sored by pharmaceutical manufacturers, the manufacturers themselves should assume responsibility in case of accidents. This is particularly necessary in the case of externally sponsored research when the subjects are not protected by social security measures.

Confidentiality of Data

33. Research may involve the collection and storage of data relating to individuals, which, if disclosed to third parties, might cause harm or distress. Consequently, arrangements should be made by investigators to protect the confidentiality of such data, as for example by omitting information which might lead to the identification of individual subjects, by limiting access to the data, or other appropriate means.

INTERNATIONAL GUIDING PRINCIPLES FOR BIOMEDICAL RESEARCH INVOLVING ANIMALS

Council for International Organizations of Medical Sciences

Preamble

Experimentation with animals has made possible major contributions to biological knowledge and to the welfare of man and animals, particularly in the treatment and prevention of diseases. Many important advances in medical science have had their origins in basic biological research not primarily directed to practical ends, as well as from applied research designed to investigate specific medical problems. There is still an urgent need for basic and applied research that will lead to the discovery of methods for the prevention and treatment of diseases for which adequate control methods are not yet available—notably the noncommunicable diseases and the endemic communicable diseases of warm climates.

Past progress has depended, and further progress in the foreseeable future will depend, largely on animal experimentation which, in the broad field of human medicine, is the prelude to experimental trials on human beings of, for example, new therapeutic, prophylactic, or diagnostic substances, devices, or procedures.

There are two international ethical codes intended principally for the guidance of countries or institutions that have not yet formulated their own ethical requirements for human experimentation: the Tokyo revision of the Declaration of Helsinki of the World Medical Association (1975), and the Proposed International Guidelines for Biomedical Research Involving Human Subjects of the Council for International Organizations of Medical Sciences and the World Health Organization (1982). These codes recognize that while experiments involving human subjects are a *sine qua non* of medical progress, they must be subject to strict ethical requirements. In order to ensure that such ethical requirements are observed, national and institutional ethical codes have also been elaborated with a view to the

protection of human subjects involved in biomedical (including behavioral) research.

A major requirement both of national and international ethical codes for human experimentation, and of national legislation in many cases, is that new substances or devices should not be used for the first time on human beings unless previous tests on animals have provided a reasonable presumption of their safety.

The use of animals for predicting the probable effects of procedures on human beings entails responsibility for their welfare. In both human and veterinary medicine, animals are used for behavioral, physiological, pathological, toxicological, and therapeutic research; for experimental surgery or surgical training; and for testing drugs and biological preparations. The same responsibility toward the experimental animals prevails in all of these cases.

Because of differing legal systems and cultural backgrounds, there are varying approaches to the use of animals for research, testing, or training in different countries. Nonetheless, their use should be always in accord with humane practices. The varying approaches in different countries to the use of animals for biomedical purposes, and the lack of relevant legislation or of formal self-regulatory mechanisms in some, point to the need for international guiding principles elaborated as a result of international and interdisciplinary consultations.

The guiding principles proposed here provide a framework for more specific national or institutional provisions. They apply not only to biomedical research but also to all uses of vertebrate animals for other biomedical purposes, including the production and testing of therapeutic, prophylactic, and diagnostic substances, the diagnosis of infections and intoxications in man and animals, and to any other procedures involving the use of intact live vertebrates.

1. Basic Principles

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 regard 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 paralyzed 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.

2. Special Provisions

Where they are quantifiable, norms for the following provisions should be established by a national authority, national advisory council, or other competent body.

2.1 Acquisition. Specialized breeding establishments are the best source of the most commonly used experimental animals. Nonspecifically bred animals may be used only if they meet the research requirements, particularly for health and quality, and their acquisition is not in contradiction with national legislation and conservation policies.

2.2 Transportation. Where there are no regulations or statutory requirements governing the transport of animals, it is the duty of the director of an institute or department using animals to emphasize to the supplier and the carrier that the animals should be transported under humane and hygienic conditions.

2.3 Housing. Animal housing should be such as to ensure that the general health of the animals is safeguarded and that undue stress is avoided. Special attention should be given to the space allocation for each animal, according to species, and adequate standards of hygiene should be maintained as well as protection against predators, vermin, and other pests.

Facilities for quarantine and isolation should be provided. Entry should normally be restricted to authorized persons.

2.4 Environmental Conditions. Environmental needs such as temperature, humidity, ventilation, lighting, and social interaction should be consistent with the needs of the species concerned. Noise and odor levels should be minimal. Proper facilities should be provided for the disposal of animals and animal waste.

2.5 Nutrition. Animals should receive a supply of foodstuffs appropriate to their requirements and of a quality and quantity adequate to preserve their health, and they should have free access to potable water, unless the object of the experiment is to study the effects of variations of these nutritional requirements.

2.6 Veterinary Care. Veterinary care, including a program of health surveillance and disease prevention, should be available to breeding establishments and to institutions or departments using animals for biomedical purposes. Sick or injured animals should, according to circumstances, either receive appropriate veterinary care or be painlessly killed.

2.7 Records. Records should be kept of all experiments with animals and should be available for inspection. Information should be included regarding the various procedures which were carried out and the results of postmortem examination if conducted.

3. Monitoring of the Care and Use of Animals for Experimentation

3.1. Wherever animals are used for biomedical purposes, their care and use should be subject to the general principles and criteria set out above as well as to existing national policies. The observance of such principles and criteria should be encouraged by procedures for independent monitoring.

3.2. Principles and criteria and monitoring procedures should have as their objectives the avoidance of excessive or inappropriate use of experimental animals and should encourage appropriate care and use before, during, or after experimentation. They may be established by specific legislation laying down standards and providing for enforcement by an official inspectorate; by more general legislation requiring biomedical research institutions to provide for peer review in accordance with defined principles and criteria, sometimes with informed lay participation; or by voluntary self-regulation by the biomedical community. There are many possible variants of monitoring systems, according to the stress laid upon legislation on the one hand, and voluntary self-regulation on the other.

4. Methods Not Involving Animals: "Alternatives"

4.1. There remain many areas in biomedical research which, at least for

the foreseeable future, will require animal experimentation. An intact live animal is more than the sum of the responses of isolated cells, tissues, or organs; there are complex interactions in the whole animal that cannot be reproduced by biological or nonbiological "alternative" methods. The term "alternative" has come to be used by some to refer to a replacement of the use of living animals by other procedures, as well as methods which lead to a reduction in the numbers of animals required or to the refinement of experimental procedures.

4.2. The experimental procedures that are considered to be "alternatives" include nonbiological and biological methods. The nonbiological methods include mathematical modeling of structure-activity relationships based on the physicochemical properties of drugs and other chemicals, and computer modeling of other biological processes. The biological methods include the use of microorganisms, *in vitro* preparations (subcellular fractions, short-term cellular systems, whole organ perfusion, and cell and organ culture), and, under some circumstances, invertebrates and vertebrate embryos. In addition to experimental procedures, retrospective and prospective epidemiological investigations on human and animal populations represent other approaches of major importance.

4.3. The adoption of "alternative" approaches is viewed as being complementary to the use of intact animals, and their development and use should be actively encouraged for both scientific and humane reasons.

Patients' Bills of Rights

DECLARATION OF LISBON ON THE RIGHTS OF THE PATIENT

Adopted by the 34th World Medical Assembly (Lisbon, September/October 1981)

Recognizing that there may be practical, ethical, or legal difficulties, a physician should always act according to his/her conscience and always in the best interest of the patient. The following Declaration represents some of the principal rights which the medical profession seeks to provide to patients.

Whenever legislation or government action denies these rights of the patient, physicians should seek by appropriate means to assure or to restore them.

a) The patient has the right to choose his physician freely.

b) The patient has the right to be cared for by a physician who is free to make clinical and ethical judgments without any outside interference.

c) The patient has the right to accept or to refuse treatment after receiving adequate information.