

EDITORIAL

Bioethical Principles of Biomedical Research Involving Animals

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. That is so called: Good Clinical Praxis (GCP). 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 Declaration of Helsinki* of the World Medical Association 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[1].

Animal experimentation is fundamental to the biomedical sciences, not only for the advancement of specific vital processes, but also for the improvement of methods of prevention, diagnosis, and treatment of disease both in man and in animals. The use of animals is also indispensable for testing the potency and safety of biological substances used in human and veterinary medicine, as well as for determining the toxicity of the rapidly growing number of molecules that never existed before in nature and which may represent a hazard to health. This extensive exploitation by man of animals implies philosophical and moral problems that are not peculiar to their use for scientific purposes, and there are no objective ethical criteria by which to judge claims and counterclaims in such matters[2]. However, there is a consensus that „deliberate cruelty is repugnant“.

While many countries have general laws or regulations imposing penalties for ill-treatment of animals, relatively few make specific provision for their use for scientific purposes. 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. In the few that have done so, the measures adopted vary widely: on the one hand, legally enforceable detailed regulations with licensing of experimenters and their premises together with an official inspectorate; on the other, entirely voluntary self-regulation by the biomedical community, with lay participation. Many variations are possible between these extremes, one intermediate situation being a legal requirement that experiments or other procedures involving the use of animals should be subject to the approval of ethical committees of specified composition.

The International Guiding Principles are the product of the collaboration of a representative sample of the international biomedical community, including experts of the World Health Organization, and of consultations with responsible animal welfare groups. The International Guiding Principles have already gained a considerable measure of acceptance internationally. European Medical Research Councils (EMRC), an international association that includes all the West European medical research councils, fully endorsed the Guiding Principles in 1984.

Here we bring the basic bioethical principles for using animals in biomedical research[3]:

1. Methods such as mathematical models, computer simulation and *in vitro* biological systems should be used wherever appropriate,
2. Animal experiments should be undertaken only after due consideration of their relevance for human or animal health and the advancement of biological knowledge,
3. The animals selected for an experiment should be of an appropriate species and quality, and the minimum number required to obtain scientifically valid results,
4. 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,
5. 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,
6. Where waivers are required in relation to the provisions of article V, the decisions should not rest solely with the investigators directly concerned but should be made, with due regard to the provisions of articles IV, and V, by a suitably constituted review body. Such waivers should not be made solely for the purposes of teaching or demonstration,
7. 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,
8. 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,
9. 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.

Also see *Draft CIOMS Guiding Principles 2011* to be used by the international scientific community to guide the responsible use of vertebrate animals in scientific and/or educational activities[4].

Alternatives for animal in biomedical research

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 non-biological "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.

The experimental procedures that are considered to be "alternatives" include biological and non-biological methods. The biological methods include the use of micro-organisms, *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. The non-biological methods include mathematical modeling of structure-activity relationships based on the physico-chemical properties of drugs and other chemicals, and computer modeling of other biological processes. In addition to experimental procedures, retrospective and prospective epidemiological investigations on human and animal populations represent other approaches of major importance.

There no need specially underline that 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.

Editor in Chief

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References

1. Council for International Organizations of Medical Sciences established jointly by WHO and UNESCO in 1949. http://www.cioms.ch/about/frame_about.htm
2. Ewald RW. The Physiologist's Ethical Dilemmas. *News in Physiological Sciences*. 2002;17 (1); pp 43-46.
3. ICLAS is an international scientific organization dedicated to advancing human and animal health. <http://www.iclas.org>.
CIOMS-ICLAS project to review the 1985 International Guiding Principles for Biomedical Research Involving Animals. April 15, 2011. <http://ora.msu.edu/ICLAS/index.html>. Comments Requested on 2011 Revised CIOMS Principles. Office of Laboratory Animal Welfare. April 20, 2011.