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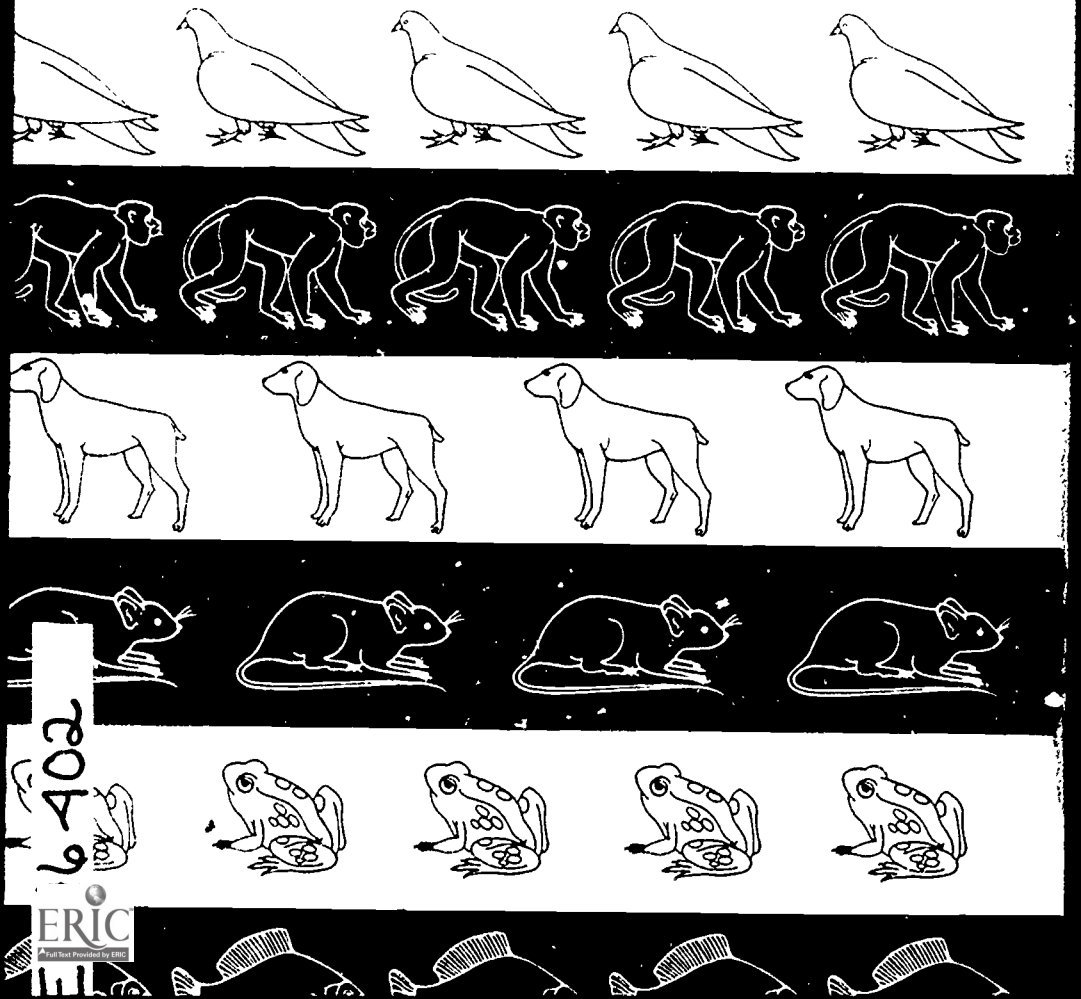
ABSTRACT

With an estimated 17-22 million animals used in laboratories annually in the United States, public interest in animal welfare has sparked an often emotional debate over such uses of animals. Concerns focus on balancing societal needs for continued progress in biomedical and behavioral research, for toxicity testing to safeguard the public, and for education in the life sciences with desires to replace, reduce, and refine the use of laboratory animals. In 1985, the United States Congress enacted three laws that dealt with laboratory animals, including amendments to the Animal Welfare Act. This assessment analyzes the scientific, regulatory, economic, legal, and ethical considerations involved in alternative technologies in biomedical and behavioral research, toxicity testing, and education. Included is a detailed examination of federal, state, and institutional regulation of animal use, and a review of recent developments in 10 other countries. The report illustrates a range of options for congressional action in seven areas of public policy regarding animals: using existing alternatives; developing new alternatives; disseminating research and testing information; restricting animal use; counting the numbers and kinds of animals used; establishing a uniform policy for animal use within federal agencies; and amending the Animal Welfare Act. (JN)

Summary

CONGRESS OF THE UNITED STATES
Office of Technology Assessment

Alternatives to Animal Use in Research, Testing, and Education



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Foreword

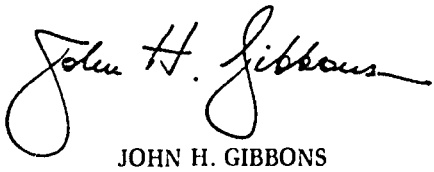
With an estimated 17 million to 22 million animals used in laboratories annually in the United States, public interest in animal welfare has sparked an often emotional debate over such uses of animals. Concerns focus on balancing societal needs for continued progress in biomedical and behavioral research, for toxicity testing to safeguard the public, and for education in the life sciences with desires to replace, reduce, and refine the use of laboratory animals. In 1985, Congress enacted three laws that dealt with laboratory animals, including amendments to the Animal Welfare Act.

In this assessment, OTA analyzes the scientific, regulatory, economic, legal, and ethical considerations involved in alternative technologies in biomedical and behavioral research, toxicity testing, and education. Included is a detailed examination of Federal, State, and institutional regulation of animal use, and a review of recent developments in 10 other countries. The report was requested by Sen. Orrin Hatch, Chairman of the Senate Committee on Labor and Human Resources.

The report illustrates a range of options for congressional action in seven principal areas of public policy regarding animals: using existing alternatives, developing new alternatives, disseminating research and testing information, restricting animal use, counting the numbers and kinds of animals used, establishing a uniform policy for animal use within Federal agencies, and amending the Animal Welfare Act.

OTA was assisted in preparing this study by an advisory panel of individuals and reviewers selected for their expertise and diverse points of view on the issues covered in the assessment. Advisory panelists and reviewers were drawn from animal welfare groups, industrial testing laboratories, medical and veterinary schools, Federal regulatory agencies, scientific societies, academia, and the citizenry at large—in short, from representatives of all parties interested in laboratory-animal use and its alternatives. Written comments were received from 144 reviewers on the penultimate draft of the assessment. In addition, at the study's inception, OTA solicited information and opinions from more than 600 interested groups and individuals.

OTA gratefully acknowledges the contribution of each of these individuals. As with all OTA reports, responsibility for the content of the assessment is OTA's alone The assessment does not necessarily constitute the consensus or endorsement of the advisory panel or the Technology Assessment Board.



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OTA appreciates and is grateful for the valuable assistance and thoughtful critiques provided by the Advisory Panel members. The views expressed in this OTA report, however, are the sole responsibility of the Office of Technology Assessment

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[1]Through December 1984
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[5]Through January 1985

Alternatives to Animal Use in Research, Testing, and Education

- *A former high school teacher in New York organizes demonstrations and advertising campaigns opposing the use of rabbits and rodents in two product-safety tests. Industry responds by giving several million dollars in grants to university scientists searching for alternatives to animal testing.*
- *Researchers induce seizures in rats, draw their cerebrospinal fluid, and use it to quell seizures in other rats; the anticonvulsant substance produced during seizures could bear on the understanding and treatment of epilepsy.*
- *Industrial toxicologists in New Jersey adopt refined methods of testing potentially poisonous chemicals, reducing by 48 percent the number of animals used in acute toxicity studies and cutting the cost of compliance with government regulations.*
- *A Virginia woman donates $1,250,000 to the University of Pennsylvania to establish the Nation's first endowed professorship in humane ethics and animal welfare. One of the goals of the chair is to investigate alternatives to animal experiments for medical research.*
- *Members of the Animal Liberation Front break into a biomedical research laboratory in California and remove dogs being used in a cardiac pacemaker experiment.*
- *Veterinary students in Washington study principles of physiology without recourse to the traditional dog dissection. Instead, they use a computer simulation of canine physiology.*

These recent events illustrate the complex political, ethical, and economic issues raised by the use of animals in research, testing, and education. Concern about the continued use of animals has led to public calls for development of alternatives.

The popular debate over animal use has been taken up by proponents holding a wide spectrum of views, ranging from belief in abolition of animal use on moral and ethical grounds to belief in free rein on the use of animals in research, testing, and education. An increasing number of groups are taking a middle ground. In the mid-1980s, it is misleading—and often impossible—to characterize many vocal groups either as simply "pro-animal" or "pro-research."

In light of requests for "a scientific evaluation of alternative methods to animal research, experimentation, and testing" from the Chairman of the Senate Committee on Labor and Human Resources, Senator Orrin G. Hatch (R-UT), and from Senator Alan Cranston (D-CA), this assessment examines the reasons for seeking such alternatives and the prospects for developing them. It describes animal and nonanimal methods used by industry, acade

mia, and government agencies; explains the roles and requirements of government regulation and self-regulation of animal use; and identifies policy issues and options that the debate over alternatives places before Congress.

The report covers three kinds of animal use: research in the biomedical and behavioral sciences; testing of products for toxicity; and education of students at all levels, including the life sciences, and medical and veterinary training. The use of animals in these three situations—research, testing, and education—differs considerably, and each has different prospects for development of alternatives.

The assessment **excludes** examination of the use of animals in food and fiber production, their use in obtaining organs, antibodies, and other biological products; and their use for sport, entertainment, and companionship. Such purposes include numbers of animals generally estimated to be many multiples greater than the numbers used for purposes described in this report. Issues of animal care, such as feeding and maintenance, are also beyond the scope of this assessment.

DEFINITION OF TERMS

In this report, animal is defined as any nonhuman member of the five classes of vertebrates: mammals, birds, reptiles, amphibians, and fish. Within this group, two kinds of animals can be distinguished—warm-blooded animals (mammals and birds) and cold-blooded animals (reptiles, amphibians, and fish). Other creatures customarily included in the animal kingdom, such as invertebrates (e.g., worms, insects, and crustaceans), are excluded by this definition. The use of human subjects is not examined in this assessment.

The concept of alternatives to animal use has come to mean more than merely a one-to-one substitution of nonanimal methods for animal techniques. **For alternatives, OTA has chosen a definition characterized by the three Rs: replacement, reduction, and refinement.**

Scientists may **replace** methods that use animals with those that do not. For example, veterinary students may use a canine cardiopulmonary-resuscitation simulator, Resusci-Dog, instead of living dogs. Cell cultures may replace mice and rats that are fed new products to discover substances poisonous to humans. In addition, using the preceding definition of animal, an invertebrate (e.g., a horseshoe crab) could replace a vertebrate (e.g., a rabbit) in a testing protocol.

Reduction refers to the use of fewer animals. For instance, changing practices allow toxicologists to estimate the lethal dose of a chemical with as few as one-tenth the number of animals used in traditional tests. In biomedical research, long-lived animals, such as primates, may be shared, assuming sequential protocols are not deemed inhumane or scientifically conflicting. Designing experimental protocols with appropriate attention to statistical inference can lead to decreases (or to increases) in the numbers of animals

used. Or several tissues may be simultaneously taken from a single animal as a result of coordination among investigators. Reduction can also refer to the minimization of any unintentionally duplicative experiments, perhaps through improvements in information resources.

Existing procedures may be **refined** so that animals are subjected to less pain and distress Refinements include administration of anesthetics to animals undergoing otherwise painful procedures; administration of tranquilizers for distress; humane destruction prior to recovery from surgical anesthesia, and careful scrutiny of behavioral indices of pain or distress, followed by cessation of the procedure or the use of appropriate analgesics. Refinements also include the enhanced use of noninvasive imaging technologies that allow earlier detection of tumors, organ deterioration, or metabolic changes and the subsequent early euthanasia of test animals.

Pain is defined as discomfort resulting from injury or disease, while distress results from pain, anxiety, or fear. Pain may also be psychosomatic, resulting from emotional distress. Although these are subjective phenomena, pain and distress can sometimes be identified and quantified by observing an animal's behavior. Pain is relieved with analgesics or anesthetics; distress is eased with tranquilizers. Widely accepted ethical standards require that

Resusci-Dog, Canine Cardiopulmonary-Resuscitation Simulator

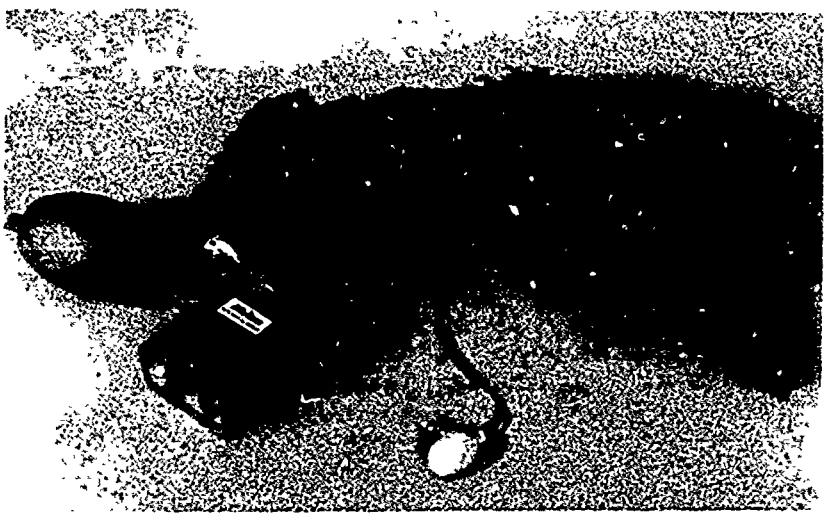

Photo credit Charles R Short, New York State College of Veterinary Medicine, Cornell University

Resusci-Dog, a plastic mannequin linked to a computer, can simulate an arterial pulse, and pressure can be applied to its rib cage for cardiac massage or cardiopulmonary resuscitation. Resusci-Dog has replaced about 100 dogs per year in the training of veterinary students at the New York State College of Veterinary Medicine.

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scientists subject animals to as little pain or distress as is necessary to accomplish the objectives of procedures. Professional ethics require scientists to provide relief to animals in pain or distress, unless administering relief would interfere with the objective of the procedure (e.g., when the objective is a better understanding of the mechanisms of pain).

HOW MANY ANIMALS ARE USED?

Estimates of the animals used in the United States each year range from 10 million to upwards of 100 million. OTA scrutinized a variety of surveys, including those of the National Research Council's Institute for Laboratory Animal Resources and the Animal and Plant Health Inspection Service (APHIS) of the U.S. Department of Agriculture (USDA). Indirect estimates of animal use were also based on data such as Federal funds spent on animal research and sales revenues of the Nation's largest commercial breeder of laboratory animals.

All these data are unreliable. No data source exists, for example, to enumerate how many institutions do not report animal use. In addition, nonreporting institutions may not be similar enough to reporting institutions to justify extrapolation. Thus every estimate of animal use stands as a rough approximation. With this caveat in mind, **the best data source available—the USDA/APHIS census—suggests that at least 17 million to 22 million animals were used in research and testing in the United States in 1983.** The majority of animals used—between 12 million and 15 million—were rats and mice. Current data permit no statement about any trends in animal use through recent years. Animal use in medical and veterinary education amounted to at least 53,000 animals in the school year 1983-84.

The Animal Welfare Act of 1966 (Public Law 89-544), as amended and presently enforced, requires research and testing facilities to report to USDA their annual use of dogs, cats, hamsters, rabbits, guinea pigs, and nonhuman primates. (About two-thirds of the reporting institutions also volunteer the number of rats and mice used.) For fiscal year 1983, the USDA reporting forms indicate the facilities used nearly 1.8 million of these six kinds of animals (see table 1).

Table 1.—Animal Use Reported to the U.S. Department of Agriculture, 1983[a]

Animal	Number used in 1983
Dogs	182,425
Cats	55,346
Hamsters	454,479
Rabbits	509,052
Guinea pigs	521,237
Nonhuman primates	59,336
Total	1,781,875

[a]Totals do not include rats or mice, two species that together represent the majority of animals used

SOURCE: Office of Technology Assessment

USDA reports are of limited utility because:

- the Department counts only six kinds of animals that together account for an estimated 10 percent of the total animals used (reporting of rats, mice, birds, and fish is not required);
- the annual summary report does not tabulate reports received after December 31st of each year, resulting in a 10- to 20-percent underestimation of laboratory use of regulated species;
- ambiguities in the reporting form ask respondents to add figures in a way that can cause animals to be counted twice; and
- terms on the reporting form are undefined (e.g., the form has room for voluntary information about "wild animals," but does not specify what animals might be included).

In the absence of a comprehensive animal census, the USDA reports will continue to provide the best data. Imprecise as they are, these reports can identify major changes in the numbers of dogs, cats, hamsters, rabbits, guinea pigs, and nonhuman primates. (It is important to note that any change in the total number of animals used may reflect not only the adoption of alternative methods, but changes in research and testing budgets as well.)

ETHICAL CONSIDERATIONS

At one end of a broad spectrum of ethical concerns about animal use is the belief that humans may use animals in any way they wish, without regard for the animals' suffering. At the other extreme is the notion—epitomized by the slogan "animals are people, too"—that each animal has the right not to be used for any purpose that does not benefit it. Each view is anchored in a school of philosophical thought, and people considering this issue can choose from a variety of arguable positions.

Prominent within the Western philosophic and religious tradition is the view that humans have the right to use animals for the benefit of humankind. This view is predicated on the assumption that human beings have special intrinsic value and thus may use natural animate and inanimate objects, including animals, for purposes that will enhance the quality of human life. Yet this tradition suggests that because animals are intelligent and sentient beings, they should be treated in a humane manner. Current policies and trends within the scientific community have reinforced this conviction by advocating that pain and suffering be minimized when animals are used in research, testing, or education.

Advocates of what generally is called animal welfare frequently question the objectives of animal use, as well as the means. They point out that animals can experience pain, distress, and pleasure. Drawing on the utilitarian doctrine of providing the greatest good for the greatest number, some animal welfare advocates weigh animal interests against human interests. In this view, it might be permissible to use animals in research to find a cure for a fatal human disease, but it would be unjust to subject animals to pain to develop a product with purely cosmetic value.

Some animal rights advocates carry this concern a step further and do not balance human and animal rights. They generally invoke the principle

of inalienable individual rights. They believe that animal use is unjustified unless it has the potential to benefit the particular animal being used. Animal rights advocates refer to the denial of animal rights as a form of "speciesism," a moral breach analogous to racism or sexism. Animals, by this reasoning, have a right not to be exploited by people.

People throughout the spectrum find common ground in the **principle of humane treatment,** but they fail to agree on how this principle should be applied. Society does not apply the principle of humane treatment equally to all animals. A cat may evoke more sympathy than a frog, for example, because the cat is a companion species and possesses apparently greater neurological sophistication than a frog, endowing it with both favored status and a familiarity that suggests to humans that they can interpret its behavior. Even within a species, all individuals are not treated consistently. Pet rabbits in the home and pest rabbits in the garden, like human friends and strangers, are treated differently.

The improvements in public health and safety made possible through the use of animals in research and testing are well known. But these questions remain: Do these advances justify animal use? How much of the improvements were actually dependent on the use of animals? Debate on these and other questions is bound to continue, but most parties agree that consideration of replacing, reducing, and refining the use of animals is desirable.

ALTERNATIVES IN RESEARCH

In research, scientists often explore uncharted territory in search of unpredictable events, a process that inherently involves uncertainty, missteps, and serendipity. Some biological research requires—and in the foreseeable future will continue to require—the use of live animals if the study of the complex interactions of the cells, tissues, and organs that make up an organism is to continue. Knowledge thus gained is applied to improving the health and well-being of humans and of animals themselves, and it may lead to the development of methods that would obviate the use of some animals.

Some nonanimal methods are becoming available in biomedical and behavioral research. As more develop, animal use in research will likely become less common. It is important to note, however, that **even if animals cannot be replaced in certain experiments, researchers can attempt to reduce the number used and also to minimize pain and distress.**

Most alternatives to current animal use in research fall into one of four categories:

- **Continued, But Modified, Use of Animals.** This includes alleviation of pain and distress, substitution of cold-blooded for warm-blooded vertebrates, coordination among investigators, and use of experimental designs that provide reliable information with fewer animals than were used previously.

- **Living Systems.** These include micro-organisms, invertebrates, and the in vitro culture of organs, tissues, and cells.
- **Nonliving Systems.** These include epidemiologic databases and chemical and physical systems that mimic biological functions.
- **Computer Programs.** These simulate biological functions and interactions.

The many fields of research—ranging from anatomy to zoology—use animals differently, and each thus has different prospects for developing and implementing alternatives. To determine the prevalence of animal and nonanimal methods in varied disciplines of research, OTA surveyed 6,000 articles published between 1980 and 1983 in 12 biomedical research journals and 3 behavioral research journals. Research disciplines were distinguished by their characteristic patterns of animal use, as measured by the percentages of published reports showing animal use, no animal use, and use of humans. Animal methods predominated in most of the journals surveyed, including the three behavioral research journals. The exceptions in the overall survey were cell biology, which used primarily nonanimal methods, and cardiology, which used primarily human subjects.

Using alternative methods in biomedical research holds several advantages from scientific, economic, and humane perspectives, including:

- reduction in the number of animals used;
- reduction in animal pain, distress, and experimental insult;
- reduction in investigator-induced, artifactual physiological phenomena;
- savings in time, with the benefit of obtaining results more quickly;
- the ability to perform replicative protocols on a routine basis;
- reduction in the cost of research;
- greater flexibility to alter conditions and variables of the experimental protocol;
- reduction of error stemming from interindividual variability; and
- the intrinsic potential of in vitro techniques to study cellular and molecular mechanisms.

Many of these alternative methods are accompanied by inherent disadvantages, including:

- reduced ability to study organismal growth processes;
- reduced ability to study cells, tissues, and organ systems acting in concert,
- reduced ability to study integrated biochemical and metabolic pathways,
- reduced ability to study behavior;
- reduced ability to study the recovery of damaged tissue;
- reduced ability to study interaction between the organism and its environment;
- reduced ability to study idiosyncratic or species-specific responses,
- reduced ability to distinguish between male- and female-specific phenomena; and
- a handicap to probing the unknown and phenomena not yet identified.

Behavior encompasses all the movements and sensations by which living things interact with both the living and nonliving components of their environment. Since one of the chief goals of behavioral research is an under-

standing of human behavior, there are obvious advantages to the use of human research subjects. There are also advantages to using animals, including the following:

- Laboratory research on animals offers a greater opportunity to control variables such as genetic background, prior experience, and environmental conditions, all of which affect behavior and can obscure the influence of the factor under study.
- The short lifespans of certain animals allow scientists to study behavior as it develops with age and across generations.
- Some animal behavior is less complex than human behavior, facilitating an understanding of basic elements and principles of behavior.
- The behavior of certain animals holds particular interest for humans. These animals include companion species, farm animals, and agricultural pests.

Although behavior is a biological phenomenon, behavioral research differs substantially from biomedical research in that researchers have fewer opportunities to study mechanisms isolated from living organisms. There is little prospect, for example, of using in vitro cultures to look at aggression, habitat and food selection, exploration patterns, or body maintenance activities—all topics studied by behavioral scientists. Yet in each of these disciplines, reduction or refinements of animal use may be possible. **It is the continued, but modified, use of animals that holds the most promise as an alternative in the field of behavioral research.**

ALTERNATIVES IN TESTING

Several million animals are used each year in testing substances for toxicity and establishing conditions for safe use. The resulting data—together with information about use and exposure, human epidemiologic data, and other information—are used in assessing and managing health risks.

As a reduction in the number of animals is a principal alternative, proper statistical design and analysis in testing protocols play an important role. The total number of animals needed for statistically significant conclusions depends on the incidence of toxic effects without administration of the test substance, the degree of variation from animal to animal for the biological effect that is of interest, and the need to determine a quantitative relationship between the size of the dose and the magnitude of the response. Statistical analysis plays a similarly important role in research.

One of the oldest and, perhaps for that reason, least sophisticated tests is the LD_{50} ("lethal dose" for "50" percent of the test animals) In this short-term, or acute, test, a group of animals, usually rats or mice, are exposed to a single substance, and the measured end point is death (although other observations may be made). The LD_{50} is the dose at which half the test animals can be expected to die. A range of doses is administered to some 30 to 100 animals and the LD_{50} is calculated from the results. **Tests providing the same information have recently been developed using as few as 10 animals, i.e., a 3- to 10-fold reduction.**

The LD_{50} is used to screen substances for their relative toxicity and mode of toxic action. Scientists and animal welfare advocates have criticized it in recent years, in part because it cannot be extrapolated reliably to humans, and in part because the imposition of a highly toxic or lethal dose seems particularly inhumane.

Another often-criticized acute toxicity assay is the **Draize eye irritancy test.** This involves placing a test substance into one eye of four to six rabbits and evaluating its irritating effects. Results are used to develop precautionary information for situations in which exposure of the human eye to the substance is possible. Substances with certain properties—e.g., a caustic pH—could be assumed to be eye irritants and not tested. **Draize procedures may also be modified to reduce pain, and in vitro methods to test for irritancy are under development.** A promising new bioassay for tissue irritancy makes use of the chorioallantoic membrane of the chick embryo (see fig. 1).

Other common tests include those for long-term chronic effects, carcinogenicity, reproductive and developmental toxicity, skin irritancy, and neurotoxicity. In addition to such descriptive toxicology (i.e., tests that focus on the response of the organism as a whole), testing may also be done to determine the mechanisms by which a substance is metabolized or excreted, and the chemical reactions by which toxic effects are produced. Such studies of mechanistic toxicology aid in the selection and design of descriptive tests.

The Federal Government plays a major role in this area, both through laws that directly or indirectly require testing and through guidelines that influence testing procedures. The greatest amount of testing is done under laws administered by the Food and Drug Administration (FDA) requiring that products be safe and effective and that labeling claims be substantiated. The Environmental Protection Agency (EPA) requires testing to support pesticide registrations and in certain other cases. For substances other than pesticides, EPA relies largely on published literature and EPA-sponsored testing. Other agencies that use animal testing data include USDA, the Consumer Product Safety Commission, the Occupational Safety and Health Administration, the Department of Transportation, the Federal Trade Commission, and the Centers for Disease Control.

Although most laws do not explicitly require animal testing, requirements of safety implicitly require that the best available means for determining safety be used. Thus, alternatives are not likely to be used widely until they can be shown to be at least as valid and reliable as the tests being replaced. Meeting these criteria is probably not overly difficult with some alternatives that involve reduction or refinement, but it may be harder to replace whole-animal testing totally with in vitro methods.

Reductions in the number of animals used can be brought about by using no more animals than necessary to accomplish the purpose of the test, by combining tests in such a way that fewer animals are needed, and by retrieving information that allows any unintentional duplication of earlier work to be avoided. Refinements include increased use of anesthetics and analgesics to ameliorate pain and tranquilizers to relieve distress. Replacements

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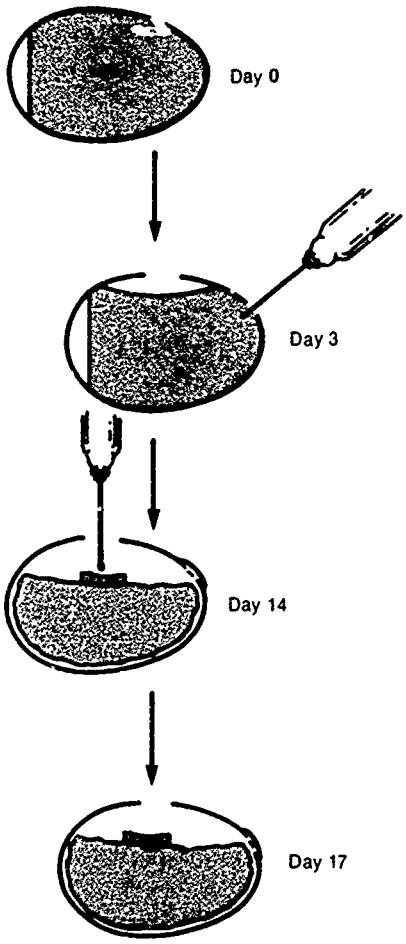
may involve human cell cultures obtained from cadavers or in surgery, animal cell cultures, invertebrates, or micro-organisms. For example, the use of an invertebrate in place of a vertebrate, as in the case of substituting horseshoe crabs for rabbits in testing drugs for their production of fever as a side effect, is increasingly accepted as a replacement.

Figure 1.—Chronological Sequence of Chick Embryo Chorioallantoic Membrane Assay



Day 0. Fertile eggs are incubated at 37° C. **Day 3.** The shell is penetrated in two places: A window is cut at the top, and 1 5 to 2 milliliters of albumin is removed with a needle and discarded The chorioallantoic membrance forms on the floor of the air space, on top of the embryo The window is taped **Day 14.** A test sample is placed on the embryonic membrane and contained within a plastic ring **Day 17.** The chorioallantoic membrane is evaluated for its response to the test substance, and the embryo is discarded.

SOURCE. J Leighton, J Nassauer, and R Tchao, "The Chick Embryo in Toxicology An Alternative to the Rabbit Eye," *Food Chem. Toxicol.* 23·293-298. Copyright 1985, Pergamon Press, Ltd.

Chick Embryo Chorioallantoic Membrane Assay

Photo credit: Joseph Leighton, Medical College of Pennsylvania

Typical reaction seen when certain concentrations of household products are placed on the 14-day-old chorioallantoic membrane and examined 3 days later on 17-day-old membranes. The thin white plastic ring has an internal diameter of 10 millimeters (0.4 inch). The area of injury occupies the entire plastic ring. Damaged blood vessels appear within the ring as an elaborate branching structure of pale, white, dead vessels of various sizes. The severity of the reaction is measured by measuring the diameter of the injury, in this instance spanning the entire ring.

The most promising in vitro methods are based on an understanding of whole-organ or organism responses that can be related to events at the cellular or subcellular level. Cells manifest a variety of reactions to toxins, including death, changes in permeability or metabolic activity, and damage to genetic material.

ALTERNATIVES IN EDUCATION

Although far fewer animals are used in education than in either research or testing, animal use in the classroom plays an important role in shaping societal attitudes toward this subject. As educational goals vary from level to level, so does the use of animals and therefore the potential for alternatives.

In elementary schools, live animals are generally present solely for observation and to acquaint students with the care and handling of different species. Although the guidelines set by many school boards and science teachers' associations limit the use of living vertebrates to procedures that neither

cause pain or distress nor interfere with the animals' health, these guidelines are not observed in all secondary schools. Science fairs are an additional avenue for students to pursue original research. The Westinghouse Science Fair prohibits the invasive use of live vertebrates, whereas the International Science and Engineering Fair has no such prohibition.

In the college classroom and teaching laboratory, alternatives are being developed and implemented because they sometimes offer learning advantages, are cheaper than animal methods, and satisfy animal welfare concerns. As a student advances, animal use at the postsecondary level becomes increasingly tied to research and skill acquisition. As graduate education merges with laboratory research and training, animal use becomes largely a function of the questions under investigation. In disciplines such as surgical training in the health professions, some measure of animal use can be helpful but is not universally viewed as essential.

Many alternative methods in education are already accepted practice. Replacements include computer simulations of physiological phenomena and pharmacologic reactions, cell culture studies, human and animal cadavers, and audiovisual materials. Clinical observation and instruction can also replace the use of animals in some laboratory exercises in medical and veterinary schools. Reduction techniques include the use of classroom demonstrations in place of individual students' animal surgery and multiple use of each animal, although subjecting an animal to multiple recovery procedures may be viewed as inhumane and counter to refined use. Refinements include the use of analgesics, euthanasia prior to recovery from surgery, observation of intact animals in the classroom or in their natural habitats, and the substitution of cold-blooded for warm-blooded vertebrates in laboratory exercises.

Humane education aspires to instill positive attitudes toward life and respect for living animals. Instruction in proper care and handling of various species may be complemented by exposure to the principles of animal use in research and testing and to alternative methods. This type of education promotes attitudes conducive to the development and adoption of alternatives.

COMPUTER SIMULATION AND INFORMATION RESOURCES

Recent advances in computer technology hold some potential for replacing and reducing the use of animals in research, testing, and education. In most cases, however, research with animals will still be needed to provide basic data for writing computer software, as well as to prove the validity and reliability of computer alternatives.

In research, scientists are developing computer simulations of cells, tissues, fluids, organs, and organ systems. Use of such methods enables less use of some animals. Limitations on the utility of computer simulations are due to a lack of knowledge of all the parameters involved in the feedback mechanisms that constitute a living system, which means the information on which the computer must depend is incomplete.

In testing, computers allow toxicologists to develop mathematical models and algorithms that can predict the biological effects of new substances based on their chemical structure. If a new chemical has a structure similar to a known poison in certain key aspects, then the new substance also may be a poison. Such screening can thus preempt some animal use.

In education, computer programs simulate classroom experiments traditionally performed with animals. The most advanced systems are videodisks that combine visual, auditory, and interactive properties, much as a real classroom experiment would. Computer simulations can eliminate both the detailed work of conducting an experiment and the effects of extraneous variables, helping students concentrate on a lesson's main point.

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One way any existing unintentional duplication might be ended, and thus animal use reduced, is to establish or refine existing computer-based registries of research or testing data. The National Cancer Institute and the National Library of Medicine (NLM) developed a limited registry in the late 1970s, but it failed: The Laboratory Animal Data Bank (LADB) had few users, as it did not serve user needs.

Any new registry should contain descriptions of the methods of data collection and the laboratory results for both experimental and control groups of animals. Inclusion of negative results (which are seldom reported in journals) could also reduce animal use. Entries should undergo peer review before inclusion in the registry; that is, studies should be scrutinized to judge the validity and reliability of the data. A registry along these lines would probably be 3 to 15 times as complex and costly as the unsuccessful LADB.

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Twenty States and the District of Columbia regulate the use of animals in research to some extent As in the case of the Federal Animal Welfare Act, most State laws address such matters as procurement rather than the actual conduct of experiments.

All 50 States and the District of Columbia allow some form of pound animal use for research and training. In some States, laws permitting or requiring research and teaching facilities to purchase stray dogs and cats from pounds and shelters have been the targets of repeal efforts. To date, 9 States prohibit in-State procurement (although not importation from out-of-State) of pound animals for research and training. Of these, Massachusetts will in October 1986 prohibit the use of any animal obtained from a pound.

Institutional and Self-Regulation

Opponents of increased government regulation of research assert that investigators and their institutions are best suited to determine what constitutes appropriate care and use of animals. To regulate animal use at this level, the scientific community relies on a variety of policies and administrative structures.

Taken together, the requirements for institutional animal committees contained in the Animal Welfare Act (as amended), the Health Research Extension Act of 1985, and the PHS *Policy* bring the overwhelming majority of experimental-animal users in the United States under the oversight of a structured, local review committee.

Institutions that receive funds from PHS for research on warm-blooded laboratory animals must have committees that oversee the housing and routine care of animals. NIH reports that about a quarter of these animal care and use committees currently review research proposals to determine whether experimental procedures satisfy concerns about animal welfare. Committees with such responsibility are not unique to research with animals. For 15 years, similar groups have been weighing ethical issues raised by the use of human research subjects, and these committees have served as models in the development of animal care and use committees.

Committees usually have included the institution's attending veterinarian, a representative of the institution's administration, and several users of research animals. Some committees also have nonscientist members, or lay members not affiliated with the institution. Nonscientist and lay seats have been filled by clergy, ethicists, lawyers, humane society officials, and animal rights advocates **Animal care and use committees at PHS-supported**

facilities are today required to consist of not less than five members, and must include at least:

- **one Doctor of Veterinary Medicine with training or experience in laboratory animal science or medicine, who has responsibility for activities involving animals at the institution;**
- **one practicing scientist experienced in research using animals;**
- **one member whose primary concerns are in a nonscientific area; and**
- **one individual who is not affiliated with the institution in any way.**

The minimum committee structure required by the PHS policy is thus more rigorous than that mandated by Federal law. The Animal Welfare Act and the Health Research Extension Act do not require, for example, that the committee veterinarian be trained in laboratory-animal medicine. The acts require a minimum committee of three individuals, whereas the PHS policy requires five.

Institutional regulation generally entails compliance with some type of minimum standards for an animal facility, usually those of the NIH *Guide for the Care and Use of Laboratory Animals*. Compliance can be checked in-house or through accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC), a voluntary private organization As of April 1985, a total of 483 institutions had received AAALAC accreditation, which requires site visits that include interviews, inspection of facilities, and review of policies and records. Accredited institutions include hospitals, universities, facilities of the Veterans' Administration (VA), and pharmaceutical manufacturers.

A number of scientific and professional societies, universities, and corporations have promulgated statements of policy concerning their members or employees' standards of conduct in animal use. These policies generally require:

- humane care and use of animals,
- minimization of the number of animals used,
- alleviation of pain and suffering, and
- supervision of animal use by qualified personnel.

Twelve of fifteen such policies reviewed by OTA encourage or require consideration of the use of alternatives. But only 3 of the 15 include enforcement provisions or mention sanctions against violators.

Regulation Within Federal Agencies

Six Federal departments and four independent agencies use laboratory animals intramurally and account for approximately one-tenth of the animal use in the United States Beginning in December 1986, Federal facilities in those departments and agencies using animals will be required by the 1985 amendments to the Animal Welfare Act to install institutional animal committees Each committee shall report to the head of the Federal agency conducting the experimentation.

Most Federal agencies that use animals in research or testing have formal policies and administrative structures to ensure that the animals receive humane treatment. At the request of the Executive Office of Science and Technology Policy, the Interagency Research Animal Committee developed a 450-word policy statement, *Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education*, to be followed by all Federal agencies supporting animal use.

No one Federal agency policy on animal care and use has all the characteristics needed to address all issues adequately. Combining certain aspects from each would produce an effective uniform Federal policy. Almost all policies today require adherence to the NIH *Guide* and the Animal Welfare Act. Most agencies also require an attending veterinarian and an animal care and use committee at each facility. The committees generally review research protocols to ensure that animals are not used in excessive numbers, that adequate provisions are made for animal care and pain relief, and that alternatives are used whenever possible. Most committees and attending veterinarians have little enforcement power, and those who have such power rarely use it.

Some agencies' policies have features that would be considered advantageous by animal welfare advocates. NIH and the National Aeronautics and Space Administration have laypeople on their animal care and use committees. The VA requires all its animal facilities to acquire AAALAC accreditation. The Department of Defense has a separate policy and committee for nonhuman primates. The Air Force has solicited evaluation of its policies by a panel of independent experts and plans to implement the group's recommendations.

International Regulation

OTA surveyed laws controlling use of experimental animals in 10 foreign nations, including countries of Western Europe (see table 2) and Australia and Canada. Comparative analysis of regulation of animal use abroad can yield lessons from foreign regulatory experiences, models for regulation, and models for funding of alternatives.

A review of foreign laws, especially those revised or instituted in the last decade, indicates three trends of note in government control of animal research:

- Attention is shifting away from intentionally or negligently "cruel" treatment and toward the avoidance of pain and suffering. This change in perspective raises the difficulty of defining prohibited conduct, and disagreement arises over the definition of animal pain and suffering. Newer statutes rely on authorized reviewers who check experimental plans in advance and apply their own sensibilities to satisfy themselves—and thereby the public interest—that pain and suffering are not being inflicted without justification.
- There is increasing emphasis on finding alternatives. The old method of justifying animal research by reference to its potential for providing

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Most State anticruelty statutes forbid both active cruelty and neglect. Many of these laws incorporate vague terms, and alleged offenders offer a variety of defenses. Enforcement may be delegated to humane societies, whose members are not well trained to build criminal cases skillfully and are underfunded for the task.

Twenty States and the District of Columbia regulate the use of animals in research to some extent. As in the case of the Federal Animal Welfare Act, most State laws address such matters as procurement rather than the actual conduct of experiments.

All 50 States and the District of Columbia allow some form of pound animal use for research and training. In some States, laws permitting or requiring research and teaching facilities to purchase stray dogs and cats from pounds and shelters have been the targets of repeal efforts. To date, 9 States prohibit in-State procurement (although not importation from out-of-State) of pound animals for research and training. Of these, Massachusetts will in October 1986 prohibit the use of any animal obtained from a pound.

Institutional and Self-Regulation

Opponents of increased government regulation of research assert that investigators and their institutions are best suited to determine what constitutes appropriate care and use of animals. To regulate animal use at this level, the scientific community relies on a variety of policies and administrative structures.

Taken together, the requirements for institutional animal committees contained in the Animal Welfare Act (as amended), the Health Research Extension Act of 1985, and the PHS *Policy* bring the overwhelming majority of experimental-animal users in the United States under the oversight of a structured, local review committee.

Institutions that receive funds from PHS for research on warm blooded laboratory animals must have committees that oversee the housing and routine care of animals. NIH reports that about a quarter of these animal care and use committees currently review research proposals to determine whether experimental procedures satisfy concerns about animal welfare. Committees with such responsibility are not unique to research with animals. For 15 years, similar groups have been weighing ethical issues raised by the use of human research subjects, and these committees have served as models in the development of animal care and use committees.

Committees usually have included the institution's attending veterinarian, a representative of the institution's administration, and several users of research animals. Some committees also have nonscientist members, or lay members not affiliated with the institution. Nonscientist and lay seats have been filled by clergy, ethicists, lawyers, humane society officials, and animal rights advocates. **Animal care and use committees at PHS-supported**

facilities are today required to consist of not less than five members, and must include at least:

- **one Doctor of Veterinary Medicine with training or experience in laboratory animal science or medicine, who has responsibility for activities involving animals at the institution;**
- **one practicing scientist experienced in research using animals;**
- **one member whose primary concerns are in a nonscientific area; and**
- **one individual who is not affiliated with the institution in any way.**

The minimum committee structure required by the PHS policy is thus more rigorous than that mandated by Federal law. The Animal Welfare Act and the Health Research Extension Act do not require, for example, that the committee veterinarian be trained in laboratory-animal medicine. The acts require a minimum committee of three individuals, whereas the PHS policy requires five.

Institutional regulation generally entails compliance with some type of minimum standards for an animal facility, usually those of the NIH *Guide for the Care and Use of Laboratory Animals*. Compliance can be checked in-house or through accreditation by the American Association for Accreditation of Laboratory Animal Care (AAALAC), a voluntary private organization. As of April 1985, a total of 483 institutions had received AAALAC accreditation, which requires site visits that include interviews, inspection of facilities, and review of policies and records. Accredited institutions include hospitals, universities, facilities of the Veterans' Administration (VA), and pharmaceutical manufacturers.

A number of scientific and professional societies, universities, and corporations have promulgated statements of policy concerning their members' or employees' standards of conduct in animal use. These policies generally require:

- humane care and use of animals,
- minimization of the number of animals used,
- alleviation of pain and suffering, and
- supervision of animal use by qualified personnel.

Twelve of fifteen such policies reviewed by OTA encourage or require consideration of the use of alternatives. But only 3 of the 15 include enforcement provisions or mention sanctions against violators.

Regulation Within Federal Agencies

Six Federal departments and four independent agencies use laboratory animals intramurally and account for approximately one-tenth of the animal use in the United States. Beginning in December 1986, Federal facilities in those departments and agencies using animals will be required by the 1985 amendments to the Animal Welfare Act to install institutional animal committees. Each committee shall report to the head of the Federal agency conducting the experimentation.

Most Federal agencies that use animals in research or testing have formal policies and administrative structures to ensure that the animals receive humane treatment. At the request of the Executive Office of Science and Technology Policy, the Interagency Research Animal Committee developed a 450-word policy statement, *Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Education*, to be followed by all Federal agencies supporting animal use.

No one Federal agency policy on animal care and use has all the characteristics needed to address all issues adequately. Combining certain aspects from each would produce an effective uniform Federal policy. Almost all policies today require adherence to the NIH *Guide* and the Animal Welfare Act. Most agencies also require an attending veterinarian and an animal care and use committee at each facility. The committees generally review research protocols to ensure that animals are not used in excessive numbers, that adequate provisions are made for animal care and pain relief, and that alternatives are used whenever possible. Most committees and attending veterinarians have little enforcement power, and those who have such power rarely use it.

Some agencies' policies have features that would be considered advantageous by animal welfare advocates. NIH and the National Aeronautics and Space Administration have laypeople on their animal care and use committees. The VA requires all its animal facilities to acquire AAALAC accreditation. The Department of Defense has a separate policy and committee for nonhuman primates. The Air Force has solicited evaluation of its policies by a panel of independent experts and plans to implement the group's recommendations.

International Regulation

OTA surveyed laws controlling use of experimental animals in 10 foreign nations, including countries of Western Europe (see table 2) and Australia and Canada. Comparative analysis of regulation of animal use abroad can yield lessons from foreign regulatory experiences, models for regulation, and models for funding of alternatives.

A review of foreign laws, especially those revised or instituted in the last decade, indicates three trends of note in government control of animal research:

- Attention is shifting away from intentionally or negligently "cruel" treatment and toward the avoidance of pain and suffering. This change in perspective raises the difficulty of defining prohibited conduct, and disagreement arises over the definition of animal pain and suffering. Newer statutes rely on authorized reviewers who check experimental plans in advance and apply their own sensibilities to satisfy themselves—and thereby the public interest—that pain and suffering are not being inflicted without justification.
- There is increasing emphasis on finding alternatives. The old method of justifying animal research by reference to its potential for providing

Table 2.—National Laws for the Protection of Animals in Selected European Countries

Provisions	Denmark	Federal Republic of Germany	Netherlands	Norway	Sweden	Switzerland	United Kingdom
Species protected	Vertebrates	All animals	Vertebrates, native species	Vertebrates, crustaceans	Vertebrates	Vertebrates	Vertebrates
Distinctions among species	Should use lowest rank, dogs, cats, monkeys purpose bred	Better to use invertebrates or cold-blooded vertebrates	Vertebrates better protected	Monkeys, dogs, cats better protected	Should use lowest rank, all purpose-bred	Should use lowest rank	Primates, dogs, cats, equidae preferred, no stray dogs
Alternatives must be used if available	Yes	Yes	Vertebrates	Yes	Alternatives promoted	Yes	Alternatives encouraged
Anesthetics, analgesics or approval required for painful experiments	Except for minor or transient pain	If pain, suffering, or injury likely	If injury or pain likely	If pain is possible (unless Board approves)	Surgery on mammals unless committee approves	Slight pain or anxiety, if too painful must forgo	Statute does not specify, but certificate may require
Educational uses	Higher education, technique	High school and above	University and vocational	Professional training	Allowed, but restricted	Not allowed	Some demonstration, not for practicing
Ban on animal use for more than one painful experiment	All dogs, cats, monkeys, most experiments	No multiple surgeries on vertebrates	Rarely reused because of pain requirements	Only one experiment allowed per animal	Rarely reused because of pain requirements	Only reused if pain was slight	If anesthetized or because of pain requirements
License/permit for dealers, facilities, and investigators	All facilities, head investigators	Dealers, facilities, investigators	Dealers (dogs and cats), facilities	Investigators or facilities licensed	Breeders, facilities	Breeders, facilities	Facilities registered, investigators licensed
Review of experiments	Most experiments need approval by national board	Not needed, proposed that facility's animal welfare officer review	Head of institute reviews	Investigator or facility (licensee) review	Notification/application, tiered system	2 State committees review	Home Office and Advisory Committee
Administration	Centralized government/ nongovernment board, licensee is responsible	States enforce and administer (proposed that facilities have animal welfare officer)	Central enforcement and reporting, administration by institute	Central coordination, some functions delegated to licensees	Central coordination with oversight by facility head and committee	Central coordination, administered by States	Centralized, shared by Head Office, Advisory Committee, Royal Society
Animal welfare representation	3 nominees to national board	Being considered	Not required, but facility reports are public	Not required	On all committees, being reconsidered	Members of national commission	Advisory Committee
Reporting	Annual report	In house recordkeeping	Annual report	Annual report	Government recordkeeping	In-house recordkeeping	Annual reports

SOURCE: Office of Technology Assessment

new knowledge is being enhanced by the greater burden of demonstrating that no less painful method is available to achieve the same result. Increasingly, animals are being viewed as having an interest in not being hurt.

- Countries with comprehensive reporting systems (e.g., the United Kingdom) have found that fewer animals are now being used in experiments. The data are insufficient to determine the reasons for these reductions or what the effect may be on the production of new information.

These trends indicate a growing interest in Western Europe in replacing, reducing, or refining the use of animals through legislation.

It is not clear whether the tighter control found in some West European countries can be applied in the United States. Most West European nations are more homogeneous than is this country of federated States. In geographical dispersal and size, the research enterprises in those countries are small—there are fewer than 300 investigators using animals in Denmark, for example. The British system functions well, despite its complexity, because it has been refined over the course of a century. New scientists are weaned on it, and the inspector is a familiar sight in the laboratory. The British system's enforcement is based more on advice and negotiation than on confrontation.

POLICY ISSUES AND OPTIONS FOR CONGRESSIONAL ACTION

Seven policy issues related to alternatives to animal use in research, testing, and education were identified during the course of this assessment. The first concerns the implementation of alternatives and examines options that might encourage the research, testing, and education communities to adopt currently available methods of replacing, reducing, and refining their use of animals. The second issue explores options for promoting research and development leading to more and better alternatives. Both recognize that scientifically valid alternative methods can make positive contributions to research, testing, and education and might therefore be promoted.

The five additional policy issues examined are: disseminating information about animal experimentation, restricting animal use, counting animal use, establishing a Federal animal use policy, and changing the implementation of or amending the Animal Welfare Act. Although these policy issues do not explicitly address either the implementation or development of alternative methods, they are inextricably linked to the replacement, reduction, and refinement of animal use.

Associated with each policy issue are several options for congressional action, ranging in each case from taking no specific steps to making major changes. The order in which the options are presented should not imply their priority. Furthermore, the options are not, for the most part, mutually exclusive. Adopting one does not necessarily disqualify others in the same category or within any other category. A careful combination of options

might produce the most desirable effects. In some cases, an option may suggest alterations in more than one aspect of alternatives to using animals. It is important to keep in mind that changes in one area have repercussions in others.

Some of the options involve direct legislative action. Others are oriented to the actions of the executive branch but involve congressional oversight or encouragement. Congress can promote alternatives in at least three ways. It can provide incentives through tax policies, grants, or educational assistance It can mandate the adoption or development of alternatives by means of appropriations or legislation. And it can provide encouragement via oversight or resolutions. Table 3 summarizes the seven policy issues and associated options derived from this assessment.

ISSUE: Should steps be taken to encourage the use of available alternatives in research, testing, or education?

Alternatives to animals become accepted practice in the research, testing, and educational communities as methods are developed through research, validated by independent measurements, gradually accepted by the scientific community, and implemented as they come to be relied on or required. Several alternatives to the use of animals are in the validation or implementation phase today; for the most part, these methods are based on reductions and refinements. Approaches that replace the use of animals have generally not been completely validated and accepted. Instead, these represent possibilities for the longer term. (An exception may be educational simulations of living systems where an adequate range of physiological variables is known.) The processes of validation and gradual implementation are certain to continue, and they could be accelerated.

Analysis of alternatives in research, testing, and education demonstrates differing availability both among and within these three areas. In research, for example, animal methods can be complemented by computer models, and experiments may be designed to provide the desired information with fewer animals. Dissemination of information within the research community may reduce any instances of unintentional duplication, thereby lowering the number of animals used. In testing, the LD_{50} protocol has in many cases been modified to use fewer animals. And eye irritancy can be assumed—without testing—for substances exhibiting strong skin irritation or having a strongly acid or alkaline pH. In educational settings, exercises not involving animals may be substituted to teach the scientific method or to introduce biological concepts. In other instances, animals are destroyed humanely following a single surgery in a teaching session, rather than experiencing multiple recovery procedures. Four options address the implementation of alternatives such as these.

Option 1: Take no action.

As alternatives are developed and validated, they are likely to continue being implemented at an uneven pace, influenced by factors largely external to Congress Science and technologies will continue to evolve, and as

Table 3.—Policy Issues Related to Alternatives to Animal Use and Options for Congressional Action

Policy issue						
Using existing alternatives	Developing new alternatives	Disseminating information	Restricting animal use	Counting animals used	Establishing a Federal animal use policy	Changing Animal Welfare Act
Options for congressional action						
Take no action Charge a Federal entity with coordinating the implementation of alternatives Encourage alternative methods in Federal testing requirements Ban procedures for which alternatives are available	Take no action Charge a Federal entity with coordinating the development of alternatives Fund development of alternatives	Take no action Mandate easy access to federally funded testing and research data Promote greater use of testing data submitted to Federal agencies Require literature searches Create new data-bases Translate foreign literature into English	Take no action Restrict use of certain kinds of animals Restrict use of certain protocols Restrict acquisition of animals from certain sources License animal users for certain protocols and/or kinds of animals Prohibit animal use	Take no action Eliminate APHIS[a] census Correct inadequacies in present APHIS[a] reporting system Expand APHIS[a] census to include rats and mice Establish independent census	Take no action Establish intramural Federal policy of minimum standards	Take no action Eliminate funding for enforcement Increase funding for enforcement Amend to expand coverage to include experimentation Amend to realign enforcement authority Amend to preempt State and local laws

[a]Animal and Plant Health Inspection Service

SOURCE Office of Technology Assessment

nonanimal methods emerge from research and validation, they may or may not be accepted and implemented by the scientific community.

This course does not necessarily pass judgment on the value of adopting alternatives per se. Nor does it mean that alternatives will not be implemented. It would merely indicate that Congress has decided against encouraging or forcing the implementation of alternatives beyond its direction in 1985 to NIH to establish a plan to develop and assess alternatives in biomedical research (Public Law 99-158). This option might illustrate the belief that external political, ethical, economic, and scientific factors are sufficient to govern the implementation of alternatives.

Further congressional action toward implementation might be judged unnecessary because various other sources are already acting to implement alternatives. For example, EPA has defined circumstances where the LD_{50} test can be replaced by a limit test, and FDA has stated that it does not require data derived from the LD_{50} test; industry is watching to gauge the practical effects of these statements. Also, members of the soap and detergent industry have implemented modifications of the LD_{50} test. Noteworthy, too, is the important role of institutional animal care and use committees in all phases of animal experimentation. In education, medical schools are conducting some laboratory exercises with computer simulations or video demonstrations in lieu of live animals. Medical students in some instances bypass experiments and training involving animals, proceeding from cadavers to people. Activities such as these are likely to continue without new congressional action.

Additional congressional steps may be deemed inappropriate because implementation of alternatives may be judged unimportant. Some people do not object to animal use, for example, in toxicological testing. They believe the status quo brings the comforts and health benefits of new products and technology and protects them from hazards.

Option 2 Require a new or existing Federal entity to coordinate the validation and implementation of alternatives.

This action is based on the assumption that validation and implementation of alternatives would occur more rapidly with enhanced Federal coordination. Along this line, an information service at the National Agricultural Library on improved methods of animal experimentation was mandated by Congress in 1985 (Public Law 99-198). A clearinghouse for resources required to implement alternatives would further hasten their adoption. This entity might, for example, be a central source for computer software or cell culture material.

Existing Federal entities that might be assigned such responsibilities include some component of the National Institutes of Health (e.g., the Division of Research Resources), the National Toxicology Program, or the National Center for Toxicological Research. Coordinating activities could include symposia, workshops, newsletters, scholarships, grants, and the issuance of model protocols or guidelines. The coordinating body could monitor both public and private initiatives. In 1985, Congress took a step toward coordination

of the use of alternatives in biomedical research conducted by or through NIH. It directed NIH to disseminate information about alternatives found to be valid and reliable to those involved in animal experimentation (Public Law 99-158).

Educational programs play a central role in this type of effort. Training scientists in replacement methods and raising awareness about reductions and refinements is likely to increase the implementation of alternatives. This type of education is closely allied with the teaching of principles of humane care and use.

Animal care and use committees at individual institutions might function as a relay between Federal coordination efforts and individual investigators. The institutional animal care and use committee might be required to suggest alternative methods as part of its review of animal care and use. Linked in this way to a Federal implementation effort, these committees would both feed into and draw on the resources of the Federal entity.

A different type of coordination, particularly in research, would be the attachment of provisions to Federal grants regarding the implementation of alternatives. Research grant applications using alternative methods could be awarded higher priority scores in the grant evaluation process or be otherwise favored. This strategy would require sufficient flexibility to ensure that valuable, state-of-the-art scientific proposals that may not involve alternatives are not handicapped. Funding mechanisms could also be used to encourage coordination between laboratories. The responsibility for overseeing the implementation of alternatives via funding mechanisms could be borne by each source of Federal funding.

Option 3: Encourage regulatory agencies to review existing testing guidelines and requirements and to substitute alternatives whenever scientifically feasible.

Through oversight or legislation, Congress could encourage or require Federal agencies to evaluate existing alternatives in testing, to participate in their validation, to adopt them where appropriate, and to report to Congress on their progress in implementing alternatives, as the NIH has been asked to do (Public Law 99-158). Such agency review would have to be a periodic or continuing effort, given rapid advances in the state of the art. Some review of testing guidelines now occurs in keeping requirements up to date, although the purpose of that review is to improve the science rather than to protect animals per se. Formal agency review of international testing guidelines, such as those of the Organization for Economic Cooperation and Development, could also be encouraged. The costs of agency review should be moderate, entailing input from agency experts, comment from outside experts, and publication. If Federal laboratories were involved in the validation of alternative testing methods, additional costs would be incurred. Such a policy could encourage industry to develop alternatives because the barriers to acceptance would be reduced.

Option 4: Ban procedures for which alternatives are available, or give a Federal agency authority to ban procedures as valid alternatives become available.

This option recognizes that prohibitions can be used to force technological change. Prohibiting procedures for which scientifically acceptable alternatives are already available would accelerate the implementation of such alternatives. Existing reductions and refinements in animal use include the greater use of analgesics in research, the use of fewer animals in the LD_{50} and Draize eye irritancy tests, and reliance on videotaped demonstrations and computer simulations in education.

A ban could not only force implementation of existing alternatives, but, over time, help focus the development of new techniques (as discussed in the next section) and allow considerable flexibility in achieving the desired end. A disadvantage of banning a specified procedure is that the replacement, or the process of developing one, may be even more politically unacceptable (e.g., the in vitro culture of human fetal nerve cells). A prohibition also takes no account of the question of judging the scientific acceptability of an alternative.

In pursuing this option or the preceding one, it is important to appreciate that the swiftest adoption of alternatives may come about if regulatory agencies avoid mandating specific testing requirements. Requiring specified tests might actually serve as a strong inhibitor to the implementation (and development) of alternative methods. Greater flexibility is achieved when testing requirements are defined in a manner that allows judgment and encourages use of alternate methods. Viewed from this perspective, the adoption of alternatives might be best stimulated by regulatory requirement for evaluation of a potential toxic response, such as mutagenicity, rather than requirement of a specified test for mutagenicity.

ISSUE: Should the more rapid development of new alternatives in research, testing, or education be stimulated?

Alternatives are currently being developed in many phases of animal use. It is worth noting that development of many of these techniques, especially their validation, cannot occur without animals being used (unless humans are used instead). In addition, many replacement systems will never be fully divorced from animal research and testing, and therefore they will serve to reduce but not eliminate animal use.

Certain research and testing methods now being developed, such as in vitro culture of animal components, bear great promise as alternatives. Similarly, the growing capabilities of computer modeling, for example biological simulation and pharmacology, may reduce the number of animals needed. Development of an enhanced ability to detect and relieve pain can help refine animal use.

Research that spawns alternatives usually takes place across traditional disciplinary lines—principally within the life sciences—but also in applied

mathematics, statistics, engineering, physics, and chemistry. The principal support for such research comes from Federal funds, predominantly NIH and the National Science Foundation. In general, there is little incentive for private investment in methodologies at a stage so remote from commercialization and, in the case of testing, so governed by regulation. Some private concerns, however, specifically fund research into alternative testing methods.

Clearly, research and development require money. Determining the optimum level of funding, however, and the best way to distribute funds remains elusive. Nonetheless, the promotion of such research is likely to increase the number of alternatives available for implementation; in turn, increased implementation is likely to spur research in this area.

Option 1: Take no action.

If Congress takes no specific steps beyond its recent charge to NIH to establish a plan for the development of alternatives in biomedical research, the development of alternatives will continue to be a function of ethical, political, economic, and scientific factors.

That alternatives are being developed in the absence of direct legislation is best illustrated by research centers at Rockefeller University and The Johns Hopkins University funded by corporate and private donations. In addition, corporations are undertaking work in-house or sponsoring it in universities, often in response to scientific, economic, animal welfare, and public relations considerations.

An uncertain pace of development marks the chief disadvantage of this option. Although alternatives may emerge, changing research priorities in both the public and private sectors will affect the rate of development. From another perspective, this is an advantage: It permits researchers to respond to changing needs and priorities with minimal Federal interference.

Option 2. Require a new or existing Federal entity to coordinate the development of alternatives.

Implementation of this option would have great symbolic value within the scientific and animal welfare communities and could lead to more rapid development of alternatives. A central clearinghouse for the development of alternatives could compile and maintain records of all federally funded research and development (R&D) on alternatives. Information on R&D in the private sector would be a valuable component of the coordination effort, though it may prove difficult to obtain.

Coordination could involve identifying research areas likely to lead to new alternatives and reviewing Federal support for those areas across agency lines. The latter responsibility might preclude housing this entity within an existing Federal agency involved in funding R&D on alternatives to avoid either a real or apparent conflict of interest.

As in the implementation of alternatives (see preceding issue), education plays a central role in the development of such approaches. Coordination of efforts aimed at informing investigators and students about animal research could be among the responsibilities of this Federal entity.

Option 3: Provide intramural and extramural Federal funding for the development of alternatives.

An effective mechanism for encouraging R&D on alternatives is funding. Small pilot programs might assess whether or not targeted development is effective.

Development of alternatives in testing within the Federal Government is a natural offshoot of and closely allied with toxicological research. The agencies most likely to produce alternatives in response to new Federal funding are the National Cancer Institute and NIH. Because testing is so closely tied to regulation, funding could also be directed to FDA, EPA, the Consumer Product Safety Commission, and the National Institute for Occupational Safety and Health. Regulatory agencies could be required to develop alternatives to specified tests or to spend funds generally toward their development.

To stimulate extramural R&D, granting agencies reviewing applications could be required to assign priority to those that contain research with promise for the development of new alternatives. Postdoctoral training programs could be established, along the lines of NIH's National Research Service Awards, to ensure a steady supply of young researchers schooled in traditional disciplines, ranging from molecular biology to animal behavior, with applications in the development of alternatives.

Financial incentives to private groups developing alternatives could take the form of tax incentives—perhaps tax credits in addition to those already in place for R&D. Such groups could also be eligible for a new program (analogous to the Small Business Innovation Research program) that would target the development of alternatives.

ISSUE: Should improvements be made in information resources to reduce any unintentionally duplicative use of animals in research and testing?

Science is able to advance rapidly because information about what has been done is disseminated. If attempts to find prior work are inadequate or prior work is not sufficiently accessible, unintentional duplication may occur. Such unnecessary repetition of experiments must be distinguished from replication of experiments to demonstrate the reproducibility of a method or to confirm the validity of results.

The amount of unintentional, largely duplicative research and testing that occurs today is unknown. Investigations into the amount and circumstances of unintentional duplication would be valuable in determining whether it results in substantial waste of animals or funds. Moreover, consultations with potential users of any new information resources would be essential in implementing certain options addressing this issue.

Although the storage and retrieval of data are costly, there are clear benefits to making information that reduces unintentional duplication readily available. Among these benefits are savings in the expense and time associated with animal research and testing. Other benefits are savings in animal lives and the additional work that might be done if resources are not wasted.

Option 1: Take no action.

By making the National Agricultural Library the focus of a service to provide information on improved methods of animal experimentation (Public Law 99-198), Congress in 1985 indicated its intention to facilitate the dissemination of information about alternatives and to prevent unintended duplication of animal experimentation.

Even if no further improvements in information resources are made specifically for the sake of avoiding unintentionally duplicative animal use, general improvements in information resources will proceed as a matter of course. Many resources already exist. The National Library of Medicine, the National Toxicology Program, and other Federal entities maintain large databases that contain information or citations to published sources. Major commercial databases exist as well. National libraries and information centers provide the full text of articles and reports. The National Technical Information Service (NTIS) catalogs, stores, and distributes on request many unpublished Federal reports. Improvements in these resources can be expected, either to fill needs for which the benefits justify the costs or to achieve other information policy goals, such as openness in government or advancement of science.

Option 2: Require that results of all federally funded research and testing be conveniently accessible.

By means of oversight authority or legislation, all Federal entities could be required to provide convenient access to the results of all federally funded animal research and testing. Implementation could be largely through mechanisms already available—publishing in the scientific literature; circulating published reports or depositing them with NTIS, NLM, the National Agricultural Library, or other entity; or entering the results in a publicly available database. New databases might also be established. Requirements that results be made conveniently accessible could apply to Federal employees, contractors (through contract terms), and grantees (as a condition of awards). Contractors and grantees, however, may not be enthusiastic about assuming the burden of publicizing their results and responding to requests for information.

This option recognizes that much research and some testing using animals is federally funded, that dissemination of research and testing results could be more comprehensive, and that better dissemination might reduce any unintentional duplication. Because publication and information dissemination are normally much less costly than obtaining original data, the benefits of enhanced communication extend beyond saving animal lives.

It is important to note that most federally funded work, indeed the vast majority of significant work, is already accessible, although access comes with different levels of convenience. And the results of federally funded work (except some grants) are available under the Freedom of Information Act (FOIA). Requiring that all results be conveniently accessible may burden databases and libraries with inconclusive results or other information that will not be used.

Option 3: Promote greater use of animal testing data submitted by industry to Federal agencies, except where confidentiality protections apply.

Industry must submit data to regulatory agencies before it can market certain products or sometimes in response to reporting requirements. Statutory and regulatory provisions already exist that make some of this information publicly available, thus theoretically avoiding unintentional duplication. In addition, information that is voluntarily submitted and not claimed as confidential is available under FOIA.

Using oversight authority or legislation, greater use of nonconfidential information could be promoted, for example, by requiring that it be put into databases, compiled in reports, or summarized in newsletters. Industry could bear the cost of information dissemination, and any data submission to the Federal Government would have to be accompanied by evidence of intent to publish nonconfidential testing data. Industry may be unenthusiastic about such a procedure, because in some cases nonconfidential data provide direct clues to confidential data. Nevertheless, greater availability of nonconfidential data could aid in avoiding unintentionally duplicative testing.

The extent to which researchers who need such data already know how to obtain them is not known. The needs of those engaged in animal testing must be carefully gauged prior to consideration of this option. A further consideration is the willingness of those who generate the data to encourage others to benefit from their investment.

Option 4: Require comprehensive literature searches to ensure that federally funded research or testing involving animals is not duplicative.

A literature review is normally conducted by an investigator in the course of preparing a grant application, contract proposal, or data submission. In addition, the reviewers of such proposals are expected to be familiar with work that has already been done. Implementation of this option would require proof of a literature search through, for example, a companion document in any proposal to conduct federally funded research or testing. The funding entity would presumably have to judge the appropriateness of the literature search. Both the investigator's act of searching the literature and the funding agency's certification of the search may reduce any unintentional duplication. To make a mandatory literature search palatable to investigators, free access to some or all of the necessary information resources may have to be provided.

An alternative strategy is to require a literature search by the funding agency, or other entity, prior to the release of any funds. The disadvantages of requiring a comprehensive literature search before work could be funded include the delay that an additional step would cause, the cost of the search itself to the Federal Government, and possibly part of the cost of developing new information resources.

Option 5: Create new databases designed to reduce unintentional duplication of animal use in research and testing.

New computerized databases might play an important role in reducing any unintentionally duplicative animal use. There are at least three types that could contribute to this end:

- **Unpublished Results, Including Negative Results.** Such a database would disseminate results that are otherwise distributed narrowly or not at all. The major problem with unpublished information is that its quality is difficult to evaluate because it is rarely subjected to peer review. Another problem is that the most useful unpublished data are owned by industry and would not be disclosed because of their proprietary value (although provision could be made for voluntary submissions). A category of special interest, particularly from the standpoint of duplicative testing, is negative results (e.g., showing the absence of toxic effects). Few journals are willing to publish negative testing results. Dissemination of negative results could spare any unintentional duplication, direct investigators away from fruitless paths, or suggest improvements in methodologies.
- **Data From Untreated, or Control, Animals.** Data pertaining to the health or behavior of animals not given a test substance could be used in choosing the best species for experimentation (e.g., a species most likely to yield unambiguous results). This information might obviate the need to use more than one species or might allow smaller control groups in some experiments. Compiling the database could be both difficult and costly because the necessary data are often not published.
- **Experimental Protocols and Results.** This database could be as narrow as abbreviated listings of methods and results, perhaps arranged by species, or as comprehensive as the on-line full text of all published scientific literature. (The full text of a scientific report includes not only protocol and results, but also discussion and interpretation of the results, tables, figures, and bibliography. At present, the full text (minus figures and images) of a few dozen scientific journals is available on-line.) The greatest obstacle to the successful creation of a database of this size is catering to the diverse needs of animal users. In its fullest incarnation, this would cost hundreds of millions of dollars to start and maintain.

Most important, the extent to which any of these databases would be used is unknown. Within the Federal Government, the NLM has the greatest expertise in establishing and operating large databases, and implementation of any form of this option is likely to build on the experience and existing resources of that library.

Option 6. Facilitate the use of foreign data by providing translations of foreign journals.

An often-overlooked source of published data is foreign-language literature, although most important scientific work is routinely published in or translated into English. The advantages of providing translations of additional work are thought by many experts to be quite limited and economically unjustifiable. English translation costs for the four principal languages of science (French, German, Russian, and Japanese) range from $40 to $88

nonanimal methods emerge from research and validation, they may or may not be accepted and implemented by the scientific community.

This course does not necessarily pass judgment on the value of adopting alternatives per se. Nor does it mean that alternatives will not be implemented. It would merely indicate that Congress has decided against encouraging or forcing the implementation of alternatives beyond its direction in 1985 to NIH to establish a plan to develop and assess alternatives in biomedical research (Public Law 99-158). This option might illustrate the belief that external political, ethical, economic, and scientific factors are sufficient to govern the implementation of alternatives.

Further congressional action toward implementation might be judged unnecessary because various other sources are already acting to implement alternatives. For example, EPA has defined circumstances where the LD_{50} test can be replaced by a limit test, and FDA has stated that it does not require data derived from the LD_{50} test; industry is watching to gauge the practical effects of these statements. Also, members of the soap and detergent industry have implemented modifications of the LD_{50} test. Noteworthy, too, is the important role of institutional animal care and use committees in all phases of animal experimentation. In education, medical schools are conducting some laboratory exercises with computer simulations or video demonstrations in lieu of live animals. Medical students in some instances bypass experiments and training involving animals, proceeding from cadavers to people. Activities such as these are likely to continue without new congressional action.

Additional congressional steps may be deemed inappropriate because implementation of alternatives may be judged unimportant. Some people do not object to animal use, for example, in toxicological testing. They believe the status quo brings the comforts and health benefits of new products and technology and protects them from hazards.

Option 2: Require a new or existing Federal entity to coordinate the validation and implementation of alternatives.

This action is based on the assumption that validation and implementation of alternatives would occur more rapidly with enhanced Federal coordination. Along this line, an information service at the National Agricultural Library on improved methods of animal experimentation was mandated by Congress in 1985 (Public Law 99-198). A clearinghouse for resources required to implement alternatives would further hasten their adoption. This entity might, for example, be a central source for computer software or cell culture material.

Existing Federal entities that might be assigned such responsibilities include some component of the National Institutes of Health (e.g., the Division of Research Resources), the National Toxicology Program, or the National Center for Toxicological Research. Coordinating activities could include symposia, workshops, newsletters, scholarships, grants, and the issuance of model protocols or guidelines. The coordinating body could monitor both public and private initiatives. In 1985, Congress took a step toward coordination

of the use of alternatives in biomedical research conducted by or through NIH. It directed NIH to disseminate information about alternatives found to be valid and reliable to those involved in animal experimentation (Public Law 99-158).

Educational programs play a central role in this type of effort. Training scientists in replacement methods and raising awareness about reductions and refinements is likely to increase the implementation of alternatives. This type of education is closely allied with the teaching of principles of humane care and use.

Animal care and use committees at individual institutions might function as a relay between Federal coordination efforts and individual investigators. The institutional animal care and use committee might be required to suggest alternative methods as part of its review of animal care and use. Linked in this way to a Federal implementation effort, these committees would both feed into and draw on the resources of the Federal entity.

A different type of coordination, particularly in research, would be the attachment of provisions to Federal grants regarding the implementation of alternatives. Research grant applications using alternative methods could be awarded higher priority scores in the grant evaluation process or be otherwise favored. This strategy would require sufficient flexibility to ensure that valuable, state-of-the-art scientific proposals that may not involve alternatives are not handicapped. Funding mechanisms could also be used to encourage coordination between laboratories. The responsibility for overseeing the implementation of alternatives via funding mechanisms could be borne by each source of Federal funding.

Option 3. Encourage regulatory agencies to review existing testing guidelines and requirements and to substitute alternatives whenever scientifically feasible.

Through oversight or legislation, Congress could encourage or require Federal agencies to evaluate existing alternatives in testing, to participate in their validation, to adopt them where appropriate, and to report to Congress on their progress in implementing alternatives, as the NIH has been asked to do (Public Law 99-158). Such agency review would have to be a periodic or continuing effort, given rapid advances in the state of the art. Some review of testing guidelines now occurs in keeping requirements up to date, although the purpose of that review is to improve the science rather than to protect animals per se. Formal agency review of international testing guidelines, such as those of the Organization for Economic Cooperation and Development, could also be encouraged. The costs of agency review should be moderate, entailing input from agency experts, comment from outside experts, and publication. If Federal laboratories were involved in the validation of alternative testing methods, additional costs would be incurred. Such a policy could encourage industry to develop alternatives because the barriers to acceptance would be reduced.

Option 4: Ban procedures for which alternatives are available, or give a Federal agency authority to ban procedures as valid alternatives become available.

This option recognizes that prohibitions can be used to force technological change. Prohibiting procedures for which scientifically acceptable alternatives are already available would accelerate the implementation of such alternatives. Existing reductions and refinements in animal use include the greater use of analgesics in research, the use of fewer animals in the LD_{50} and Draize eye irritancy tests, and reliance on videotaped demonstrations and computer simulations in education.

A ban could not only force implementation of existing alternatives, but, over time, help focus the development of new techniques (as discussed in the next section) and allow considerable flexibility in achieving the desired end. A disadvantage of banning a specified procedure is that the replacement, or the process of developing one, may be even more politically unacceptable (e.g., the in vitro culture of human fetal nerve cells). A prohibition also takes no account of the question of judging the scientific acceptability of an alternative.

In pursuing this option or the preceding one, it is important to appreciate that the swiftest adoption of alternatives may come about if regulatory agencies avoid mandating specific testing requirements. Requiring specified tests might actually serve as a strong inhibitor to the implementation (and development) of alternative methods. Greater flexibility is achieved when testing requirements are defined in a manner that allows judgment and encourages use of alternate methods. Viewed from this perspective, the adoption of alternatives might be best stimulated by regulatory requirement for evaluation of a potential toxic response, such as mutagenicity, rather than requirement of a specified test for mutagenicity.

ISSUE: Should the more rapid development of new alternatives in research, testing, or education be stimulated?

Alternatives are currently being developed in many phases of animal use. It is worth noting that development of many of these techniques, especially their validation, cannot occur without animals being used (unless humans are used instead). In addition, many replacement systems will never be fully divorced from animal research and testing, and therefore they will serve to reduce but not eliminate animal use.

Certain research and testing methods now being developed, such as in vitro culture of animal components, bear great promise as alternatives. Similarly, the growing capabilities of computer modeling, for example biological simulation and pharmacology, may reduce the number of animals needed. Development of an enhanced ability to detect and relieve pain can help refine animal use.

Research that spawns alternatives usually takes place across traditional disciplinary lines—principally within the life sciences—but also in applied

mathematics, statistics, engineering, physics, and chemistry. The principal support for such research comes from Federal funds, predominantly NIH and the National Science Foundation. In general, there is little incentive for private investment in methodologies at a stage so remote from commercialization and, in the case of testing, so governed by regulation. Some private concerns, however, specifically fund research into alternative testing methods.

Clearly, research and development require money. Determining the optimum level of funding, however, and the best way to distribute funds remains elusive. Nonetheless, the promotion of such research is likely to increase the number of alternatives available for implementation; in turn, increased implementation is likely to spur research in this area.

Option 1: Take no action.

If Congress takes no specific steps beyond its recent charge to NIH to establish a plan for the development of alternatives in biomedical research, the development of alternatives will continue to be a function of ethical, political, economic, and scientific factors.

That alternatives are being developed in the absence of direct legislation is best illustrated by research centers at Rockefeller University and The Johns Hopkins University funded by corporate and private donations. In addition, corporations are undertaking work in-house or sponsoring it in universities, often in response to scientific, economic, animal welfare, and public relations considerations.

An uncertain pace of development marks the chief disadvantage of this option. Although alternatives may emerge, changing research priorities in both the public and private sectors will affect the rate of development. From another perspective, this is an advantage: It permits researchers to respond to changing needs and priorities with minimal Federal interference.

Option 2: Require a new or existing Federal entity to coordinate the development of alternatives.

Implementation of this option would have great symbolic value within the scientific and animal welfare communities and could lead to more rapid development of alternatives. A central clearinghouse for the development of alternatives could compile and maintain records of all federally funded research and development (R&D) on alternatives. Information on R&D in the private sector would be a valuable component of the coordination effort, though it may prove difficult to obtain.

Coordination could involve identifying research areas likely to lead to new alternatives and reviewing Federal support for those areas across agency lines. The latter responsibility might preclude housing this entity within an existing Federal agency involved in funding R&D on alternatives to avoid either a real or apparent conflict of interest.

As in the implementation of alternatives (see preceding issue), education plays a central role in the development of such approaches. Coordination of efforts aimed at informing investigators and students about animal research could be among the responsibilities of this Federal entity.

Option 3: Provide intramural and extramural Federal funding for the development of alternatives.

An effective mechanism for encouraging R&D on alternatives is funding. Small pilot programs might assess whether or not targeted development is effective.

Development of alternatives in testing within the Federal Government is a natural offshoot of and closely allied with toxicological research. The agencies most likely to produce alternatives in response to new Federal funding are the National Cancer Institute and NIH. Because testing is so closely tied to regulation, funding could also be directed to FDA, EPA, the Consumer Product Safety Commission, and the National Institute for Occupational Safety and Health. Regulatory agencies could be required to develop alternatives to specified tests or to spend funds generally toward their development.

To stimulate extramural R&D, granting agencies reviewing applications could be required to assign priority to those that contain research with promise for the development of new alternatives. Postdoctoral training programs could be established, along the lines of NIH's National Research Service Awards, to ensure a steady supply of young researchers schooled in traditional disciplines, ranging from molecular biology to animal behavior, with applications in the development of alternatives.

Financial incentives to private groups developing alternatives could take the form of tax incentives—perhaps tax credits in addition to those already in place for R&D. Such groups could also be eligible for a new program (analogous to the Small Business Innovation Research program) that would target the development of alternatives.

ISSUE: Should improvements be made in information resources to reduce any unintentionally duplicative use of animals in research and testing?

Science is able to advance rapidly because information about what has been done is disseminated. If attempts to find prior work are inadequate or prior work is not sufficiently accessible, unintentional duplication may occur. Such unnecessary repetition of experiments must be distinguished from replication of experiments to demonstrate the reproducibility of a method or to confirm the validity of results.

The amount of unintentional, largely duplicative research and testing that occurs today is unknown. Investigations into the amount and circumstances of unintentional duplication would be valuable in determining whether it results in substantial waste of animals or funds. Moreover, consultations with potential users of any new information resources would be essential in implementing certain options addressing this issue.

Although the storage and retrieval of data are costly, there are clear benefits to making information that reduces unintentional duplication readily available. Among these benefits are savings in the expense and time associated with animal research and testing. Other benefits are savings in animal lives and the additional work that might be done if resources are not wasted.

Option 1: Take no action.

By making the National Agricultural Library the focus of a service to provide information on improved methods of animal experimentation (Public Law 99-198), Congress in 1985 indicated its intention to facilitate the dissemination of information about alternatives and to prevent unintended duplication of animal experimentation.

Even if no further improvements in information resources are made specifically for the sake of avoiding unintentionally duplicative animal use, general improvements in information resources will proceed as a matter of course. Many resources already exist. The National Library of Medicine, the National Toxicology Program, and other Federal entities maintain large databases that contain information or citations to published sources. Major commercial databases exist as well. National libraries and information centers provide the full text of articles and reports. The National Technical Information Service (NTIS) catalogs, stores, and distributes on request many unpublished Federal reports. Improvements in these resources can be expected, either to fill needs for which the benefits justify the costs or to achieve other information policy goals, such as openness in government or advancement of science.

Option 2. Require that results of all federally funded research and testing be conveniently accessible.

By means of oversight authority or legislation, all Federal entities could be required to provide convenient access to the results of all federally funded animal research and testing. Implementation could be largely through mechanisms already available—publishing in the scientific literature; circulating published reports or depositing them with NTIS, NLM, the National Agricultural Library, or other entity; or entering the results in a publicly available database. New databases might also be established. Requirements that results be made conveniently accessible could apply to Federal employees, contractors (through contract terms), and grantees (as a condition of awards). Contractors and grantees, however, may not be enthusiastic about assuming the burden of publicizing their results and responding to requests for information.

This option recognizes that much research and some testing using animals is federally funded, that dissemination of research and testing results could be more comprehensive, and that better dissemination might reduce any unintentional duplication. Because publication and information dissemination are normally much less costly than obtaining original data, the benefits of enhanced communication extend beyond saving animal lives.

It is important to note that most federally funded work, indeed the vast majority of significant work, is already accessible, although access comes with different levels of convenience. And the results of federally funded work (except some grants) are available under the Freedom of Information Act (FOIA). Requiring that all results be conveniently accessible may burden databases and libraries with inconclusive results or other information that will not be used.

Option 3: Promote greater use of animal testing data submitted by industry to Federal agencies, except where confidentiality protections apply.

Industry must submit data to regulatory agencies before it can market certain products or sometimes in response to reporting requirements. Statutory and regulatory provisions already exist that make some of this information publicly available, thus theoretically avoiding unintentional duplication. In addition, information that is voluntarily submitted and not claimed as confidential is available under FOIA.

Using oversight authority or legislation, greater use of nonconfidential information could be promoted, for example, by requiring that it be put into databases, compiled in reports, or summarized in newsletters. Industry could bear the cost of information dissemination, and any data submission to the Federal Government would have to be accompanied by evidence of intent to publish nonconfidential testing data. Industry may be unenthusiastic about such a procedure, because in some cases nonconfidential data provide direct clues to confidential data. Nevertheless, greater availability of nonconfidential data could aid in avoiding unintentionally duplicative testing.

The extent to which researchers who need such data already know how to obtain them is not known. The needs of those engaged in animal testing must be carefully gauged prior to consideration of this option. A further consideration is the willingness of those who generate the data to encourage others to benefit from their investment.

Option 4. Require comprehensive literature searches to ensure that federally funded research or testing involving animals is not duplicative.

A literature review is normally conducted by an investigator in the course of preparing a grant application, contract proposal, or data submission. In addition, the reviewers of such proposals are expected to be familiar with work that has already been done. Implementation of this option would require proof of a literature search through, for example, a companion document in any proposal to conduct federally funded research or testing. The funding entity would presumably have to judge the appropriateness of the literature search. Both the investigator's act of searching the literature and the funding agency's certification of the search may reduce any unintentional duplication. To make a mandatory literature search palatable to investigators, free access to some or all of the necessary information resources may have to be provided.

An alternative strategy is to require a literature search by the funding agency, or other entity, prior to the release of any funds. The disadvantages of requiring a comprehensive literature search before work could be funded include the delay that an additional step would cause, the cost of the search itself to the Federal Government, and possibly part of the cost of developing new information resources.

Option 5: Create new databases designed to reduce unintentional duplication of animal use in research and testing.

New computerized databases might play an important role in reducing any unintentionally duplicative animal use. There are at least three types that could contribute to this end:

- **Unpublished Results, Including Negative Results.** Such a database would disseminate results that are otherwise distributed narrowly or not at all. The major problem with unpublished information is that its quality is difficult to evaluate because it is rarely subjected to peer review. Another problem is that the most useful unpublished data are owned by industry and would not be disclosed because of their proprietary value (although provision could be made for voluntary submissions). A category of special interest, particularly from the standpoint of duplicative testing, is negative results (e.g., showing the absence of toxic effects). Few journals are willing to publish negative testing results. Dissemination of negative results could spare any unintentional duplication, direct investigators away from fruitless paths, or suggest improvements in methodologies.
- **Data From Untreated, or Control Animals.** Data pertaining to the health or behavior of animals not given a test substance could be used in choosing the best species for experimentation (e.g., a species most likely to yield unambiguous results). This information might obviate the need to use more than one species or might allow smaller control groups in some experiments. Compiling the database could be both difficult and costly because the necessary data are often not published.
- **Experimental Protocols and Results.** This database could be as narrow as abbreviated listings of methods and results, perhaps arranged by species, or as comprehensive as the on-line full text of all published scientific literature. (The full text of a scientific report includes not only protocol and results, but also discussion and interpretation of the results, tables, figures, and bibliography. At present, the full text (minus figures and images) of a few dozen scientific journals is available on-line.) The greatest obstacle to the successful creation of a database of this size is catering to the diverse needs of animal users. In its fullest incarnation, this would cost hundreds of millions of dollars to start and maintain.

Most important, the extent to which any of these databases would be used is unknown. Within the Federal Government, the NLM has the greatest expertise in establishing and operating large databases, and implementation of any form of this option is likely to build on the experience and existing resources of that library.

Option 6. Facilitate the use of foreign data by providing translations of foreign journals.

An often-overlooked source of published data is foreign-language literature, although most important scientific work is routinely published in or translated into English. The advantages of providing translations of additional work are thought by many experts to be quite limited and economically unjustifiable. English translation costs for the four principal languages of science (French, German, Russian, and Japanese) range from $40 to $88

per thousand words. An estimated $4 billion to $5 billion would be required, for example, to translate the current foreign-language holdings of the NLM into English, with an ongoing yearly translation cost of $150 million. Copyright protections might involve costly inconvenience as well. The impact of this option is uncertain, as English abstracts are today available for most foreign journals, and translations can be obtained on an ad hoc basis by those interested in a particular report.

ISSUE: Should animal use in research, testing, or education be restricted?

The use of animals for research, testing, and educational purposes is not closely restricted in the United States. Only four types of constraints can be identified. The Animal Welfare Act requires humane handling, care, and treatment of nonhuman primates, dogs, cats, rabbits, guinea pigs, and hamsters. However, any regulation of these animals within an actual experimental protocol is specifically excepted by the Animal Welfare Act. Second, at the State and local levels, cruelty to animals is generally proscribed, although such statutes are generally not applied to animal use during experimentation. Third, self-regulation takes place at individual institutions and facilities through the implementation of Federal policies. These call for assessment of animal care, treatment, and practices in experimentation by institutional animal care and use committees. Fourth, the Department of Defense was prohibited in fiscal years 1984 and 1985 from expending any funds for training surgical personnel by treating in dogs and cats wounds that had been produced by weapons.

The few existing restrictions on animal use illustrate two phenomena. First, they show that primates and pets have a privileged position in public policy. The Animal Welfare Act names only six kinds of animals, omitting the rats and mice that together constitute approximately 75 percent of the animals used in research, testing, and education. It requires exercise for dogs and a physical environment adequate to promote the psychological well-being of primates. In the case of the DOD appropriation, dogs and cats were named, while goats and pigs (also used in surgical wound training) were not.

Second, the restrictions demarcate the longstanding frontier of legislative province over animal use—the laboratory door. The actual conduct of experiments stands largely outside of any specific mandatory provisions of law. (In contrast, British investigators are licensed to carry out specified procedures using specified animals and face inspection visits to the laboratory bench by government officials.) Solely in the case of the prohibition of DOD expenditures is one use of two particular species addressed.

Considering the issue of restriction of animal use may require the resolution of four difficult questions:

- Are there **some kinds of animals** on which experimentation is inherently inappropriate?
- Are **some methods or procedures** beyond the realm of societal acceptability?
- Should **some sources of animals** be deemed off limits for animal use in research, testing, or education?

- Should **licensed investigators alone** be permitted to engage in animal experimentation?

The resolution of these questions turns on science, law, politics, and, to a large degree, ethics. Six options for congressional action have been identified.

Option 1: Take no action.

In the absence of new restrictions, animal use in research, testing, and education will continue to be governed loosely at the Federal level. Like the American system of education, control of animal use can be largely a local issue, and institutional animal care and use committees stand as the arbiters of community standards. One drawback of a minimal Federal role is the possible development of conflicting or confusing State and local policies.

Maintenance of the status quo would reaffirm that Congress concurs that no methods or procedures are beyond the realm of societal acceptability (except the training of military personnel in surgical techniques on wounded dogs and cats in fiscal years 1984 and 1985). Maintenance of the status quo would leave unaffected the acquisition of animals for research, testing, and education: Sources of animals today include breeders, dealers, pounds, and in-house breeding. Some States will continue to bar the acquisition of pound animals for research. Finally, in the absence of a licensing scheme, investigators and their areas of inquiry will remain wholly a function of available resources and individual interests.

Option 2: Restrict the use of certain kinds of animals.

Some people feel it is wrong to use particular animals in research, testing, or education. This belief may stem from respect for apparent intelligence, and animals most closely related to humans, such as nonhuman primates, may be considered off limits for investigation or manipulation. Similarly, attachment to companion animals such as dogs and cats or to pet species such as hamsters may lead to a desire for their legislated immunity from experimentation.

A restriction of this nature is likely to have several consequences. The restricted species would be protected while investigators faced, at a minimum, an inconvenience until new methods are developed. Development of new model systems would likely necessitate the generation of new fundamental data about the characteristics of the model system, while the existing base of data—which could be large—about the restricted animal is set aside because it is no longer useful. In some cases, new methods would lead to a substitution of a less favored species for the restricted one. Perhaps the most important consequence would be that where the restricted species (e.g., monkey or dog) is the most scientifically appropriate model for research or testing, a prohibition on the use of that species may affect the ability to extrapolate results to humans.

Given that few, if any, kinds of animals are exclusively used in testing, research, and education, a restriction of this nature would be difficult to impose How, for example, might a restriction distinguish between primates under behavioral observation in a field colony and those observed by tourists

at a safari-style game preserve? Restriction of the use of particular kinds of animals may be inconsistent with the popular treatment and use of those same animals (e.g., circus, zoological park, sport, hunt, or farm) throughout the United States. Combining this option with the next one—to restrict the use of a species in a certain protocol—would yield a more limited, more practicable form of restriction than a blanket prohibition on use of a species.

Option 3: Restrict the use of particular protocols.

Some people feel that it is inhumane to manipulate animals in certain ways, irrespective of the motivation for the procedure. Such concerns usually focus on procedures that cause the animal pain or are painful for humans to watch. The Draize eye irritancy test is such a procedure, as are inflictions of blunt head trauma in neurology research and of bullet wounds in surgical training.

In research, blanket prohibitions either of a particular animal's use (the preceding option) or of a specified procedure entail a risk of being overly inclusive. They could have unintended or unforeseen consequences, especially in the face of incomplete knowledge about how animals are used and in what protocols and what the results might portend. One risk of such a restriction would be the elimination of the use of animal models that may be the best available or the sole method of studying conditions present in humans but that do not lend themselves to systematic study in humans.

In testing, procedures like the Draize test and the LD_{50} are used in part because investigators believe that Federal regulatory agencies, such as FDA and EPA, require the results of these tests in data submissions. Exercise of oversight authority could induce Federal regulatory agencies to make explicit their disinterest in data derived from objectionable tests and to demonstrate their ready acceptance of data obtained through alternate means. Such oversight action, coupled with active research into alternative methods, would probably end most use of the targeted procedures.

It is likely that review of protocols by committee, particularly a committee with expertise in bioethics, laboratory animal science, and anesthesia, would effectively restrict procedures to those that are generally accepted as humane. In both research and testing, banning animal use for a specific purpose would reflect the judgment that knowledge gained via that procedure could never justify the cost in animal suffering or lives.

Option 4: Restrict the acquisition of animals from particular sources.

For several decades, States and municipalities have wrestled with the issue of the release of dogs and cats from pounds to research and educational institutions. Some people feel that the release of pound animals for experimentation is wrong, because the animals are former pets or are too unhealthy to be proper subjects for study. In some jurisdictions, research and educational institutions are barred from acquiring pound animals, while other jurisdictions require that pound animals be released to researchers after a certain number of days in captivity.

As pound animals are usually sold at low cost, banning their sale would lead to higher procurement costs as the pound animals were replaced with

animals that are purposely bred for experimentation. (Some animals are already purpose-bred because certain pound animals are not suitable candidates for experimentation.) The purposeful breeding of such animals for experimentation in parallel with routine euthanasia of pound animals would probably work out to a net increase in dogs and cats being killed.

Option 5: License animal users (e.g., for specified uses or for particular kinds of animals).

Animal users could be granted licenses specifying the procedures they are authorized to perform or the animals with which they may work. Such a system is in place in the United Kingdom under the auspices of the Home Office. Given that at least five to six times as many animals are used in the United States annually (17 million to 22 million) as in the United Kingdom (3 million to 4 million), achieving and maintaining licensure here would be a considerably larger and more costly enterprise than now exists in any country.

Implementation of this option would require a Federal licensing body with inspection and enforcement capability. If the British system is the model, licenses would be legally enforceable personal documents. A license to perform a particular experiment or a series of experiments or to work with a particular species would be nontransferable. Confidentiality would be guaranteed in order to protect, for example, an investigator's claim to priority in research results. Comprehensive annual reporting by licensees and auditing by an oversight body—both integral parts of the British system—would be necessary. It is noteworthy that in the United Kingdom this system allows every animal experiment to be logged.

The British system works. It relies heavily on a tradition of cooperation between experimenter and Home Office inspector. The feasibility of such a system in the United States is difficult to predict because the dimensions of animal use are so poorly characterized. Hence, the number of licensees and the resources required for monitoring are unknown. Perhaps most important, the extent to which the parties involved would cooperate is uncertain.

Option 6: Prohibit the use of animals in research, testing, and education.

No other country and no jurisdiction in the United States has completely banned animal use in research, testing, or education. In Switzerland, a binding referendum of this nature was presented to the public for a vote in December 1985, but it was defeated.

Action to ban animal use fully is the most extreme of the six options related to the issue of restriction. It would undeniably provide great impetus toward implementing alternatives. Indeed, the alternatives of **reduction** and **refinement** of animal use would be immediately and completely achieved. However, the development of many **replacements** to animal use depends itself on animals. A ban would, for example, eliminate the use of organ cultures, nonhuman tissue cultures, and cell cultures, except for those self-perpetuating ones already in existence. Replacements would have to be drawn from among human and veterinary patients, micro-organisms, plants, chemical and physical systems, and simulations of living systems.

The development of new computer simulations would falter, with new data from animal systems being unavailable. The ability to verify new simulations or proposed replacements would also come to a halt.

Implementation of this option would effectively arrest most basic biomedical and behavioral research and toxicological testing in the United States. Education would be affected too, although perhaps not as severely as research and testing. In the advanced life sciences and in medical and veterinary training, students might be handicapped, although not to as great a degree as once thought. Some medical schools today, for example, use no animals in physiology curricula.

The economic and public health consequences of a ban on animal use are so unpredictable and speculative that this course of action must be considered dangerous. Caution would demand, for example, that any new products or processes have substantial advantages over available ones to merit the risk of using them without animal testing.

ISSUE: Should more accurate data be obtained on the kinds and numbers of animals used in research, testing, and education?

Accurate data on the kinds and numbers of animals used in research, testing, and education in the United States do not exist. The best numbers now available on the use of certain species (nonhuman primates, dogs, cats, rabbits, guinea pigs, and hamsters) are produced by the Animal and Plant Health Inspection Service of the USDA. The APHIS *Animal Welfare Enforcement Report* submitted to Congress each year is best viewed as a rough estimate of animal use. It records approximately 10 percent of all animals used annually; omitted are rats, mice, birds, fish, reptiles, and amphibians.

Estimates of animals used yearly in the United States range to 100 million and more. Although the development and implementation of alternatives do not require an accurate count, public policy formation would be helped by better data. Regulating animal use, for example, or funding the development or validation of alternatives to a particular procedure, may depend on how many animals are used and what fraction of the total this represents. Trends in animal use have similar applications. In the United Kingdom, the exact animal use records kept since 1876 have influenced policymakers.

Some animal welfare advocates suggest that the moral and ethical issues surrounding animal use are independent of the precise number of animals used. Others question whether the value of the data obtained is worth the cost of obtaining accurate numbers. A rough estimate based on minimal data may be all that is necessary to put the relevant issues into context. Selecting among the following options will depend, therefore, on judgment of how important it is to know the number and kinds of animals used, who uses them, and what trends exist.

Option 1: Take no action.

The primary advantage of this option is that no additional funding would be required, since nothing within the system would change. Continued fund-

ing of current APHIS activities would keep yielding rough estimates of the use of six kinds of animals that account for about 10 percent of total animal use.

The major disadvantage of maintaining the status quo is that an inaccurate and ambiguous reporting system would be perpetuated, yielding marginally useful analysis of animal use in the United States. The APHIS counting system is ineffective because of problems with ambiguous reporting forms and a failure to audit the forms that are returned.

Funding for the APHIS survey has been derived from the approximately $5 million allocated annually in recent years to APHIS to enforce the Animal Welfare Act. Depending on the uses to which data on animal use are put, maintaining the status quo may be adequate, an unnecessary expense, or not nearly enough.

Option 2: Eliminate the APHIS reporting system.

If the value of the information obtained by the APHIS system is not justified by the money allocated for its collection, the APHIS reporting system could be terminated. In adopting this option, Congress would signal a willingness to rely on estimates produced by nongovernment organizations and individuals without the benefit of reports or inspections.

Option 3: Correct inadequacies in the present APHIS system of reporting use of animals mandated by the Animal Welfare Act.

To gain a more accurate picture of the use of nonhuman primates, dogs, cats, rabbits, guinea pigs, and hamsters in the United States, oversight authority could be used to require that APHIS alter its present practices in one or more of the following ways:

- correct its reporting form to eliminate ambiguities;
- change the reporting deadline or publication schedule for the annual *Animal Welfare Enforcement Report*, so that fewer institutional reports are excluded;
- audit or spot-check the "Annual Report of Research Facility" forms and facilities;
- strictly enforce the regulation requiring that all institutions within the United States using mandated species register with APHIS and complete the "Annual Report of Research Facility" forms as required by law; or
- allocate more of APHIS' resources for enforcement of the Animal Welfare Act to reporting.

These changes would require little additional government funding or expenditure by regulated entities, although it could affect how they allocate their resources. Adoption of this option would bring APHIS closer to delivering the information it is obliged to deliver under the Animal Welfare Act.

Option 4: Alter the APHIS system to count additional kinds of animals (e.g., rats and mice).

Rats and mice account for approximately 75 percent of the animals used in research, testing, and education in the United States. They go uncounted because a USDA regulation under the Animal Welfare Act excludes them from its definition of animals. There is, however, some voluntary reporting

of the use of these species on the APHIS "Annual Report of Research Facility" forms.

Data on rats and mice (or other currently unregulated animals) could be obtained in either of two ways. Congressional oversight of the Secretary of Agriculture could lead to a requirement that the use of rats and mice be reported. This would require additional funding for APHIS, because the number of facilities under the act's regulations would increase. On the other hand, the counting mechanism is already in place, and only minor changes would be needed.

Expanding the APHIS animal counting requirement to include rats and mice would raise costs for some members of the research and testing communities. Accurate counting of these species, including categorization of experiments for pain and pain relief, is a labor-intensive activity and hence costly. Such costs will be of exceptional concern to institutions using large numbers of rats and mice, and these users can be expected to question whether accounting needs for policy evaluation require the extra expense.

A broadening of the APHIS census to include rats and mice would still leave some uncounted. The Animal Welfare Act's definition of research facility covers any institution that uses primates, dogs, cats, rabbits, guinea pigs, hamsters, or other warm-blooded animals, as the Secretary of Agriculture may determine are used in experimentation, and that either purchases or transports animals in commerce or receives Federal funds for experiments. Thus, a facility that breeds all its animals in-house– most likely rats or mice—falls outside the scope of the Animal Welfare Act and accompanying USDA regulations. The number of facilities breeding and using rats and/or mice exclusively is unknown. Some toxicological testing laboratories are likely to fall into this group.

Option 5: Establish an independent census of animal use, either on a one-time or periodic basis.

Fundamental changes could be made in the ways animals are counted. An animal census could be periodic—e.g., occurring every 2, 5, or 10 years. An organization other than APHIS, such as the private Institute for Laboratory Animal Resources (ILAR) of the National Research Council, could do the counting. In 1986, ILAR will undertake another in its series of surveys of laboratory-animal facilities and resources in the United States. (The last survey was conducted in 1978.) ILAR will survey the use of two classes of vertebrates—mammals and birds—at approximately 3,000 facilities.

Another approach to gathering information on the kinds and numbers of animals used would be to conduct a comprehensive, one-time study of research, testing, and education. Such a study could survey all species acquired or bred for research, testing, and education; count the number of animals actually used in experimentation; record the length of stay in animals in the facility, and categorize the purposes of the experimental-animal use. Such a comprehensive survey would not merit repetition every year—the purposes of animal use in research, for instance, do not change that quickly.

A different way to count animals used would be to obtain figures from breeders on the number of animals bred for experimentation. This would not take into account the percentage of animals bred that are never used in experimentation, or animals bred within a laboratory, but it would yield a valuable index of animal use. Yet another source of information would be to count the number of facilities or individuals using animals for specified activities.

It is noteworthy that the revised PHS *Policy on Humane Care and Use of Laboratory Animals by Awardee Institutions* (effective Dec. 31, 1985) requires listing the average daily inventory, by species (with none excepted), of each animal facility, as part of each institution's annual report to the NIH Office for Protection from Research Risks. Thus, PHS-supported facilities are now required to report more complete census data to NIH than facilities covered by the Animal Welfare Act report to APHIS. Consequently, a portion of animal use in research (e.g., NIH-supported animal research) and testing (e.g., FDA-supported animal testing) is about to become more closely censused.

The choice among census types under this option will depend on the ways in which the information is to be used, the resources available for obtaining it, and the utility of the new census required by PHS.

ISSUE: Should Federal departments and agencies be subject to minimum standards for animal use?

The Federal Government has six cabinet departments and four independent agencies involved in intramural animal research or testing. These departments and agencies account for at least 1.6 million animals for intramural research. Federal agencies have generally followed the existing PHS policy and as of December 1986 will be required to operate institutional animal committees (Public Law 99-198). Many departments and agencies also follow the NIH *Guide for the Care and Use of Laboratory Animals*. Yet there is no stated, detailed policy of minimum standards for animal use within the Federal Government. Therefore, this issue has just two options: either maintaining the present system or establishing a minimum policy for intramural animal use. Financial considerations are not a major factor because funds will be needed either to continue the present system of variable policies or to implement and enforce a minimum, government-wide policy.

Option 1: Take no action.

The advantages of the present system are its flexibility and minimal bureaucratic structure. The policies mentioned previously, along with the Interagency Research Animal Committee's *Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*, allow each agency or department to have policies and mechanisms unique to its situation. The disadvantages are the potential for conflicting policies and the lack of a neutral enforcement authority.

Option 2: Establish minimum standards for all intramural animal use in Federal departments and agencies.

This option would require that a policy be developed and perhaps that an organizational entity be established to oversee its implementation and

enforcement. This could be accomplished by an interagency committee or by a designated agency. Setting minimum standards would still give each agency and department the flexibility to tailor specific policies to unique situations, yet it would establish a Federal model for standards of animal care in experimentation and ensure humane procedures in Federal facilities.

A Federal intramural policy might incorporate policies and procedures that address facility accreditation and institutional review of research proposals. A composite, minimum Federal policy could reflect the most progressive parts of various current agency standards.

It is noteworthy that this type of action has been taken to protect human research subjects. A *Model Federal Policy for the Protection of Human Research Subjects* involved in research conducted, supported, or regulated by Federal departments or agencies is now in draft form. The policy will be implemented through routine policy and procedural channels of the departments and agencies. The advantage of minimum standards is that all concerned parties know the policy and can immediately and permanently put in place the appropriate organizational structure and facilities to guarantee adherence.

ISSUE: Should the Animal Welfare Act of 1966 be further amended, or its enforcement enhanced?

One criticism of the Animal Welfare Act is the lack of coverage of practices other than anesthesia and analgesia during actual experimentation. Although the most recent amendments to the act, in 1985, direct institutional animal committees to assess practices in experimentation and require that professionally acceptable standards are followed during experimentation, the act at the same time forbids any regulation related to the design or performance of experiments. Additional complaints concern the adequacy of resources for its enforcement, the enforcement structure, the choice of APHIS as the primary enforcement agency, and the cumbersome record-keeping.

In considering whether the act should be strengthened, some related issues must be kept in mind. First, a change in authority may require funding for implementation and enforcement. Second, any change must take into account the present resources of those affected and their ability to achieve compliance without compromising other objectives. Thus, an important consideration is whether or not regulated institutions have sufficient institutional and independent veterinary resources to effect meaningful compliance with a strengthened law and still meet their testing or research objectives. Finally, strengthening the Animal Welfare Act in the face of differences within the scientific and animal welfare communities will carry considerable symbolic value.

Option 1: Take no action.

By maintaining the status quo, Congress would give a strong signal to all concerned parties that it is satisfied with the present regulatory structure for animal use in the United States and that no change is deemed necessary. More specifically, selection of this option would imply that current enforce-

ment efforts are sufficient and that it is not necessary to regulate rats and mice used in experimentation.

Option 2: Eliminate funding for enforcement of the Animal Welfare Act.

Elimination of funding for enforcement of the Animal Welfare Act by APHIS would save the Federal Government approximately $5 million annually. Without these funds, there would be no inspections of facilities (including exhibitors, dealers, and research institutions) using nonhuman primates, dogs, cats, rabbits, guinea pigs, or hamsters and no annual census of these six kinds of animals. Action taken by APHIS against violators would cease. Therefore, the objective of the Animal Welfare Act—to safeguard the humane care and treatment of certain animals—would no longer be met.

Option 3: Increase funding for enforcement of the Animal Welfare Act.

Increased funding for the enforcement of the Animal Welfare Act would bolster enforcement of the present law. Additional funds could be used to:

- increase the training of inspectors;
- increase the number of enforcement agents in the field, so as to raise the number of inspections;
- oversee consistent interpretation of existing regulation by inspection and enforcement agents in the field; and/or
- replace voluntary assurances and simple certifications of compliance with more rigorous procedures.

Additional funding could help stimulate the present passive regulatory situation to become a more active, aggressive regulatory environment. Such a transition would rest on APHIS' level of enthusiasm for enforcing the Animal Welfare Act.

Option 4: Expand the jurisdiction of enforcing agencies to include standards of care, treatment, and use during the actual conduct of experimentation.

The Animal Welfare Act exempts the treatment of animals while they are actually involved in experimentation, except for a requirement for appropriate anesthesia or analgesia and the use of professionaliy acceptable standards in the care, treatment, and use of animals. The original law exempted actual experimentation because Congress did not want to interfere with the conduct of the scientific process. Animal care and treatment are essentially regulated only before and after a scientific procedure. Implementation of this option would broach the design and execution of experimental protocols and would require statutory change. Such action would increase the responsibility of APHIS and its enforcement would require additional funding. A deterrent to implementation of this option is APHIS' lack of expertise in reviewing experimental protocols.

Option 5. Realign existing and any new responsibilities for enforcement among Federal departments and agencies.

APHIS spends little of its resources, either monetary or personnel, enforcing the Animal Welfare Act. It was selected by Congress in 1966 to enforce the act because it had some expertise in animal issues but did not have the conflict of interest that an entity such as NIH or DHHS might have.

Enforcement power could be changed by transferring enforcement authority for violations of the Animal Welfare Act from USDA (APHIS) to DHHS. This would set up a potential conflict of interest: A single department would both sponsor animal experimentation and have oversight authority. In addition, many of the regulations in the Animal Welfare Act affect areas in which DHHS has no expertise (e.g., animal use by exhibitors).

In amending the Animal Welfare Act in 1985, Congress mandated that the Secretary of Agriculture consult with the Secretary of Health and Human Services prior to issuing regulations under authority of the act. The implementation of this provision may lead to DHHS having increased influence on the enforcement of the act.

Option 6: Amend the Animal Welfare Act to preempt State and local laws concerning animal use in areas not already covered by the Animal Welfare Act.

Although the *Edward Taub* case in Maryland did not decide the preemption question, it did bring up the issue of whether the Animal Welfare Act could preempt a State statute. Congress may wish to examine its authority to preempt State anticruelty statutes and may then wish to specify for the judiciary whether it intended its law to supersede any State or local laws on this issue. In doing so, Congress could remove uncertainty in the law by making clear whether it intends the Animal Welfare Act to be a comprehensive, exclusive system of control over the use of animals in experimental facilities and activities in interstate and foreign commerce. Without such clarification, the possibility exists for local criminal prosecution, seizure of animals, injunctions to close facilities, and cessation of animal investigations.

Current State and local efforts to assure humane treatment have been criticized for several reasons. Compliance schemes are overly complex, training and resources are inadequate, and existing laws are not specific enough in their standards for care, treatment, and use. If Federal preemption is not exercised, then State and local laws will be considered concurrent and complementary to existing Federal laws.

It is important to note that Federal preemption means that the administrative system for monitoring, including on-site inspection, should be made adequate to ensure continued compliance with national standards for humane treatment. Otherwise, State-level organizations with a sincere and reasonable concern about the care of animals will be justified in demanding local enforcement and surveillance of research, testing, and education involving animals.

Finally, it should be recognized that if Federal preemption is deemed necessary, the constitutional question of whether the Federal Government has the authority to assert itself into areas traditionally regulated by the States (e.g., pound animal use) may well land in the courts.

Assessments in Progress as of February 1986

Technologies To Maintain Biological Diversity
Integrated Renewable Resource Management for U S. Insular Areas
Low Resource Agriculture in Developing Countries
Evaluation of Agent Orange Protocol
Technology and Indian Health Care: Effectiveness, Access, and Efficiency
Technologies for Detecting Heritable Mutations
Technologies for Child Health
Life-Sustaining Technologies and the Elderly
Disorders Causing Dementia
New Developments in Biotechnology
Technology and the American Economic Transition
Western Surface Mine Reclamation
High-Technology Ceramics and Polymer Composites
Technologies for Prehistoric and Historic Preservation
International Competition in the Service Industries
Reduction of Industrial Hazardous Wastes
Technology Transfer to China
Alternatives for Improving NATO's Defense Response
Federal Government Information Technology: Key Trends and Policy Issues
Intellectual Property Rights in an Age of Electronics and Information
New Communications Technology: Implications for Privacy and Security
Wastes in the Marine Environment: Their Management and Disposal
Technologies To Control Illegal Drug Traffic
Hazardous Materials Transportation: Technology Issues
Science Policy Special Projects

(NOTE. For brief descriptions of these studies in progress, see OTA booklet on "Assessment Activities"—available from OTA's Publishing Office, 224-8996.)

NOTE: Copies of the full report "Alternatives to Animal Use in Research, Testing, and Education" can be purchased from the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402, GPO stock No. 052-003-01012-7.

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