

Animal Care and Use Committees: Structural Problems Impair Usefulness

PHYSICIANS COMMITTEE FOR RESPONSIBLE MEDICINE

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Introduction

The Animal Welfare Act (AWA) requires that institutional animal care and use committees (IACUCs) be established at research facilities that use animals covered under the Act. The Public Health Service and the Interagency Research Animal Committee supplement the AWA by requiring IACUCs at many institutions where vertebrate animals are used, including federal research facilities and those receiving PHS funding.

Under the AWA, the IACUC's job is to review every proposed experiment which involves animals to ensure that pain is minimized. Specifically, the IACUC is supposed to ensure, among other things, that researchers have considered alternatives to painful procedures, that experiments do not unnecessarily duplicate previous experiments, and that painful procedures will be performed only with appropriate anesthetics unless their omission is for scientific reasons. Also, the committee is to inspect experimentation and holding areas and the condition of the animals.

IACUCs are intended to provide a measure of protection for animals in laboratories. Unfortunately, experience has shown that many IACUCs provide inadequate protection. Examples abound in which the committees have approved patently inhumane and scientifically questionable projects. In a few cases, such experiments were prevented from going forward because of intervention by Congress, a court, or a federal agency, while in other cases, the experiments have gone forward. For instance, at the University of Washington, an experiment was proposed in which infant monkeys were to be reared in total isolation in order to cause them to self-mutilate, with the intent of mimicking the behavior of children with brain damage or genetic disorders. The monkeys were to be killed at three-month intervals, and their brains were to be compared to those of other, non-isolated monkeys. While the IACUC expressed reservations about the potential suffering entailed in the project and noted that alternative research methodologies might exist, it approved the proposal without modification. The committee was apparently unaware that a multicenter research project of a similar nature was already in progress. The National Institutes of Health then assigned the proposal such low priority that it was denied funding.

In another example of inadequate IACUC review, the

Letterman Army Institute of Research IACUC considered a project in which a large section of bone would be removed from the legs of over a hundred dogs formerly used in racing. The bones were to be replaced with a synthetic compound, which was to be assessed for its potential in treating battlefield injuries. Independent orthopedic surgeons noted numerous technical problems with the experiments, including that they did not simulate real battlefield injuries, used poor anesthetic technique, and involved a poor choice of experimental subjects. In addition, information about the test substance was not presented to the committee when it reviewed the proposal. Nonetheless, the IACUC approved the project. A court issued a temporary restraining order that stopped the project after it was determined that the dogs had been illegally obtained. Congress later voted to withhold funding until the Army provided a better justification for the project.

In order to identify ways to improve IACUC performance, the Physicians Committee for Responsible Medicine obtained information from a panel of former members of IACUCs: Jan Polon Novic (Letterman Army Institute of Research committee), Kim Sturla (University of California-Berkeley committee), Anne Phillips (University of Tennessee College of Veterinary Medicine committee), Thomas Poulton, M.D. (Creighton University School of Medicine committee), Pamela Krausz (University of Pennsylvania committee), Steve Sapontzis, Ph.D. (Lawrence Berkeley Lab committee), and Bruce Max Feldmann, D.V.M. (Codon Company committee). In addition, PCRM consulted Barbara Orlans, Ph.D., a research associate at the Kennedy Institute of Ethics at Georgetown University who has written extensively on IACUCs, Martin Stephens, Ph.D., with the Humane Society of the United States, Christine Stevens with the Animal Welfare Institute, and Nedim Buyukmihci, V.M.D., associate professor of ophthalmology at the University of California, Davis. Andrew Rowan, Ph.D., director of the Tufts Center for Animals and Public Policy, offered comments on this report. Dr. Michael Allen Fox, professor of philosophy at Queens University in Canada, Dr. Brigitte Rusche with the Animal Welfare Academy in Germany, and Karin Gabrielson with the Swedish Society Against Painful Experiments on Animals provided information on animal care and use committees in their countries. Veterinary evaluations of necropsy reports by Eric Dunayer, V.M.D., and Bernard Feldman, D.V.M., and reviews

of animal care and use programs at a number of research facilities were also reviewed. This report's conclusions are those of PCRMA and are not necessarily those of each individual consulted.

Evaluation of IACUCs is made difficult by the fact that many do not release substantive information to the public, which obviates the possibility of statistical conclusions.

The panel cited proposals which would be considered cruel by most people and which had little scientific merit, but were approved by the IACUCs anyway. One involved castrating rabbits and/or giving them estrogen to study erectile problems. Another experiment involved euthanizing horses as part of an effort to study exercise-induced bleeding in race horses. A protocol designed to teach students the effects of alcohol on short-term memory entailed forcing animals to ingest a solution of alcohol and water for up to four weeks, with this solution being the animals' only source of fluid. A protocol for a college physical education course involved putting rats on a moving treadmill and electrically shocking them if they stopped running, until they became exhausted and would stop running despite being shocked. Experiments were also approved in which substances were to be administered to animals until 50% of them died (the lethal dose 50 (LD50) test); cocaine was given to pigs and piglets; insects fed on the shaven skin of rabbits; and pigs were bled to the verge of death and revived.

IACUCs have failed to assure proper veterinary care and comfort for animals at some sites. Overcrowding, cramped cages, lack of socialization, and poor veterinary care have been cited by IACUC members and in veterinary evaluations of necropsy reports. For example, necropsy reports on squirrel monkeys who died at the Uniformed Services University of the Health Sciences (USUHS) indicated deficiencies in care. A female monkey at USUHS was dehydrated and emaciated after she was found dead following brain surgery. Dr. Dunayer postulates that "unless the monkey suffered massive loss of fluid following surgery (a loss preventable with proper veterinary care), dehydration would require days to occur. Emaciation could develop only over a period of weeks." Parasites were found in the lung and intestines of another monkey, also found dead after brain surgery. Dr. Dunayer concludes that "the facility, then, seems to have failed to provide proper veterinary care." Necropsy reports from the Armed Forces Radiobiology Research Institute dated from September 1988 through May 1989 also indicated emaciation of animal subjects. Dr. Feldman suggests that emaciation could be due to improper animal care. These problems occurred in spite of the presence of IACUCs.

Structural Deficiencies with the Committees

The panel identified the following problems which limit the usefulness of IACUCs:

1. There is considerable bias toward approving experiments as proposed or with minimal modification. This is due, in part, to the committee composition. The committee is appointed by the chief executive officer of the research facility and is to include at least three members. One member must be a veteri-

narian. Another must be a person who is not affiliated in any other way with the facility, in order to represent the "general community interests in the proper care and treatment of animals," in the words of the Animal Welfare Act. U.S. Public Health Service policy goes a bit further than the Animal Welfare Act. It requires that IACUCs be comprised of five members, including at least one veterinarian, a practicing scientist, a non-scientist, and a person not otherwise affiliated with the institution. However, most members tend to be researchers or other employees of the research facility. Committee members are sometimes subordinates of investigators at the facility. The committee chairs are often animal researchers, and there are cases in which the chairs' own proposals have been considered by the committee, an obvious conflict of interest.

2. There have been conflicts of interest in monitoring animal care at research facilities. A review of Air Force animal research programs found that at two facilities the committee chairs were chief veterinary officers whose animal care programs were to be monitored by the committees.

3. At some facilities, most IACUC members are excluded from inspections of animal facilities and study areas. Of the fifteen-member IACUC at the University of Tennessee College of Veterinary Medicine, only three IACUC members, selected by lottery, conducted each inspection. In two and a half years on the committee, the unaffiliated member participated in only one inspection. Documents show that at the Army Medical Research Institute of Infectious Diseases in 1991, two Army veterinary reservists conducted the semi-annual inspections of the animal facilities and then submitted a report to the IACUC. IACUC members were invited to accompany the reservists but were not expected or required to participate.

4. There is little inclusion of persons representing community perspectives, particularly of those with expertise in animal welfare. In some cases, the unaffiliated representative has had no previous experience or interest in animal welfare issues. In other cases, the unaffiliated member, while not directly employed at the research facility, is affiliated with institutions that have close ties with the facility. Army documents show that in 1991 the unaffiliated member of the Walter Reed Army Institute of Research committee was a chaplain from the Walter Reed Army Medical Center. In 1990, the two unaffiliated members on the committee at the Army Medical Research Institute of Chemical Defense were a veterinarian assigned to the Army Environmental Hygiene Agency and a post chaplain, both of whom apparently were military officers. At the Army Aeromedical Research Laboratory in 1990, the unaffiliated member was a civilian "employed on post."

5. Procedures on voting, minority reports, and removal of committee members are not clearly prescribed by law, and vary from committee to committee in such a way that the committees' mission can be compromised. Removal of committee members is often left to the discretion of facility officials. Attempts have been made to prohibit members from casting a

negative vote. At the University of California-Berkeley, for instance, the chairperson of the IACUC tried vigorously to prevent an unaffiliated member from casting a negative vote on many proposals if he believed the member's rationale to be insufficient. Members may not be informed that they can file a minority report, and minority reports are subject to editing. At the University of California-Berkeley, the IACUC chairperson deleted sections of an unaffiliated member's minority report. After the member appealed to a top school official, the chairperson was ordered to discontinue censuring minority reports.

6. Some panel members reported a pronounced lack of tolerance for opinions critical of individual experiments or committee procedures. The unaffiliated IACUC member at University of California-Berkeley mentioned in the previous paragraph was frequently criticized by other members of the committee, including the chairperson, for dissenting opinions. An IACUC member at another institution was removed after suggesting changes in the committee's review process. Questions and criticisms of proposed projects are often ignored or are met with disparaging remarks.

7. There is often little turnover in the committees and a resultant lack of new personnel and new ideas within the committees.

8. The IACUCs' authority is vague. In conflicts with investigators, it is unclear to what extent the committees can impose decisions upon them. Some IACUCs have developed in-house policy statements which address their authority, but most are without such rules.

9. IACUCs often do not consider the scientific merit of proposed projects. Essentially pointless projects have been approved by committees, such as the horse racing and physical education experiments noted above. While some IACUCs attempt to review scientific merit, others have established policies that they will not, under any circumstances, address merit. In some instances not involving a federal grant or contract, an IACUC may be the only formal review of a project involving animals. Some interpret the Public Health Service law to require that, when Public Health Service funds are involved and when there is no separate institutional peer review committee charged with reviewing merit, IACUCs must perform merit review.¹

10. The unaffiliated member's effectiveness is often compromised by the high volume of protocols and the lack of interpretation of technical wording of proposals. In some cases, members have only a few days to evaluate protocols. They may be prohibited from consulting with outside scientific experts to assist them in the evaluation.

11. IACUCs are largely unaccountable to the public. At many, perhaps most, institutions, committee meetings are closed and records unavailable to the public. Minority reports and dissenting opinions may not be reported outside the committee.

A comprehensive survey of the accessibility of IACUC meetings and records is not currently available.

12. It may be difficult for IACUCs to determine if there is other ongoing research that makes proposed projects redundant, as was the case in the proposed study at University of Washington discussed above.

Do IACUCs Help At All?

IACUCs offer some advantages. IACUCs may require experimenters to give additional thought to using animals in projects. In one case, a professor agreed to use a non-animal method in a teaching lab after reading minority reports written by IACUC members. IACUCs may deter some projects from being proposed. Where meetings and records are available to the public, IACUCs may also be good sources of information on experiments.

In a study by Rebecca Dresser of Case Western Reserve University, 32 IACUCs reviewed four hypothetical animal research protocols involving painful or potentially painful procedures. The hypothetical protocols were real studies purposely altered to raise questions about applying government standards to the protocols, and the protocols were intentionally vague and brief. The committees were informed about the study objectives and hypothetical nature of the protocols. Most or all of the committees made one of the following three decisions for each protocol: a) approval contingent on acceptable response to committee recommendations or questions b) deferral pending receipt of additional information, or c) disapproval unless major modifications were made.² This suggests some commitment by IACUCs to reducing laboratory animal pain.

As the author points out, the study did not include negotiation between researchers and the committees. She notes that when the committees questioned the justification for a procedure, their comments implied that researchers could go forward with the experiment by providing additional information. Since many committees refused to participate in the study, the study committees may, in the author's words, "disproportionately represent the more active and enthusiastic review committees." The brevity and vagueness of the protocols may have provoked an unusually large amount of questions. Committee awareness of the study objectives and nature of the protocols may have led to more vigorous reviews than customarily.

Animal Care and Use Committees in Sweden, Germany, and Canada

A review of the Swedish, German, and Canadian equivalents of American IACUCs reveals significant differences between countries in committee structure and function:

1. Sweden

Role of the Committee

Under Swedish law, committees on animal experiments conduct "examinations on ethical grounds" of animal research

proposals. There are seven committees, and each committee examines proposals for a particular region of Sweden. The committees have only an advisory function, although their decisions reportedly are influential.

Guidelines for Committee Review of Proposals

Approval of proposals is based on scientific significance, public interest, whether the experiment can be achieved without the use of laboratory animals, whether the experiment can be performed in a more humane manner, and whether the experiment unnecessarily duplicates previous experiments.

Committee Composition

The members of the ethical committees on animal experiments are appointed by the National Board for Laboratory Animals, whose membership is appointed by the Ministry of Agriculture. The committees are composed of a chairperson, a vice-chairperson, and twelve other members. Half of the twelve must be laypersons, and currently two of the laypersons on each committee are from animal protection organizations. While committee members are appointed for not more than three years at a time, members can be re-appointed.

2. Germany

Role of the Committee

Regionally-based advisory committees on animal experiments advise local governments on whether to permit proposed animal experiments. Local governments are not obligated to follow the committee recommendations. It is rare for committees to recommend that governments refuse permission for experiments to go forward, and it is not uncommon for the governments to approve experiments when the committees have recommended that the experiments not be granted permission.

Guidelines for Committee Review of Proposals

In reaching their decision about proposed experiments, the committees weigh animal suffering against the potential for gain from the experiments, as well as whether the experimenters have considered alternatives.

Committee Composition

The local governments appoint committee members, of whom one-third come from animal welfare organizations, and two-thirds are from the scientific community. The committee members serve three-year terms but can be reappointed.

3. Canada

Role of the Committee

National law does not require local animal care committees in Canada, but there is a de facto obligation to form these committees at every institution conducting animal research, because funding agencies require committee approval of experiments, and the province of Ontario legally requires the committees. Among the committees' responsibilities is to ensure that no experiments are commenced without prior committee approval.

Guidelines for Committee Review of Proposals

In deciding whether to approve proposed experiments, the committee is supposed to "review protocols from the viewpoint of the ethical aspects of the procedures and the acceptability of the methodologies proposed."³ For those projects not subject to a scientific merit review by another body, the committee may require that an external merit review be conducted or may itself review the protocol for scientific merit.

Committee Composition

The head institutional official appoints the committee members, which include scientists, a veterinarian, a non-animal user, and at least one person representing the community. The members serve set terms, which are renewable.

Recommendations

The IACUC structural deficiencies and the examination of committees in other countries suggest reforms that would improve IACUCs:

1. Increase the proportion of unaffiliated members on the committees. All proposals should be reviewed by at least one non-institutional member. At least one-third of the committees' membership should be from outside the institution, which would be consistent with the proportions in the Animal Welfare Act requirements. Unaffiliated members should not be from other institutions where animal research is conducted or from institutions that are closely connected with the research facility.
2. The committee should include, when possible, at least one scientist or clinician unaffiliated with the facility with experience in animal welfare advocacy.
3. Federal regulations should clearly outline the authority of the committees.
4. Each committee member should be authorized to file unedited minority reports and negative votes.
5. Members should be permitted to consult with outside scientists, with the understanding that consultants will maintain the confidentiality of protocols in those instances where confidentiality is required.
6. Guidelines should be established for the periodic turnover of committee members, including the chairperson.
7. Guidelines, including an appeals process, should be established for removing members from the committee. Voting records, raising questions about proposals, and criticism of committee procedure should not be grounds for dismissal.
8. Committee meetings, records, and reports should be available to the public, except where national security or control over trade secrets would be threatened.

9. IACUCs should be explicitly required to consider the significance and scientific merit of proposed research or educational projects. IACUCs should also be provided with adequate information on potential harm to the animals.

10. Mechanisms should be established so that the IACUC is aware of similar research projects, conducted concurrently or previously, in order to prevent duplicative projects.

11. Shifting the responsibility for appointing committee members from the research facility's chief executive officer to a government or government-affiliated body, such as in Swe-

den and Germany, should be considered. Establishing committees on a regional rather than an institutional basis should also be considered. These changes could increase the independence of the committees from the institutions that conduct animal research.

References

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