 requires specific authorization of the authority where an animal may experience severe pain that is likely to endure. Authorization must be refused if the authority judges that the procedure is not of ex-

ceptional importance for meeting the essential needs of humans or animals, including the solution of scientific problems.

Article 10 declares that an animal under procedure remains subject to the provisions of article 5, except where those provisions are incompatible with the object of the procedure.

Article 11 provides for a decision at the end of procedures whether the animal shall be kept alive or killed by a humane method, subject to the condition that it shall not be kept alive if, even though it has been restored to normal health in all other respects, it is likely to remain in lasting pain or distress. Such decisions must be made by a veterinarian or a person responsible for the procedure. If an animal is not to be kept alive it should be killed by a humane method as soon as possible. Finally, the article provides that no animal be used in more than one painful procedure unless the second procedure is one in which the animal is subject throughout to general anesthesia, from which it is not allowed to recover, or the further procedure will involve minor interventions only.

Article 12 permits experimental animals to be set free as part of the procedure provided that the maximum practicable care has been taken to safeguard the animal’s well-being. Procedures that involve setting the animal free are not permitted solely for educational or training purposes.

Authorization

Article 13 provides that procedures authorized by article 2 may be performed only by authorized persons or persons under their direct responsibility, or if the project is authorized by the legislation of a member country. Only persons deemed competent by the responsible authority may be so authorized.

Breeding or Supplying Establishments

The four articles contained in this part establish principles for breeders and suppliers of experimental animals, who would be required to:

- register and comply with article 5 (article 14);
- specify a competent person in charge with authority to administer or arrange for suitable care (article 15);
- keep detailed records on breeding, shipment, and transfer, to be maintained at least 3 years from the date of last entry (article 16); and
- mark humanely for identification dogs and cats and maintain complete records to promote their identification (article 17).

User Establishments

Under the provisions of the seven articles in this part, users (i.e., experimental facilities) would be required to:

- register with national authorities and comply with article 5 (article 18);
- provide equipment and facilities appropriate for species used and to ensure that the procedures are performed as effectively as practicable with the minimum number of animals and the minimum degree of pain, suffering, distress, or lasting harm (article 19);
- identify persons administratively responsible for care and equipment, provide sufficiently trained staff, and make adequate arrangements for veterinary advice and treatment (article 20);
- use only animals supplied by registered breeders or suppliers, subject to national exceptions (article 21);
- use only mice, rats, guinea pigs, golden hamsters, rabbits, dogs, cats, or quail originating in or acquired directly from registered breeding establishments, subject to national exemptions (member countries would add species to the list, particularly primates, as soon as there is a reasonable prospect of a sufficient supply of purpose-bred animals; straying domestic animals cannot be used and exemptions are not permitted) (article 22);
- conduct procedures outside their establishments only where authorized by the national authority (article 23); and
- keep records adequate to meet the requirements of article 27 and, in addition, to show the number and species of all animals acquired, from whom acquired, and date of arrival, and to make such records available for inspections by the responsible authority (article 24).

Education and Training

Article 25 specifies that professional and training procedures must be approved by responsible authorities before being used and must be carried out by or under the supervision of a qualified person. Procedures are not permitted at or below the secondary level except when it is specifically directed to preparing for a career involving treatment or care of animals and the procedures entail no severe or enduring pain or suffering. Only the minimum measures absolutely necessary for the purpose are permitted, and only if their objective cannot be achieved by audio-visual or any other suitable methods. Article 26 requires that persons who carry out, take part in, or take care of animals used for procedures, including supervisors, must have adequate education and training.

Statistical Information

Article 27 requires each agreeing nation to collect and make public, where lawful, statistical information on animals in experimentation, including:

- numbers and kinds of animals used;
 - . numbers of animals, by categories, used in procedures directly concerned with medicine and in teaching and learning;
 - . numbers of animals, by categories, used in procedures for the protection of humans and their environment; and
- numbers of animals, by categories, used in procedures required by legislation.

Article 28 specifies that, subject to its own secrecy laws, each nation must submit information annually in the form set out in Appendix B to the Secretary General of the Council, who is required to publish it. Each nation is invited to send the name and address of the corresponding authority, to be included in the Secretary General's compilation of statistics.

Recognition of International Procedures

Article 29 binds agreeing nations to share information on results of procedures and to provide mutual assistance in order to avoid unnecessary repetition of procedures for the purposes of satisfying national legislation on health and safety.

Final Provisions

Articles 30 through 36 specify the manner and conditions under which the Convention will become ratified and effective (i.e., 6 months after four member states express their consent to be bound and, for any ratifying or acceding state after that, 6 months after written ratification or accession), and reserve a member state's right to reservation, partial application, or denunciation (2).

Appendix A of the Draft Convention

Appendix A, *Guidelines on Accommodation and Care of Animals*, contains detailed specifications for physical facilities, holding-room environments and environmental control, and care. Though the specifications are comprehensive, article 5 does refer to them as "suggested" (3).

Appendix B of the Draft Convention

Appendix B consists of *Statistical Tables and Guidance Notes for Their Completion in Fulfillment of the Requirements in Articles 27 and 28 of the Draft European Convention for the Protection of Vertebrate Ani-*

reals Used for Experimental and Other Scientific Purposes. The appendix would require submission by agreeing nations of experimental-animal data, reported to the Secretary General for each calendar year under the general classifications established by the referenced articles. The method of data collection is left to each member nation (4).

Guidelines of the Council for International Organizations of Medical Sciences

Through the World Health Organization (WHO), headquartered in Geneva, Switzerland, more than 150 nations exchange information and share resources for laboratory-animal science training, technical information, consultative support, and other activities.

In 1985, in the culmination of a 3-year effort initiated in 1982, the Council for International Organizations of Medical Sciences (CIOMS), an international nongovernmental organization representative of many branches of medicine and cognate disciplines that was established under the auspices of WHO and UNESCO in 1949, issued *International Guiding Principles for Biomedical Research Involving Animals* (7).

Modeled after the Tokyo revision of the *Declaration of Helsinki* by the World Medical Association in 1975 and CIOMS's *Proposed International Guidelines for Biomedical Research Involving Human Subjects*, issued in 1982, the CIOMS *International Guiding Principles* are intended to provide a conceptual and ethical framework for whatever regulatory measure each country chooses to adopt with respect to animal use (7).

The *International Guiding Principles* enumerate 11 basic principles, as follows (7):

- I. The advancement of biological knowledge and the development of improved means for the protection of the health and well-being both of man and of animals require recourse to experimentation on intact live animals of a wide variety of species.
- II. Methods such as mathematical models, computer simulation and in vitro biological systems should be used wherever appropriate.
- III. Animal experiments should be undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge.
- IV. The animals selected for an experiment should be of an appropriate species and quality, and the minimum number required, to obtain scientifically valid results.
- V. Investigators and other personnel should never fail to treat animals as sentient, and should re-

gard their proper care and use and the avoidance or minimization of discomfort, distress, or pain as ethical imperatives.

- VI. Investigators should assume that procedures that would cause pain in human beings cause pain in other vertebrate species although more needs to be known about the perception of pain in animals.
 - VII. Procedures with animals that may cause more than momentary or minimal pain or distress should be performed with appropriate sedation, analgesia, or anesthesia in accordance with accepted veterinary practice. Surgical or other painful procedures should not be performed on unanesthetized animals paralysed by chemical agents.
 - VIII. Where waivers are required in relation to the provisions of article VII, the decisions should not rest solely with the investigators directly concerned but should be made, with due regard to the provisions of articles IV, V, and VI, by a suitably constituted review body. Such waivers should not be made solely for the purposes of teaching or demonstration.
 - IX. At the end of, or when appropriate during, an experiment, animals that would otherwise suffer severe or chronic pain, distress, discomfort, or disablement that cannot be relieved should be painlessly killed.
 - X. The best possible living conditions should be maintained for animals kept for biomedical purposes. Normally the care of animals should be under the supervision of veterinarians having experience in laboratory animal science. In any case, veterinary care should be available as required.
 - XI. It is the responsibility of the director of an institute or department using animals to ensure that investigators and personnel have appropriate qualifications or experience for conducting procedures on animals. Adequate opportunities shall be provided for in-service training, including the proper and humane concern for the animals under their care.
- Additional special provisions accompany the basic principles. These deal with sources of supply of animal subjects; transport conditions; housing, including space allocation, hygienic standards, and protection against vermin; environmental conditions, including temperature, humidity, lighting, and social interaction; nutrition appropriate to the species; provision of veterinary care; and the keeping of records (7).
- The CIOMS statement also urges that the development and use of alternatives be actively encouraged. Specifically mentioned are nonbiological methods—such as the study of structure-activity relationships or

computer modeling—and biological methods, including the use of micro-organisms, *in vitro* preparations, and sometimes animal embryos (7).

Organization for Economic Cooperation and Development

The Organization for Economic Cooperation and Development (OECD) is a group of nations whose membership accounts for two-thirds of the world's chemical production, including the United States, Canada, Japan, and most of the countries of Western Europe. It also embraces six organizations that have a major role in international efforts to regulate chemicals (6).

In 1979-80, an international group of experts convened under the OECD's Special Program on the Control of Chemicals drafted and recommended for the Council's approval *OECD Principles of Good Laboratory Practice*. The Council approved the document in 1981 (OECD, *Guidelines for Testing of Chemicals, C(81)30* (Final), Annex 2).

Though the main purpose for adopting the *Principles* was to promote international harmonization of chemical-testing practices and thereby help safeguard the integrity of test results required under health and environmental safety laws, the document is patterned very much after good laboratory practice regulations adopted in 1978 by the U.S. Food and Drug Administration (see ch. 13). Following the *Principles'* general command would certainly have an impact on use of test animals, but they do not contain the same detailed language on animal care, management, and housing that domestic regulations do, nor are any sanctions to be levied for failure to observe them.

Appendix E References

1. Caufield, C., "Animal Treaty is No Protection," *New Scientist* 1417:43, 1984.
2. Council of Europe, Ad Hoc Committee of Experts for the Protection of Animals, *Final Activity Report, Addendum I: Draft European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes and Draft Explanatory Report* (Strasbourg, France: May 18, 1983).
3. Council of Europe, Ad Hoc Committee of Experts for the Protection of Animals, *Final Activity Report, Addendum 11: Draft European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Appendix A—Guidelines on Accommodation and Care of Animals* (Article 5 of the Draft Convention) (Strasbourg, France: May 18, 1983).
4. Council of Europe, Ad Hoc Committee of Experts for the Protection of Animals, *Final Activity Report, Addendum III: Draft European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes, Appendix E—Statistical Tables and Guidance Notes for Their Completion in Fulfillment of the Requirements in Articles 27 and 28 of the Draft Convention* (Strasbourg, France: May 18, 1983).
5. Gravitz, M., "Primates Get Top Priority," *The Animals Agenda* 5(5):4-5, 1984.
6. Held, J., "Animals in Research: An International Overview," *Cal. Vet.* 1:93-95, 1983.
7. Howard-Jones, N., "A CIOMS Ethical Code for Animal Experimentation," *WHO Chronicle* 39:51-56, 1985.
8. Japan Science Council, *On the Adoption of Guidelines for Animal Experimentation*, 80th General Meeting, Nov. 5, 1980.
9. Lazarowitz, A., Management Authority, Division of Research, Fish and Wildlife Service, U.S. Department of the Interior, Washington, DC, personal communication, August 1984.
10. Leavitt, E. (ed.), *Animals and Their Legal Rights* (Washington, DC: Animal Welfare Institute, third ed., 1978), Appendix.
11. Nay, A., et al., *Animal Welfare Laws in Foreign Countries* (Washington, DC: Library of Congress, 1976).
12. *Humane Society News*, "Update: The Good With the Bad," 28:24, 1983.
13. Rowan, A. N., *Of Mice, Models, & Men: A Critical Evaluation of Animal Research* (Albany, NY: State University of New York Press, 1984).
14. Vallier, G., "European Concepts on the Use of Laboratory Animals in Relationship With Animal Welfare Problems," *Dev. Biol. Stand.* 45:189-195, 1980.
15. Weiderkehr, M., "The Council of Europe's Conventions," *Council of Europe Forum*, March 1982, p. 7.