Sigma Xi Statement on the Use of Animals in Research

Approved unanimously by the Sigma Xi Board of Directors on November 16, 1991

Early in 1990, the Executive Committee of Sigma Xi requested that the Society's Committee on Science and Society develop a general mechanism for responding to controversial issues affecting the scientific research community. Dr. John Ahearne, Executive Director of Sigma Xi, suggested that the Committee first consider the issue of the use of animals in research. He noted that a number of scientists who do not use animals in their own research, as well as some who do, were concerned that resistance to the use of animals in biomedical research reflected a general questioning of all scientific investigation.

In response to this request, Alan McGowan, Chair of the Committee on Science and Society, convened a workshop on the use of animals in research at Sigma Xi's 1990 Annual Meeting. At the Annual Meeting, Dr. Colin Blakemore, Waynflete Professor of Physiology at Oxford University, received Sigma Xi's John P. McGovern Award in Science and Society, in recognition of his contributions to the public understanding of this issue. Professor Blakemore participated in the workshop on the use of animals, which was attended by more than 200 Society members. Participants in the workshop overwhelmingly recommended that Sigma Xi become involved in this issue.

Based on this recommendation, the Board of Directors of Sigma Xi requested commentary from all chapters and clubs of the Society, as well as from individual Society members. More than 90 chapters and clubs and 100 individual members responded, and the response was overwhelming: Sigma Xi should take a stand supporting the responsible use of animals in research. In April 1991, having reviewed a summary of responses from chapters and clubs and from individual members, the Board of Directors requested that a draft statement of Sigma Xi's position be developed for discussion during the 1991 Annual Meeting.

A small group was convened in July 1991 to provide more specific comments and to discuss what issues such a statement should include. That group included members and nonmembers of Sigma Xi; scientists who use animals in research and those who do not; representatives of other professional organizations; and individuals who have long been involved in the national discussion of the use of animals in research. Input from this group and from Sigma Xi members, responding via chapters and clubs and individually, was used to prepare the following statement outlining Sigma Xi's position on the use of animals in research. The statement is one step in a series of activities planned to address this issue.

Sigma Xi, The Scientific Research Society, advocates sound research. The Society recognizes the importance and value of animals in scientific research and science education, and it supports responsible use of animals in research and teaching. Sigma Xi opposes unnecessary restrictions on the use of animals in these endeavors, and it encourages public education on the importance of continuing animal research to support advances in scientific knowledge and medical applications. Freedom of opinion and discussion concerning the use of animals in research must be safeguarded. However, attacks on life or property, hostile campaigns against individuals, and the use of distorted, inaccurate, or misleading evidence should be publicly condemned.

Issues Associated with the Use of Animals in Research

Sigma Xi's strong support for the use of animals in research follows from a balanced and thorough consideration of three separate, but related, aspects of animal research: its importance for science, its value, and its conduct. These three issues are considered first in a general way, and subsequently within the context of the research process.

Importance of Animal Research. The use of animals in research and teaching is important for science. Much research is performed primarily to advance basic knowledge. This basic research is vital to the success of the research process, often in ways that are not fully evident at the time the research is being performed.

For centuries, thoughtful research with animals also has advanced understanding of chemical, biological, and behavioral processes that provide a direct application to medical treatment. For example, Pavlov won a Nobel prize for studies of digestion in dogs, even before his discovery of classical conditioning in the same subjects. Most recently, research in neuroscience, using rats as subjects, has provided basic knowledge for the development of diverse pharmacological agents and for the investigation of Alzheimer's disease and other human disorders. These examples emphasize the importance of major advances resulting from animal research. As important as these striking contributions are, however, most progess in research does not come from such major advances, but from the slow accumulation of results from many studies.

Theories, methods, and concepts derived from the study of animals stimulate hypotheses, not only within closely

related fields, but also in distant ones. Darwin's theory of evolution by natural selection is an exemplar case. Thus, to some extent, restrictions imposed on animal research are restrictions on the entire research enterprise and on the substantial advances it fosters. These advances are perhaps most obvious in medicine, but are also present in many other areas of research.

Value of Research Using Animals. Well-conducted research with animals has provided, and continues to provide, information, ideas, and applications that can be obtained in no other way. Much medical research produces clear benefit for human health care: Medical advances have contributed substantially to decreased infant mortality and increased life expectancy. (In addition, medical and related research also contribute to the quality and length of life for many animals—pets, zoo animals and wildlife, including endangered species.)

Results from work with animals have led to understanding mechanisms of bodily function in humans, with substantial and tangible applications to medicine and surgery (e.g., antibiotics, imaging technologies, coronary bypass surgery, anti-cancer therapies), public health (e.g., nutrition, agriculture, immunization, toxicology, and product safety), and also propagation of endangered species (e.g., via captive breeding). As the Surgeon General has stated, research with animals has made possible most of the advances in medicine that we today take for granted. An end to animal research would mean an end to our best hope for finding treatments that still elude us. Animal research has also contributed substantially to the understanding of behavior patterns and ecological principles and to developing the means for responding to environmental problems.

The Society recognizes the importance and value of animals in scientific research and science education, and it supports responsible use of animals in research and teaching

Research with animals has been remarkably successful in generating both basic and applied knowledge. Without such research, many of us would not have survived diseases that were once common. Without further research with animals, there will be no vaccine for AIDS and dramatically fewer advances for treating and preventing heart disease, cancer, and other serious health problems. For this reason, the overwhelming majority of Sigma Xi members providing input on this matter believes that the benefits accrued from this increase in knowledge justifies the responsible use of animals in research.

Conduct of Animal Research. Significant issues regarding the conduct of animal research include the treatment, number, and appropriate use of animals; the efficiency of experimental designs; the use of alternatives to animal research; and the duplication of results.

State and federal agencies have established numerous regulations addressing housing, handling, and experimental procedures for research animals. Disciplinary professional societies representing practicing scientists in North America and abroad have also adopted guidelines for the use of animals in research. These regulations were instituted to ensure humane treatment of animal subjects, and they have become increasingly detailed and comprehensive. Currently, before federally funded research with animal subjects can be undertaken in the United States, the experimental protocol and treatment of subjects must first be approved by an institutional animal care and use committee of prescribed membership (including a veterinarian, a lay person, and a person from outside the institution). Scientists recognize that the health and well-being of animal subjects is essential to good research: Healthy animals are needed to ensure valid and reliable results. However, the level of detail of some mandated procedures far exceeds what is needed to ensure humane treatment of subjects and may, in fact, impede even well-designed animal research. New regulations for personnel, equipment, procedures, and facilities mandated by recent regulations have made research with animals increasingly difficult and expensive. For some researchers, these regulations have limited the scope of research. For others, particularly those at smaller institutions (such as liberal arts colleges) that cannot institute mandated structural and personnel changes, these regulations have interfered more substantially with research and research training.

The use of statistical models and the application of proper experimental designs can help determine the number of animals needed to test hypotheses. With knowledge of certain parameters, one can determine the minimum number of subjects needed to produce results of required statistical power. This approach to research addresses both the naive and unnecessary use of too many subjects, and the equally wasteful use of fewer subjects than are needed to produce valid and statistically reliable results. Sigma Xi advocates the use of sound statistical methodology and recognizes that following good scientific practice (e.g., replication, control groups, and adequate sample size) may actually increase the total number of animals used. Courses providing formal instruction in statistics and experimental design have long been a standard part of the undergraduate curriculum in the social sciences and in some areas of biology. Supporting and strengthening such courses, providing similar courses for all of the life sciences, and re-educating current investigators who do not use these methods would result in more efficient use of animal subjects.

The use of alternatives to animals in research is at an early stage. Animals have been used for many routine tests because they represent the best methods currently available. Biochemical, bioenzymatic, or radioimmunologic procedures have replaced *in vivo* tests in some instances (e.g., pregnancy assessment). The goal of developing such procedures was to provide the fastest, cheapest, most reliable and simplest test. For many purposes, tests using animals are rarely as cheap, reliable, or as sensitive as desired. Therefore, we can expect that more biochemical tests will be developed and instituted, replacing tests using whole animals for these specific purposes. Yet, the biochemical tests for pregnancy could not have been developed without using animals to reveal the basic details of reproductive biology underlying these

procedures. Indeed, even when the newest procedures (using antibodies produced in cell cultures) are used, animals remain the original source of antibodies (and tumor cell lines) for these procedures. Thus, instituting biochemical methods for specific procedures may reduce the number of animals used for that purpose, but will not necessarily eliminate the use of animals.

The development and validation of computer simulations and cell and tissue culture techniques may in the future diminish the number of animals used in some routine procedures. However, these developments will not entirely replace the use of animals. Indeed, the number of animals used in research may actually increase, for several reasons: First, virtually all of these alternative methods are now adjuncts to the use of animal subjects in research, not replacements for such subjects. Second, because of complex interactions between organ systems, some physiological processes cannot be studied in isolation, but require entire animals. Third, new lines of animal research (e.g., transgenic animals) will be needed to reap the benefits of recent progress in fields such as molecular biology and genetics. Finally, results of computer simulations may raise research questions that can be addressed only by the use of animal subjects.

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Some scientists do object to the use of animals in product—especially cosmetic—safety testing (which represents less than 1 percent of all animal testing). However, if products are to be marketed, they should be tested by some means to ensure reasonable safety. The use of animals is critical in many instances for the testing of products, especially pharmaceuticals. The challenge is to develop, validate, and institute reliable and cost-effective procedures that require a minimal number of animal subjects to achieve satisfactory test performance. As in the case of *in vitro* pregnancy testing, alternative methods of assuring product safety may involve the use of fewer animals.

Replication of results is a necessary and beneficial part of the scientific research enterprise. Computerized data bases and literature searches provide a mechanism for scientists to determine the extent of published replication, preventing unnecessary repetition of investigations. Grant and publication review processes also contribute to preventing excess replication of results.

Using animals for teaching may appear to represent unnecessary duplication of results. However, the purpose of teaching is not to get a result, but rather to provide a learning experience. As an example, textbooks, lectures, videotapes, models, and simulations can teach some aspects of anatomy. Yet, they cannot provide the training for a surgeon that a real specimen can. In some cases, using alternatives may meet educational goals more effectively than using animals. For example, a number of computer programs simulate the effects of specified selective forces on successive generations of animals, or the effects of altering ion concentrations on neural membrane potentials. These simulations do not entirely replace the use of animals. However, they can be effective adjuncts to animal use by illustrating for students phenomena that cannot be easily demonstrated in the classroom. By contrast, careful use of animal material with clear educational goals (e.g., teaching surgery to veterinary or medical students or teaching morphology to biology majors) is an essential part of professional training.

Ethical Basis for the Use of Animals in Research. The importance of animals for scientific study and the value of such investigations for the public constitute valid reasons for using animals in research. Additionally, establishing and enforcing standards for the care and use of animal subjects ensures that animals so used are well treated. However, the more complex issue, from an ethical perspective, is to determine the conditions under which humans should use members of other species in research. This issue has been raised particularly in the case of research that produces discomfort or pain. To be sure, discomfort or pain should not be produced when a method exists to alleviate pain or discomfort without affecting the results of the study. Beyond this point, however, the issue becomes more difficult.

Do non-human animals have rights? A useful distinction is made between animal rights and animal welfare. In the discussion of ethics, the term "right" is generally reserved for a legitimate claim to a particular treatment or resource, a claim that carries concomitant responsibilities. We do not attribute responsibilities to nonhuman animals, and we do not attribute rights. By contrast, the position for animal welfare asserts that animals should be treated with respect, that animals should be used only for legitimate purposes, and that (within the limitations of an experiment) every reasonable effort should be made to minimize or reduce pain or discomfort. We conclude that, although nonhuman animals intrinsically cannot have rights in the sense that humans do, researchers who enjoy these rights assume with them the strong responsibility to provide for animal welfare.

What, then, are appropriate ethical criteria for using animals in research? The above discussion suggests that: 1) a reasoned judgment must be made that the benefit derived from the research is sufficient to justify the use of animals in the experiment, and 2) when animals are used, reasonable means be employed to provide for the welfare of subjects. How these criteria are applied is best addressed within the context of the research process.

Use of Animals and the Research Process

Scientific research proceeds within the framework of designing and completing systematic studies to test well-defined research hypotheses. These hypotheses make specific, often highly quantitative, predictions based upon the results of previous studies. The research hypothesis often defines a small set of highly probable—but contradictory—results. Thus, an experiment or series of experiments must be performed to determine which results occur under particular conditions. For example, the chemical structure of a newly synthesized compound may

resemble a class of antibiotics that work in a particular way. Based on this information, one might hypothesize similar activity for the new compound. However, the extent of antibiotic activity, and the conditions under which the compound shows such activity, must be determined by experiments based on results from similar, related compounds. Moreover, experiments must be conducted to determine effective dosage and possible side effects of the compound. These characteristics may be predictable from structural similarities with other compounds, but they must nonetheless be empirically verified, particularly if the antibiotic is to be marketed for use in humans or animals.

This process of scientific hypothesis testing has several implications for the use of animals in research. First, although carefully planned studies most often yield results falling within a set of predicted outcomes, the precise results are rarely known before the experiments are performed. Therefore, even if one could state that the use of animal subjects would be justified by a given result, such logic is difficult to employ. It is often impossible to know in advance what the result will be and, therefore, to weigh its importance.

Sigma Xi recognizes that the use of animals in research carries serious responsibilities for the welfare of the animals

Second, on occasion, a study yields an entirely unpredicted result. Such results may reflect the serendipitous discovery of the effect of an important—but previously unrecognized—variable. Thus, despite their rarity and unpredictability, unexpected results may make valuable contributions to the direction and progress of research. Yet, given that one cannot predict when such a result may occur, one cannot weigh its importance before the experiment is performed.

Third, a low yield is intrinsic to the research process. Experiments often suggest unexpected questions that must be addressed before a clear-cut answer can be obtained to the original question. Therefore, many experiments must often be performed to provide an unequivocal advance in knowledge. To be sure, scientists attempt to design and perform experiments in order to maximize the information obtained from each experiment. Yet, when dealing with complex systems about which little is known, multiple experiments are often necessary to isolate important variables and to determine with a high degree of certainty the relations of cause and effect. Consequently, although a line of research using animal subjects very well may yield substantial useful information, any one experiment in that line of research may appear unimportant.

Fourth, the body of scientific data generally increases by painstaking research that advances knowledge in small, incremental steps. Many such advances are usually needed to produce significant breakthroughs, and the value and importance of individual experiments are difficult to assess until the entire process has been completed. Therefore, it often is impossible to estimate the value of such experiments soon after they are finished, and thus to consider their worth in relation to any animals that may be used in the work.

Fifth, not only is it difficult to predict the value of results before an experiment is performed, or even immediately afterward, but the ultimate value may be unrecognized for some time. In advance of contributions to a line of research or other applications, we can not determine with certainty which results will have applications, what these applications may be, or when that application will arise. Long before AIDS appeared, veterinary scientists investigated retroviral infections of livestock. Their knowledge of how to work with these viruses provideda basis for initial work on AIDS. The common delay in application of research findings further complicates attempts to justify the use of animals in research in terms of the benefits of an experiment or line of research.

Sixth, repeating studies, often under slightly different conditions, are necessary to validate results in all fields of science. Duplication may appear to contribute no new information. However, both replication (under similar conditions) and systematic replication (in which parameters are systematically altered) are necessary to document the reliability of phenomena, to address the extent to which results may be generalized, and to isolate important (but otherwise undetected) variables. Concern over apparently needless duplication of experiments should be tempered by considering the possible contributions of studies completed under both similar and dissimilar conditions.

Scientists are concerned about the humane treatment of animals. Because of their work, investigators using animals in research have a heightened awareness concerning the issues surrounding animal welfare. In addition to their own personal feelings, those who work with animals recognize that to achieve valid, reliable results, one must have healthy subjects that are well treated. Under laboratory conditions, animals are not exposed to competition, parasitism, predation, or the level of disease present under natural conditions.

Conclusion

Sigma Xi supports the responsible use of animals in scientific investigations and in science education. The use of animals in research has been essential for advances in the life sciences and medicine, resulting in enormous benefit to human health and welfare. Their use will continue to be necessary for future progress. Given the world's health and other problems, it seems unwise to curtail research that is likely to have a major impact on these problems. Sigma Xi recognizes that the use of animals in research carries serious responsibilities for the welfare of the animals. Therefore, mechanisms must be in place to ensure that unnecessary suffering is avoided and the number of animals used is not excessive. Sigma Xi also supports the development of alternatives to animal experimentation when such alternatives can meet the scientific objectives of a study. Finally, Sigma Xi encourages public education on the importance of animal research in the production of scientific advances and medical treatment and the education, early in their careers, of scientists on the proper use of animals.